

AM 100
STANDARD OPERATING PROCEDURES FOR
ADMINISTRATIVE MANAGEMENT

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AM 101

STANDARD OPERATING PROCEDURE ON SOPs

1. PURPOSE

Standard operating procedures (SOPs) are intended to establish or prescribe methods to be followed routinely for the performance of designated operations or in designated situations. By defining UCDHS processes, SOPs are instrumental in developing a culture of compliance.

This SOP specifics the procedure for development, review, approval and maintenance of UCDHS SOPs for clinical research.

2. PROCEDURES

A. Formatting

- i. Each SOP will contain, at a minimum, four sections:
 - Purpose
 - Procedures
 - Scope
 - Responsibility

If applicable, a fifth section entitled “Applicable Regulations and Guidelines” will be added.

- ii. New SOPs will be numbered sequentially within the appropriate subsection.
- iii. The footer of each SOP page will contain a number assigned by combining the subsection number followed by the page number (e.g. 202.2 will be followed by 202.3).
- iv. The header of each SOP page will contain the current approval date and administrative change date, if applicable.

B. Review and Approval

- i. Once written, the SOP will be distributed to the Translational Research Integration and Compliance Committee (TRICC) for review and approval.
- ii. Revised SOPs will be returned to committee for final review and approval.

C. SOP Access

- i. The SOPs will be available online and in paper format.

D. Continuing Review and Revision

- i. All SOPs will be reviewed for accuracy and/or obsolescence no less than once every two years from the approval date, and upon new issuance of federal or state regulation changes.

- ii. The TRICC coordinator will assemble the SOP Advisory Panel when an SOP is within six months of its expiration date.
 - a. If revisions are necessary, the SOP will be revised and then returned to TRICC for review and approval.
 - b. If no revisions are necessary, the SOP will be issued a new expiration date two years from the new approval date.
- iii. All modifications and/or revisions will be summarized in the SOP.

E. Version Control

- i. Only the most currently approved version of an SOP will be maintained on the Web and in paper manuals.
- ii. Superseded versions will be maintained in paper format only.

3. SCOPE

This SOP specifies the guidelines for development of all standard operating procedures for clinical research.

4. RESPONSIBILITY

The SOP Advisory Panel is responsible for ensuring that all SOPs are developed in accordance with this SOP. The TRICC coordinator is responsible for maintaining SOP hardcopies and ensuring version control. The Translational Research Integration and Compliance Committee is responsible for final SOP approval.

5. APPLICABLE REGULATIONS AND GUIDELINES

| | |
|---------------|--|
| 21 CFR 312.60 | General Responsibilities of Investigators |
| ICH GCP | Guidelines for the Monitoring of Clinical Investigations |
| FDA 7348.811 | Compliance Program Guidance Manual: Clinical Investigators |

AM 101
STANDARD OPERATING PROCEDURE ON SOPs

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|---|------------------------------|----------------------------|
| SOP: AM 101 Version No: 1 Effective Date: 5/10/2007 | ADMINISTRATIVE MANAGEMENT | Supercedes version: N/A |
|---|------------------------------|----------------------------|

Originated by: Cancer Center CTSU

Modified by: CTSC SOP Advisory Panel

Approved by: Translational Research Integration & Compliance Committee

Approval date: 5/10/07

Expiration date: 5/10/09

AM 102

TRAINING AND DEVELOPMENT REQUIREMENTS

1. PURPOSE

Research studies will be conducted according to FDA regulations and ICH guidelines to protect the safety and welfare of study subjects. Standardized training and continuing skill development of all clinical research professionals is of the utmost importance. Proper training will foster growth and ensure that all personnel are adhering to department, University, State and Federal regulations.

2. POLICY AND PROCEDURES

A. New Employee Requirements

- i. In accordance with UCDHS policy, all new research staff will attend the “New Employee Orientation” and “Annual JCAHO Safety Training”.

B. IRB Administration Requirements

- i. All persons listed in the “Research Personnel” section of the Description of Study (DOS) are required to complete the IRB’s web-based education module in order to fulfill their educational certification requirement. The module can be accessed at <http://www.research.ucdavis.edu/home.cfm?id=OVC,1,1448,1446>
- ii. Once the module is completed, the IRB Administration is notified electronically.
- iii. Recertification is required every two years.

C. Dangerous Goods Shipping Requirements

- i. In accordance with IATA regulations, all research staff involved with shipping specimens must complete the Dangerous Goods-Infectious Substances Shipping Training every two years.
- ii. The class covers the shipment of Class 6.2 Infectious Substances and Diagnostic Specimens and Class 9 Miscellaneous Substances (e.g., dry ice).
- iii. This training is offered by the School of Medicine, Sponsored Programs Safety Officer. Call the Safety Officer at 530-752-9996 for training dates and locations.
- iv. Specific shipping instructions can be found in the Patient Management (PM) SOPs.

D. Blood-borne Pathogen and Medical Waste Training

- i. In accordance with UCDHS policy, and local, county, state and federal training requirements for laboratory safety training, all research staff working with specimens must complete Blood-borne Pathogen and Medical Waste training annually.
- ii. This class covers working with human blood, body fluids and unfixed tissue, which falls under the category of working with potential/known blood-borne pathogens.

- iii. This training is offered quarterly by the School of Medicine, Sponsored Programs Safety Officer. Call the Safety Officer at 530-752-9996 for training dates and locations.

E. JCAHO Refresher Training Requirement

- i. In accordance with UCDHS Policy & Procedure #1617, all UCDHS employees must complete an annual JCAHO refresher training.
- ii. This training may occur in one of two ways:
 - a. Through the JCAHO training course given by Human Resources twice per month
 - b. Through the web-based training available at <http://safety.ucdmc.ucdavis.edu/>

F. Clinical Research Training Program

- i. The UC Davis Clinical and Translational Science Center (CTSC) offers a CME-approved Clinical Research Training Program for investigators, physicians, pharmacists, nurses, research coordinators and support staff. Mentorship opportunities with various departments and divisions are included. New personnel conducting clinical research in human subjects are encouraged to attend. Participants who complete the program will receive a certificate.

G. Annual Continuing Education Requirement

- i. All clinical research coordinators are required to attend at least two hours of continuing education annually. The UC Davis CTSC offers monthly training through their CME-approved Educational Series, featuring seminars, workshops and brown-bag meetings. More information can be found on their Web site: <http://www.ucdmc.ucdavis.edu/ctsc>
- ii. Additional courses may be found through the following sources:
 - Society of Clinical Research Associates (SoCRA) Web site: <http://www.socra.org/>
 - Association of Clinical Research Professionals (ACRP) Web site: <http://www.acrpnet.org>
 - UCDHS Human Resources, Training and Development Web site: http://www.ucdmc.ucdavis.edu/hr/hrdepts/training_and_development/
 - UCDHS Office of Continuing Medical Education: <http://www.ucdmc.ucdavis.edu/cme>

3. SCOPE

This SOP specifies the training and continuing education requirements for all clinical research personnel.

4. RESPONSIBILITY

Date of version: 5/10/07
Replaces previous version: N/A

The research administrator or department manager is responsible for ensuring that the above requirements are met by research personnel. All research personnel are responsible for completing the training relevant to their position.

5. APPLICABLE REGULATIONS AND GUIDELINES

| | |
|---------------|---|
| 21 CFR 312.60 | General Responsibilities of Investigators |
| 45 CFR 46 | Protection of Human Subjects |
| 21 CFR 812 | Responsibilities of Investigators |
| ICH GCP | Consolidated Guideline (E6 4.2.4) |
| NIH OD-00-029 | Required Education in the Protection of Human Research Participants |

AM 102
TRAINING AND DEVELOPMENT REQUIREMENTS

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|---|------------------------------|-------------------------|
| SOP: AM 102 Version No: 1 Effective Date: 5/10/2007 | ADMINISTRATIVE MANAGEMENT | Supercedes version: N/A |
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Originated by: Cancer Center CTSU

Modified by: CTSC SOP Advisory Panel

Approved by: Translational Research Integration & Compliance Committee

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AM 103

ROLES AND RESPONSIBILITIES OF THE RESEARCH TEAM

1. PURPOSE

The Principal Investigator (PI) assumes the authority and responsibility for the conduct of a clinical study. By signing Form FDA 1572, the Statement of Investigator, the PI agrees to comply with the conditions required by FDA for use of an investigational drug or device. The PI has the authority to delegate responsibility to members of the research team; however, the PI is ultimately responsible for the conduct of the study.

2. POLICY AND PROCEDURES

A. Principal Investigator

- i. The Principal Investigator (PI) promotes good clinical practice (GCP) in the conduct of clinical studies. The PI assumes the following essential roles and responsibilities:
 - a. Is qualified by education, training and experience
 - b. Discloses applicable conflicts of interest (COIs)
 - c. Assures protocol compliance through a thorough understanding of the protocol
 - d. Assures initial and ongoing review/approval by the Institutional Review Board (IRB)
 - e. Determines that adequate resources are available to conduct the study
 - f. Manages the medical care of participants
 - g. Protects the rights and welfare of participants
 - h. Assures the validity of the data reported to the sponsor
 - i. Assures documentation of study-related procedures, processes and events
 - j. Assures the proper use and storage of investigational products
 - k. Is responsible for the overall conduct of the study
 - l. Ensure privacy and security of research data

B. Research Nurse/Clinical Research Coordinator

- i. The primary responsibility of the research nurse/coordinator is to manage all aspects of the conduct of the clinical trial. Collectively referred to as Clinical Research Coordinators (CRCs), the CRC is required to have in-depth knowledge of the protocol and good clinical practice (GCP) per federal regulations. The CRC responsibilities include, but are not limited to, the following:
 - a. Assures protocol compliance through a thorough understanding of the protocol
 - b. Assists with study start up
 - c. Screens and enrolls study participants
 - d. Tracks participant compliance with the research drug, device or procedure
 - e. Completes source documents, if applicable, and case report forms (CRFs)
 - f. Tracks, reports and monitors adverse events and deviations
 - g. Prepares regulatory documents as needed for the FDA (e.g., Form 1571, 1572) and Institutional Review Board (e.g. Description of Study, Informed Consent Form).
 - h. Complies with sponsor and/or FDA audit requests
 - i. Assists with study close out
 - j. Trains and supervises other research support staff, as needed
 - k. Protects all research data in accordance with UCDHS privacy and security requirements

3. SCOPE

This SOP defines the roles and responsibilities of the research team for conducting clinical studies at UCDHS.

4. RESPONSIBILITY

The PI can delegate authority to members of the research team; however, the PI is ultimately responsible for the conduct of the study.

5. APPLICABLE REGULATIONS AND GUIDELINES

| | |
|---------------|--|
| 21 CFR 312.53 | Selecting Investigators and Monitors |
| 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 |
| 21 CFR 54 | Financial Disclosure by Clinical Investigators |
| 21 CFR 812 | Responsibilities of Investigators |
| ICH GCP | Consolidated Guideline |

AM 103
ROLES AND RESPONSIBILITIES OF THE RESEARCH TEAM

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|---|------------------------------|-------------------------|
| SOP: AM 103 Version No: 1 Effective Date: 5/10/2007 | ADMINISTRATIVE MANAGEMENT | Supercedes version: N/A |
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Originated by: CTSC SOP Advisory Panel

Modified by:

Approved by: Translational Research Integration & Compliance Committee

Approval date: 5/10/07

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AM104 ESSENTIAL DOCUMENTS

1. PURPOSE

The purpose of this standard operating procedure (SOP) is to provide guidance to research personnel when a system of records is established. Essential documents are those documents that individually and collectively permit evaluation of both the conduct of a clinical trial and the quality of the data that are produced. These documents are generated throughout the various stages of a clinical trial, from study start-up to completion or termination of the trial.

Essential documents serve to demonstrate the compliance of the investigator, sponsor, and monitor with the standards of good clinical practice (GCP) and with all applicable regulatory requirements. These documents are also the ones that are usually audited by the sponsor and regulatory authorities as part of the compliance process to confirm the validity and integrity of the data.

2. PROCEDURES

- i. The list of essential documents in this SOP includes a description of the purpose and/or requirements of each document, a recommendation as to whether the document should be filed in the regulatory binder or the participant's research record, and a reference to the pertinent federal regulation/guidance.
- ii. It is acceptable to combine some of the documents, as long as the individual elements are readily identifiable. All documents do not have to be combined in one regulatory file.
- iii. Regulatory files must be maintained for all trial sites. It is acceptable for a main site/center/unit to maintain regulatory files for their affiliated sites/subunits if necessary.
- iv. A trial site is the location where the research is conducted and the term site is generally used in this document in place of the terms: unit, main unit, subunit, affiliated site, or center.
- v. All of the documents addressed in this SOP must be available for audit/inspection by the sponsor and regulatory authorities.
- vi. Documents may be saved in an electronic format when appropriate.
- vii. Always refer to state, federal, and/or Institutional Review Board (IRB) policies/regulations for additional guidance.
- viii. Destruction or retention of Informed Consent Forms (ICFs), Case Report Forms (CRFs) and other regulatory documents should be in accordance with the protocol or federal regulations, whichever is longer. Current FDA policy states retention for two years following the date an FDA marketing application is approved for the drug/device. If no application is to be filed, retention is limited to two years after the investigation is discontinued and FDA is notified.
- ix. Resource tools (e.g., Lab Processing Charts) are not included as essential documents.

3. SCOPE

This SOP is based upon the Code of Federal Regulations (CFR), guidance that applies to the involvement of human participants in clinical research, and standards for Good Clinical Practice (GCP). This SOP is applicable to all UCDHS clinical research studies involving drugs, devices, or procedures.

4. RESPONSIBILITY

It is the responsibility of the research team to ensure compliance with university, local, state and federal guidelines related to these essential documents. The Principal Investigator is ultimately responsible for the conduct of the study.

5. APPLICABLE REGULATIONS AND GUIDELINES

See below.

Essential Documents

| Document | Requirement / Purpose | File | Reference |
|--------------------------|--|---|---|
| Assent Form | <p>Assent of children and permission of parents or legal guardians as determined by the IRB/IEC is required as per the provisions of 45CFR46.</p> <ul style="list-style-type: none"> • State law where the research is taking place defines the age of a minor and requirements for emancipation. • The Assent Form is used for children ages 12-17. • The requirement for assent of children and/or permission of their parents or legal guardians may be waived by the IRB as long as the criteria for waiving consent in the regulations (45CFR46) are met. • Keep on file all versions submitted and approved by the IRB. | <ul style="list-style-type: none"> • Regulatory binder • Participant's research record | <ul style="list-style-type: none"> • 45CFR46, Subpart D • 21CFR50 • 21CFR56 • FDA Information Sheets, Guidance for IRBs and Investigators 1998 Update, FAQ Nos. 47 and 48; and Page 5 |
| Assurance Number | <p>The Institution is responsible for obtaining and maintaining a current Health & Human Services (HHS) Assurance through the Office of Human Research Protection (OHRP).</p> <ul style="list-style-type: none"> • The principal investigator (PI) is responsible for ensuring that a current Assurance is in effect while conducting research on human participants in HHS funded studies. • All performance sites: <ul style="list-style-type: none"> ➢ Main site ➢ All affiliated sites that meet the OHRP requirements for having an Assurance. • Must be renewed prior to expiration. • Keep on file the Assurance number and expiration date. | <ul style="list-style-type: none"> • Regulatory binder <p>Note: A copy of the actual Assurance document must be on file with the Institution and/or IRB.</p> | <ul style="list-style-type: none"> • 45CFR46 • OHRP Procedures for Registering IRBs and Filing Federalwide Assurances of Protection for Human Subjects (FWA) |
| Case Report Forms | <ol style="list-style-type: none"> 1. Dated, completed case report forms (CRFs): <ul style="list-style-type: none"> • To document that the investigator or authorized member of the investigator's staff confirms the observations recorded. • To document all changes/ additions or corrections made to CRFs after initial data were recorded. • Signed if required by Group SOPs or if used as source documentation. 2. Originals retained by sponsor after study completion and/or site closure. 3. Site retains copy. | <ul style="list-style-type: none"> • Regulatory binder • Participant's research record • Data file | <ul style="list-style-type: none"> • 21CFR312 • FDA Guidance: E6 Good Clinical Practice (GCP), Sections 1.11, 4.9, 5.5, 5.23, 8.3.14, 8.3.15 |
| Communications | <ol style="list-style-type: none"> 1. All relevant communications, other than site visits, to document any agreements or significant discussions regarding trial administration, protocol violations, trial conduct, adverse event (AE) reporting, etc. For example: <ul style="list-style-type: none"> • Letters • Meeting notes • Notes of telephone calls • Email messages 2. Includes communications to and from the Sponsor and/or the protocol team. 3. Communications about a specific participant must be filed with source documents in the participant's research record. 4. Save electronic media, originals, and/or certified copies. | <ul style="list-style-type: none"> • Regulatory binder | <ul style="list-style-type: none"> • FDA Guidance: E6 GCP, Sections 4.4, 4.9, 8.3.11 |

| Document | Requirement / Purpose | File | Reference |
|---|---|---|---|
| <p>Curriculum Vitae (CV)</p> | <ol style="list-style-type: none"> 1. The site must have on file CVs and/or other relevant documents evidencing qualifications and eligibility to conduct the trial and/or provide medical supervision of participants. Includes the following key personnel: <ul style="list-style-type: none"> • Principal investigator (i.e., individual responsible for the grant/contract at the site). • Investigator responsible for day-to-day activities of the site. • For IND studies: <ul style="list-style-type: none"> ➢ Investigator of Record (IOR) ➢ All other investigators/subinvestigators and any other clinicians listed on a Form FDA 1572, Box # 6. • For non-IND studies, all other investigators/subinvestigators and any other clinicians listed on an authorized prescribers list. • Study coordinator • Pharmacist of record 2. Update to reflect significant changes: <ul style="list-style-type: none"> • Affiliation • Education • Responsibilities | <ul style="list-style-type: none"> • Regulatory binder | <ul style="list-style-type: none"> • 21CFR312 • FDA Guidance: E6 GCP, Sections 4.1, 4.3, 5.6, 8.2.10, 8.3.5 |
| <p>Final / Close-Out Monitoring Report</p> | <ol style="list-style-type: none"> 1. A close-out report by the monitor to document that all activities required for site close-out are completed and essential documents are in the appropriate files. Includes the following: <ul style="list-style-type: none"> • Disposition of participants • Location of research records • Disposition of specimens • Disposition of study drug • IRB notification 2. Applies only to sites being closed (i.e., no longer enrolling new participants or following any participants on-study). | <ul style="list-style-type: none"> • Regulatory binder | <ul style="list-style-type: none"> • 21CFR312 • FDA Guidance: E6 GCP, Sections 4.13, 8.4.5 |
| <p>Final Study Report</p> | <p>Final report by the investigator to the IRB, and where applicable, to the regulatory authorities to document completion of the trial. Include the following information:</p> <ul style="list-style-type: none"> • Disposition of participants • Location of research records • Disposition of specimens • Disposition of study drug • Other information as required by the IRB (e.g., number of patients screened, number enrolled, serious adverse experiences, etc.). | <ul style="list-style-type: none"> • Regulatory binder | <ul style="list-style-type: none"> • 21CFR312 • FDA Guidance: E6 GCP, Sections 4.13, 8.4.7 |
| <p>Financial Disclosure</p> | <ol style="list-style-type: none"> 1. To document financial aspects of the trial and the financial agreement between the investigator / institution and the sponsor for the trial. 2. Certification or Disclosure <ul style="list-style-type: none"> • Certify that there is no financial interest, or • Disclose specific financial interests. • Must complete Office of Research form 700U and FDA forms 3454 or 3455, or equivalent forms. 3. Applies to investigators and subinvestigators 4. Applies to individuals who fit any of the following criteria: | <ul style="list-style-type: none"> • Regulatory binder | <ul style="list-style-type: none"> • 21CFR54 • 42CFR50, Subpart F • 21CFR312 • FDA Guidance: E6 GCP, Section 8.2.4 • FDA Guidance: |

| Document | Requirement / Purpose | File | Reference |
|---|--|---|--|
| | <ul style="list-style-type: none"> • Sign the Form FDA 1572 (Investigator of Record) • Identified as an investigator in initial submissions or protocol amendments under an IND. • Identified as an investigator in the NDA. • For studies not conducted under an IND, the individuals whom the sponsor considers to be investigators and subinvestigators. • Individuals who actually conduct and take responsibility for an investigation. • Individuals who have the ability and opportunity to significantly impact the data <i>as determined by the site</i>. • Spouses and dependent children of individuals indicated above. <p>5. The IRB may have additional requirements.</p> | | <p>Financial Disclosure by Clinical Investigators</p> <ul style="list-style-type: none"> • NIH Notice OD-00-040 |
| <p>Form FDA 1572 (Statement of Investigator)</p> | <ol style="list-style-type: none"> 1. Required for each initial protocol registration submission of a new protocol with an Investigational New Drug (IND) application (Form FDA 1571) 2. The Investigator listed in Box 1 of the 1572 is the individual who must sign and date the form. This individual is referred to as the Investigator of Record (IOR). 3. Only laboratories not specified in the protocol need to be listed in Section 4. 4. Section 6 must list any individual: <ul style="list-style-type: none"> • Responsible for the medical management of participants. • Authorized to prescribe study medication. • This may include, but is not limited to, the following: <ul style="list-style-type: none"> ➢ MDs ➢ Pharmacists ➢ Nurse Practitioner ➢ Physician's Assistant ➢ Study Coordinator • If there are no individuals that need to be listed, then record "NONE". 5. Update as study personnel and/or other data on the form change. Updated forms must be signed and dated by the IOR. 6. The original version and any updated forms must be submitted to the sponsor (if applicable) and the FDA. 7. A copy of the forms must be kept on file at the site. | <ul style="list-style-type: none"> • Regulatory binder | <ul style="list-style-type: none"> • 21CFR312 • FDA Guidance: E6 GCP, Sections 4.1, 4.3 |
| <p>Information Given to Study Participant</p> | <ol style="list-style-type: none"> 1. To document that participants will be given appropriate written information (content and wording) to support their ability to give fully informed consent. 2. To document that recruitment measures are appropriate and not coercive. 3. Include the following: <ul style="list-style-type: none"> • Informed consent form • All applicable translations • Advertisement for participant recruitment (if used) • Education materials (protocol specific) • Any other written information | <ul style="list-style-type: none"> • Regulatory binder | <ul style="list-style-type: none"> • 45CFR46 • 21CFR50 • 21CFR56 • FDA Guidance: E6 GCP, Sections 4.8, 8.2.3 |

| Document | Requirement / Purpose | File | Reference |
|---|---|--|---|
| <p align="center">Informed Consent Form</p> | <ol style="list-style-type: none"> 1. Written informed consent form to document that consent is: <ul style="list-style-type: none"> • Obtained in accordance with regulations, GCP, and protocol. • Dated prior to participation of each participant in trial. • Provided for direct access to records. 2. Non-English speaking participants must be consented in a language they can understand. <ul style="list-style-type: none"> • Save all written translations. 3. Consents obtained for screening purposes must be retained even if the participant was not enrolled in the protocol. 4. To document revisions of these trial-related documents that take effect during trial, save all versions submitted and approved by site's IRB: <ul style="list-style-type: none"> • Informed consent form. • Any other written information provided to participants. 5. Continual reviews are at the directive of the IRB. 6. Changes in consent forms due to protocol amendments and important safety information must be submitted and approved by the IRB. | <ul style="list-style-type: none"> • Regulatory binder • Participant's research record | <ul style="list-style-type: none"> • 45CFR46 • 21CFR50 • 21CFR56 • 21CFR312 • FDA Guidance: E6 GCP, Sections 1.28, 4.8, 8.3.12, 8.2.3, 8.3.2 • OHRP Informed Consent Guidance Information |
| <p align="center">Investigator's Brochure (IB)</p> | <ol style="list-style-type: none"> 1. To document that relevant and current scientific information about the investigational drug/agent has been provided to the investigator. 2. Include updates to document that investigator is informed in a timely manner of relevant information as it becomes available. 3. Keep on file a copy for EACH of the study drugs/agents used within the protocol. 4. Include the following: <ul style="list-style-type: none"> • Only the most recent version. <ul style="list-style-type: none"> ➢ All obsolete versions must be removed. ➢ Obsolete IBs must be shredded since they may contain proprietary information. ➢ Shred upon removal from file, or, upon trial completion. • Addendum to IBs (e.g., all IND safety reports related to the drug/agent). | <ul style="list-style-type: none"> • Regulatory binder | <ul style="list-style-type: none"> • 21CFR312 • FDA Guidance: E6 GCP, Sections 1.36, 5.12, 7, 8.2.1, 8.3.1 |

| Document | Requirement / Purpose | File | Reference |
|---|---|--|---|
| <p style="text-align: center;">IRB Approvals</p> | <ol style="list-style-type: none"> 1. Copies of all materials submitted to the IRB, including any local committees as required by the IRB, for example but not limited to: <ul style="list-style-type: none"> • Cancer Center Scientific Review Committee • Radiation Use Committee • Other Hospital Committees per IRB requirements 2. Dated proof of submission and IRB approval of the following for both initial submissions and revisions (if any). Revised documents must be labeled (e.g., date and/or version number) to differentiate them from previous versions. <ul style="list-style-type: none"> • Advertisements – to document that recruitment measures are appropriate and not coercive. • Continuing/interim review of trial in accordance with federal regulations and IRB policy. • Informed consent form • Protocol • Protocol Amendments and/or Letters of Amendment • Protocol-specific education materials • Participant compensation • Any other documents receiving IRB approval or their favorable opinion. • Any other written information to be provided to participants, to document that participants will be given appropriate written information (content and wording) to support their ability to give fully informed consent. • Any other pertinent communications with IRB or documentation required by the IRB. • Clarification memos <i>as required by the IRB</i>. 3. Dated proof of IRB submission of the following for both initial submissions and revisions (if any). Revised documents must be labeled (e.g., date and/or version number) to differentiate them from previous versions. <ul style="list-style-type: none"> • IND Safety Reports, Safety Memos, and Safety Alerts (reported with yearly renewal, unless serious, unexpected and related to study, in which case, reported within 5 days of becoming aware of the event.) • Investigator’s Brochures | <ul style="list-style-type: none"> • Regulatory binder | <ul style="list-style-type: none"> • 45CFR46 • 21CFR50 • 21CFR56 • 21CFR312 • FDA Guidance: E6 GCP, Sections 3, 4.4, 4.5, 4.10, 5.11, 5.17.3, 8.2.3, 8.2.7, 8.3.2, 8.3.3, 8.3.19 • OHRP IRB Guidebook |
| <p style="text-align: center;">Laboratory</p> | <ol style="list-style-type: none"> 1. To document competence of local, central, or Group laboratories to perform protocol required tests and support reliability of results of medical/laboratory/standardized procedures/tests, one of the following must be on file: <ul style="list-style-type: none"> <u>Laboratories located in the United States</u> <ul style="list-style-type: none"> • CLIA Certification of Compliance • CLIA Certification of Accreditation AND the agency certificate (e.g., CAP Certification of Accreditation) <u>Laboratories located outside the United States</u> <ul style="list-style-type: none"> • Results of established quality control and/or external quality assessment • Other validation 2. To document current competency, update files when: <ul style="list-style-type: none"> • Existing certification/accreditation/validation expires. • A new laboratory is added or replaces an existing laboratory. 3. Document normal values/ranges for medical/laboratory/standardized procedures/tests included in the protocol. | <ul style="list-style-type: none"> • Normal values/reference ranges may be filed in participant records (e.g., on lab report) | <ul style="list-style-type: none"> • 21CFR58 • 21CFR312 • 42CFR493.3 • FDA Guidance: E6 GCP, Sections 4.2, 8.2.11, 8.2.12, 8.3.6, 8.3.7 |

| Document | Requirement / Purpose | File | Reference |
|---|--|--|---|
| | <ul style="list-style-type: none"> Update when they are revised during the trial. Does not apply to tests that do not have established normal values/ranges. 4. The preceding (1-3) do NOT apply to laboratories that test protocol specimens but do NOT report any participant-specific results for the diagnosis, treatment or assessment of the health of participants. | | |
| Monitoring Log | Dated signature of monitor for each study visit. | <ul style="list-style-type: none"> Regulatory binder | <ul style="list-style-type: none"> 21CFR312 FDA Guidance: Monitoring FDA Guidance: E6 GCP, Section 5.18 |
| Monitoring Reports | Copies of all site visit reports (hard copy or electronic) to document both the site visits and findings of the monitor. | <ul style="list-style-type: none"> Regulatory binder | <ul style="list-style-type: none"> 21CFR312 FDA Guidance: E6 GCP, Sections 1.39, 5.18, 8.3.10 |
| Pharmacy Accountability Records | Accountability records must be kept for all study drugs/agents provided as part of the protocol. | <ul style="list-style-type: none"> IDS Pharmacy file | <ul style="list-style-type: none"> 21CFR312 FDA Guidance: E6 GCP, Sections 4.6, 5.13, 5.14, 8.2.15, 8.3.8, 8.3.23, 8.4.1 |
| Protocol | To document investigator and sponsor agreement to the protocol, amendments and CRFs; and, to document revisions of trial-related documents that take effect during trial: <ul style="list-style-type: none"> Initial version that the site was registered Amendments and Letters of Amendment Subsequent versions Clarification memos Case report forms | <ul style="list-style-type: none"> Regulatory binder | <ul style="list-style-type: none"> 21CFR312 FDA Guidance: E6 GCP, Sections 1.44, 1.45, 4.5, 5.23, 6, 8.2.2, 8.3.2 |
| Protocol Training | Documentation that trial procedures were reviewed with the investigator and investigator's trial staff: <ul style="list-style-type: none"> Summary of start-up calls Training meetings | <ul style="list-style-type: none"> Regulatory binder | <ul style="list-style-type: none"> 21CFR312 FDA Guidance: E6 GCP, Sections 4.5, 5.23, 8.2.20 |
| Record of Retained Body Fluids and/or Tissue Samples | If any blood specimens, other body fluids and/or tissue samples are retained for long-term storage at the site, document location and identification of the retained samples. (e.g., A laboratory data management or tracking system.) | <ul style="list-style-type: none"> Regulatory binder Laboratory file | <ul style="list-style-type: none"> FDA Guidance: E6 GCP, Section 8.3.25 OHRP Guidance: Issues to Consider in the Research Use of Stored Data or Tissues |
| Screening and | | | |

| Document | Requirement / Purpose | File | Reference |
|--|--|---|--|
| Enrollment / Randomization Logs | <ol style="list-style-type: none"> To document identification of participants who entered pretrial screening. To document chronological enrollment of participants by trial number Screening and enrollment/randomization logs may be separate or combined. Include the following information: <ul style="list-style-type: none"> Initials of all patients screened for each study Study ID if patient receives one Date screened Date randomized <ul style="list-style-type: none"> ➤ If not randomized, indicate reason | <ul style="list-style-type: none"> Regulatory binder | <ul style="list-style-type: none"> 21CFR312 FDA Guidance: E6 GCP, Sections 8.3.20, 8.3.22 |
| Participant Identification Code List | <ol style="list-style-type: none"> To document that the investigator keeps a confidential list of names of all participants allocated to trial numbers upon enrolling in the trial. Allows investigator/institution to permit identification of all participants enrolled in the trial in case follow-up is required. List needs to be kept in a confidential manner. | <ul style="list-style-type: none"> Regulatory binder | <ul style="list-style-type: none"> FDA Guidance: E6 GCP, Sections 1.58, 8.3.21, 8.4.3 |
| Serious Adverse Events (SAE) and Safety Reports | <ol style="list-style-type: none"> Notification by originating investigator to sponsor of serious adverse events, related reports, and other safety information. Notification by sponsor to investigators of safety information. Where applicable, notification by sponsor or investigator to regulatory authorities and the IRB: <ul style="list-style-type: none"> Unexpected, serious and related adverse drug reactions (within 5 days) Other safety information (at yearly review) | <ul style="list-style-type: none"> Regulatory binder | <ul style="list-style-type: none"> 45CFR46 21CFR50 21CFR56 21CFR312 FDA Guidance: E6 GCP, Sections 1.1, 1.2, 1.50, 1.60, 4.11, 5.16, 5.17, 8.3.16, 8.3.17, 8.3.18 |
| Signature Log | <ol style="list-style-type: none"> To document the signatures of individuals using initials in place of a full signature to sign CRFs and source documents. To document the signatures and initials of all persons authorized to make entries and/or corrections on CRFs. Include all site staff working on a study, such as: <ul style="list-style-type: none"> Clinicians Physicians Pharmacists Data personnel Any other individuals authorized to make entries and/or corrections on CRFs. Key/log must include: <ul style="list-style-type: none"> Initials Printed Signature Legal Signature, including first and last name Credentials (if appropriate) | <ul style="list-style-type: none"> Regulatory binder | <ul style="list-style-type: none"> FDA Guidance: E6 GCP, Section 8.3.24 |
| Signed Agreements | <p>To document agreements between involved parties, if any. These must be signed by an individual authorized by the institution to sign on behalf of The Regents of the University of California. This includes Confidential Disclosure Agreements</p> | <ul style="list-style-type: none"> Office of Research file | <ul style="list-style-type: none"> 21CFR312 FDA Guidance: E6 GCP, Sections 4.9.6, 5.6, 8.2.6 |

| Document | Requirement / Purpose | File | Reference |
|-------------------------|--|---|--|
| | (CDAs), Nondisclosure Agreements (NDA), Material Transfer Agreements (MTAs) and Clinical Trial Agreements (CTAs). For example: <ul style="list-style-type: none"> • Investigator/institution and sponsor (e.g., contracts, grants) • Investigator/institution and affiliated sites (e.g., contracts) • Investigator/institution and authorities (where required) | | |
| Source Documents | <ol style="list-style-type: none"> 1. To document the existence of the participant and substantiate integrity of trial data collected. 2. To include original documents related to the trial, medical treatment, history of participant, and participant's condition while on-study or in follow-up. 3. Electronic media, original documents or certified copies. | <ul style="list-style-type: none"> • As required by UC Davis/IRB policies and procedures | <ul style="list-style-type: none"> • 21CFR11 • 21CFR312 • FDA Guidance: E6 GCP, Sections 1.51, 1.52, 5.20, 8.3.13 |
| Unblinding | A copy of the Sponsor's SOP for unblinding must be on file at the site. | <ul style="list-style-type: none"> • Regulatory binder • IDS Pharmacy | <ul style="list-style-type: none"> • 21CFR312 • FDA Guidance: E6 GCP, Sections 1.10, 4.7, 8.2.17, 8.4.6 |

AM 104
ESSENTIAL DOCUMENTS

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|---|------------------------------|-------------------------|
| SOP: AM 104 Version No: 1 Effective Date: 5/10/2007 | ADMINISTRATIVE MANAGEMENT | Supercedes version: N/A |
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Originated by: CTSC SOP Advisory Panel

Modified by:

Approved by: Translational Research Integration & Compliance Committee

Approval date: 5/10/07

Expiration date: 5/10/09

AM 105 LABORATORY PROCEDURES TRAINING

1. PURPOSE

Research personnel may be required to use equipment and workspace in a UCDHS Clinical Laboratory. The purpose of this document is to provide an outline of general procedures to be used when working in a clinical laboratory.

2. POLICY AND PROCEDURES

All research personnel should be trained on the procedures outlined below prior to processing any samples independently. In addition, research personnel are expected to adhere to UC Davis' Environmental Safety Policies.

A. General Precautions

- i. It is standard practice to always wear gloves when handling, loading, or unloading samples and also when cleaning the lab or equipment.
- ii. **Do not eat or drink *anything*, do not chew gum, do not smoke, and do not apply cosmetics** in the laboratory. In addition, do not store or handle food or beverages in laboratory areas, including refrigerators used for chemical storage.
- iii. Many chemicals are absorbed through the skin, avoid direct skin contact. If you suspect skin contact with chemical substances, such as bottled reagents, wash off these substances with large quantities of water.
- iv. Wash your hands thoroughly with soap and water before leaving the laboratory.
- v. While you are working in the labs, make sure everything you need is clean and ready to use, and that all of your samples and containers are labeled.
- vi. Always learn the location of all of the safety equipment you will need while in the lab and in case of an emergency.
- vii. In case of emergency, eye wash stations are available. Please learn to locate eyewash stations, preferably with your eyes closed.
- viii. To avoid contamination never take a pen from your desk into the lab. If you need a pen, use one located in the lab.
- ix. For information not covered in this document, refer to the UC Davis Chemical Laboratory Safety Manual (http://ehs.ucdavis.edu/chem/chem_mnl/index.cfm).

B. Workbench Preparation

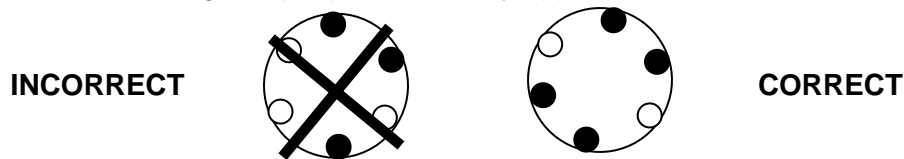
The following procedures should be completed prior to processing any samples.

- i. Remove all unnecessary items from the workbench.

- ii. Wipe down the workbench and any required equipment with alcohol wipes.
- iii. Cover the workbench with a plastic backed drop cloth.
- iv. Place all required samples and equipment on the workbench.

C. Centrifuge Instructions

- i. Do not operate centrifuges with the lids open.
- ii. Balance the contents of the centrifuge before operating. For example, if there is only one sample to be centrifuged, a tube identical in size and volume of solution contained must be placed in the rotor opposite the sample tube. For every sample placed in the rotor, there must be a balancing sample placed directly opposite.



- iii. Do not open the centrifuge lid until the rotor has stopped spinning.
- iv. Spin samples with lids on to avoid creating aerosols.
- v. Use only tubes that are specified as appropriate for that particular centrifuge

D. Workspace Clean-up

The following procedures should be completed once all samples have been processed.

- i. Dispose of all used equipment/instruments properly. All glass items should be placed in a “sharps” container. All non-glass items should be placed in a biohazard garbage receptacle.
- ii. Ship or store all samples as specified in the protocol.
- iii. Return all other items to their proper locations.
- iv. Once the workbench is empty, wipe down the workbench and any equipment with alcohol wipes.
- v. Wash your hands before leaving the lab.

3. SCOPE

This SOP specifies laboratory procedures to be followed by all research personnel.

4. RESPONSIBILITY

The research administrator or department manager is responsible for ensuring that all research personnel understand and are properly trained on all laboratory procedures. All research personnel are responsible for adhering to the laboratory procedures as outlined above.

AM 105
LABORATORY PROCEDURES TRAINING

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|---|------------------------------|----------------------------|
| SOP: AM 105 Version No: 1 Effective Date: 5/10/2007 | ADMINISTRATIVE MANAGEMENT | Supercedes version: N/A |
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Originated by: Cancer Center CTSU

Modified by: CTSC SOP Advisory Panel

Approved by: Translational Research Integration & Compliance Committee

Approval date: 5/10/07

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AM 106 PRESTUDY SITE VISITS

1. PURPOSE

Prestudy site visits are conducted by the study sponsor to meet with study personnel and review their qualifications for the study, assess the facilities, and evaluate the possibility of collaboration. This visit is conducted after the Confidential Disclosure Agreement (CDA) or Nondisclosure Agreement (NDA) has been signed by the Office of Research, Sponsored Programs.

2. POLICY AND PROCEDURE

A. Conducting the Prestudy Site Visit

- i. Identify research personnel likely to be involved in the study under consideration. This includes the principal investigator (PI), potential subinvestigators, a research administrator, research nurses/coordinators, or other support staff.
- ii. At a minimum, prestudy site visits will include a review of:
 - a. Research team member responsibilities
 - b. Facilities and equipment, including the laboratory and pharmacy, if applicable
 - c. Eligibility criteria for enrolling study participants
 - d. Treatment schedule
 - e. Pretreatment/screening procedures

B. After the Prestudy Site Visit

- i. If selected as a site, prepare and submit the following documents (if applicable):
 - a. IRB Application, including the Description of Study (DOS) based on the protocol
 - b. Informed Consent Form (ICF) as part of the IRB submission
 - c. Study budget – submit to Decision Support Services (DSS) for review/approval
 - d. School of Medicine Grant/Contract Transmittal Form
 - e. Office of Research Data Sheet for Contract and Grant Proposals
- ii. Submit the Clinical Trials Agreement (CTA) to the Office of Research, Sponsored Programs for negotiation, approval and signature

3. SCOPE

This SOP specifies the procedures for conducting the prestudy site visit for all phases of clinical studies falling under Investigational New Drug (IND) regulations.

4. RESPONSIBILITY

All members of the research team are responsible for adhering to the SOP as outlined above.

5. APPLICABLE REGULATIONS AND GUIDELINES

| | |
|---------------|--|
| 21 CFR 312.50 | General Responsibilities of Sponsors |
| 21 CFR 312.53 | Selecting Investigators and Monitors |
| 21 CFR 312.60 | General Responsibilities of Investigators |
| ICH GCP | Guidelines for the Monitoring of Clinical Investigations |

AM 106
PRESTUDY SITE VISITS

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|---|------------------------------|-------------------------|
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