PM 300
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PM 301
INFORMED CONSENT PROCESS

1. PURPOSE

The informed consent process for clinical trials is just one part of a larger system in place to safeguard participants who voluntarily participate in new practices that may improve treatment, supportive care, screening, and prevention, while perhaps benefiting from these new methods. This system ensures that clinical trials are conducted ethically, without undue risk to participants.

The informed consent process provides the participant with ongoing explanations that will help them make educated decisions about whether to begin or continue participating in a trial. Before a participant makes their decision on whether to participate in a trial, the research team will discuss the trial's purpose, procedures, risks and potential benefits, and their rights as a participant. If the participant volunteers to participate, the research team will continue to update them on any new information that may affect their situation.

As the trial proceeds, the research team may discover new information that could affect the subject's health, welfare, or willingness to remain in the study. This information will be shared with the subject and the subject may be asked to sign a new Informed Consent Form (ICF). Thus, informed consent is an ongoing, interactive process, rather than a one-time information session.

2. PROCEDURE

A. Consent Version

i. The Clinical Research Coordinator (CRC) must ensure that only the most current ICF for the study is being used.

ii. The CRC must ensure that the ICF is stamped by the IRB and that the approval has not expired.

B. Consent Review

i. The Principal Investigator (PI) or the CRC for the study will provide a copy of the ICF to the potential study participant. If possible, the participant should take the ICF home to review before signing. This will allow the participant time to review the requirements of the study, discuss the study with family and friends, and form questions about study participation prior to signing the consent form. All participants should be given ample time to make a decision regarding participation without pressure or coercion.

ii. The PI and/or the CRC will review the elements of the ICF with the study participant and address any questions within his/her scope of responsibility. This ensures that the potential study participant understands the content and meaning of the ICF.

iii. If a participant is not able to understand the ICF in English, two consenting options exist:

1) the entire ICF may be translated into the patient's native language

OR

2) a “short form” and an Experimental Subject’s Bill of Rights translated into the subject’s primary language may be used.

For complete instructions on consenting non-English speaking participants, please see the IRB Administration’s policy on “Enrollment of Non-English Speaking Subjects.” (http://www.research.ucdavis.edu/home.cfm?id=OVC,1,1081,1433)

C. Documenting the Informed Consent Process

i. The informed consent process will be documented with chronologic summaries of all interactions with a prospective subject.

ii. Documentation of the informed consent process will begin when a prospective participant is given the informed consent document.

a. If a prospective subject is mailed an informed consent document a note documenting the mailing will be written.
b. If a prospective subject is given an informed consent document in clinic, a note documenting the visit will be written.

c. Documentation of all encounters will continue until the prospective subject decides not to participate or signs the ICF. If the participant agrees to participate, a note must be made in the research chart including the following ***sample*** statement, “Prior to any study-related procedures, the participant was given ample time to review the informed consent and ask questions regarding the study. Once all questions and concerns were answered, the participant agreed to participate and signed the informed consent form. The participant was given a copy of the consent for their records.”

D. Signature Requirements

i. The ICF must be signed and dated prior to the initiation of any study-related treatment.

ii. The CRC will ensure that the study participant signs and dates the first page and last page, and initials each of the remaining pages of the study specific ICF. One original copy is required.

iii. Ensure that additional boxes for optional studies (i.e. biopsies) have been checked or initialed appropriately.

iv. The study subject must sign the study specific *Authorization for Release of Personal Health Information (Protected Health Information) for Research Purposes* form (HIPAA Release) in addition to the ICF. Once signed, a copy of the informed consent and HIPAA Release Form should be given to the patient.

v. The PI, or their IRB-approved representative, must sign and date the last page of the ICF as soon as possible after the study participant has signed. The CRC must verify that the investigator signing the ICF is listed on the IRB-approved Research Personnel list for the study. If the investigator is unable to sign the consent form on the same day as the participant, a note to file must be attached to the consent explaining why the delay occurred.

E. Distribution of ICF

i. One copy of the signed ICF and HIPAA Release will be kept in the participant's research record.

ii. A copy of the signed ICF and HIPAA Release will be sent to Health Information Maintenance (HIM) along with the IRB-approved Description of Study (DOS).

iii. The study participant will be given a copy of the signed ICF and HIPAA Release for his/her personal records.

iv. For participants receiving study drug, the Investigational Drug Service (IDS) Pharmacy will be given a copy of the last page of the ICF.

v. For surgery trials, a full copy of the ICF and HIPAA Release should be included with the pre-op packet.

F. Amendments and Reconsenting

Occasionally, changes are made to the protocol that require changes in the ICF. In such cases, the enrolled participants may be required to sign the revised ICF and the informed consent process will need to be documented again.

i. If the ICF is amended during the course of the study, due to a change in risks, the PI must ensure that all active study participants sign an amended ICF as soon as possible (***if required by the sponsor of the study or the IRB***.)

ii. The participant will be given a copy of the revised ICF. If possible the changes should be highlighted.

iii. A chronologic summary of the informed consent process will be created for each participant.

3. SCOPE

This SOP specifies the guidelines for the informed consent process for all participants enrolled in a UCDHS clinical trial.

4. RESPONSIBILITY

The PI is responsible for compliance with this SOP and for ensuring that informed consent is obtained properly from each study participant. The PI and CRC are responsible for discussing all elements of the ICF with the study participant and providing them with a copy of the ICF.

5. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 50.25	Elements of Informed Consent
21 CFR 56.109	IRB Review of Research
21 CFR 312.60	General Responsibilities of Investigators
45 CFR 46.116	General Requirements for Informed Consent
45 CFR 46.117	Documentation of informed consent.

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INFORMED CONSENT PROCESS

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PM 302
PARTICIPANT ENROLLMENT

1. PURPOSE

It is essential that the Clinical Research Coordinator (CRC) become familiar with the specific clinical trial protocol onto which he/she may be entering patients. The CRC must review all eligibility criteria follow-up requirements and correlative requirements within the study. Participants failing to meet all protocol eligibility requirements may not be enrolled.

The guidelines below should be used as a summary only – please refer to the individual protocol for specific enrollment procedures. Please note: Research participants enrolled in clinical research involving the use of UCDHS facilities should be registered in Invision.

2. PROCEDURE

A. Industry/Pharmaceutical Protocols

i. Determining Study Eligibility

Prior to beginning a prestudy participant work-up, the Clinical Research Coordinator (CRC) should verify that the study is open to accrual. Participants failing to meet all protocol eligibility requirements may not be enrolled in the study. Once a study number is assigned, a participant is followed per the protocol.

1. Confirm all regulatory requirements have been met and assure the protocol has undergone Institutional Review Board (IRB) approval within the past year.
2. Verify the informed consent form has been signed.
3. Verify all appropriate pretreatment tests have been completed within the period defined in the protocol.
4. If applicable, ensure that drug has been ordered and adequate inventory is on hand.

If a participant is screened for a specific protocol but found to be ineligible, their information should be retained in a research folder for "Screen Failures."

5. All protocol deviations, regardless of nature, reason or PI authorization must be reported to the IRB Administration with annual renewal.

ii. Clinical Trials Billing (Bulk) Account Establishment

1. Once eligibility has been verified, a clinical trials bulk account should be established. For detailed instructions, please see UCDHS P&P #1815 "Establishing a Bulk Account."

iii. Registration

1. If the study involves the use of UCDHS facilities or procedures, the participant should be registered according to UCDHS P&P #2382 "Research Subjects Patient Registration."

B. Investigator-Initiated Protocols

i. Determining Eligibility

1. Review all amendments affecting eligibility. Confirm all legal requirements have been met and assure the protocol has undergone Institutional Review Board (IRB) approval within the last year.
2. If pathology review is required, confirm with the Pathologist that materials are available for submission.
3. Verify informed consent has been signed and dated appropriately and that additional boxes for optional studies have been checked.
4. Verify all required prestudy tests have been completed within the time frame specified in the protocol and that all eligibility criteria are met.
5. Complete all information on the Eligibility Checklist in black ink, if available.

3. SCOPE

This SOP specifies the guidelines for participant enrollment into a UCDHS clinical trial.

4. RESPONSIBILITY

The Clinical Research Coordinator, with the oversight of the Principal Investigator, is responsible for ensuring that all participants enrolled meet the protocol's eligibility criteria and that enrollment occurs as outlined by the protocol.

APPLICABLE REGULATIONS AND GUIDELINES

UCDHS Policy and Procedure 1815
UCDHS Policy and Procedure 2832

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PARTICIPANT ENROLLMENT

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PM 303
SCHEDULING

1. PURPOSE

Each clinical trial is designed to collect important data at specific time points during the study, making the scheduling process an important aspect of conducting a clinical trial. Therefore, it is important to follow the schedule outlined in each trial. In order for the trial to be completed successfully and according to protocol, the CRC must become the liaison between the participant and various other departments.

2. PROCEDURES

A. Clinics

i. Turn in scheduling form to appointment scheduling clerk.
ii. There will be times when there is no open slot available for clinic and the investigator will then need to decide when and with whom the participant will be seen. If a research treatment delay occurs, the CRC will then need to document the reason in the participant's research record, as well as on any case report forms.

B. Radiology and Miscellaneous Diagnostic Exams

If the radiology or diagnostic exam is being done for research purposes only and will billed to the study's bulk account, please notify the scheduler to ensure proper billing.

i. X-Rays, CT Scans, PET Scans

a. Obtain a "Diagnostic Imaging Request" form and complete all requested information (i.e. type of exam, clinical history, suspected diagnosis, allergy information). This form may be handwritten or computer generated.

1. For baseline exam (prior to going on a clinical trial), use the ICD-9 diagnostic code.

2. For follow-up exams (once a patient has been enrolled on a trial), you must include the clinical trials code v70.7 on the ICD-9 code line, in addition to the ICD-9 diagnostic code. You must also write the bulk account number on the form to ensure proper billing.

ii. Echocardiograms

a. Complete a "UC Davis Heart Center" form and follow above instructions.

iii. Pulmonary Function Test

a. Review protocol test schedule for list of all tests required when obtaining this exam (DLCO, arterial blood gas, etc.)

b. Complete "Pulmonary Function Test" form

iv. EKG

a. An EKG may be done prior to or following a clinic appointment provided there is adequate staff and room availability. Two originals will be provided, one copy to medical records, the other for the participant's research record.

b. If the EKG is unable to be obtained in the clinic, complete the "Cardiology Department Non-Invasive Cardiology" form. This form can then be given to participant to hand carry to the Heart Station located in the South Tower RM #1311, as no appointment is needed.

C. Hospital Admittance Request (HAR)

i. Short Stays

a. There will be times when a participant's treatment will involve a "short stay" visit to the hospital.

b. Complete a "HAR" form with the following information:

- Unit number
- Patient name
- Admission date (line 17) – enter the date the patient will be admitted
- Length of stay (line 17) – enter < 24 hrs
- Admitting physician (along with PI #) (line 18)
  - *Note: The admitting physician is not necessarily the participant's investigator. The admitting physician listed on the HAR will be the attending ward physician during the time of the proposed hospital stay.*
- Type of Admission (line 19) – in most cases check "short stay"
- Admitting diagnosis with ICD-9 code (line 21)
- Proposed Surgery/Treatment (line 22) – enter treatment to be given
- Special Instructions (line 23) – if the participant will be contacted when bed is available enter "Please call patient at home when bed is available"

c. Take the completed HAR to the clinic authorization clerk. Ask that the clerk contact you once the authorization is received.

d. When picking up the HAR, verify the authorization information/number is written on the form.

e. Make two copies of the protocol and participant's signed consent form.

f. If the clinical trial involves investigational drugs provided by the study, a copy of the participant's signed consent form must be faxed to the Investigational Drug Service (IDS) Pharmacy, along with the research treatment orders.

g. Take the protocol and consent copies, along with the original treatment orders, to the Short Stay Unit.

- Give the original treatment order, one copy of the protocol and one copy of the Informed Consent Form (ICF) to the pharmacy.
- The remaining protocol and ICF copies should be given to the Davis 8 nursing station. You should also advise them of when the participant is scheduled to be treated.

D. Indwelling Venous Access Device Placement

i. Port-a-cath (and all other devices placed through Interventional Radiology)

a. Obtain a "Diagnostic Imaging Request" form and complete all requested information (e.g., type device (i.e. single lumen Port-a-Cath), clinical history, allergy information). This form may be handwritten or computer generated.

b. Give this form to the scheduler. The scheduler will phone you once he/she has obtained the authorization number and the form is ready for pick up.

c. The participant will need to be given lab requisitions for an INR, PTT, CBC w/diff and Chem 7, to be completed no more than two weeks before the scheduled placement.

ii. PICC Line

a. The PI should write an order for PICC line placement on a standard "Physicians Order" form.

b. Contact Vascular Access (734-3732 or 762-5379) to schedule the placement. Vascular Access will request the following information:
- Participant's ICD-9 code
- Allergies
- List of any blood thinners the participant may be taking

3. SCOPE

This SOP specifies the guideline for scheduling visits, infusions, admissions and exams for participants enrolled in a UCDHS clinical trial.

4. RESPONSIBILITY

The CRC or Research Nurse is responsible for scheduling all clinical trial-related clinic visits, infusions/injections and exams/tests needed for participants enrolled in clinical trials. The Research Nurse is responsible for scheduling all PICC line placements and urgent/emergent HARs.

PM 303
SCHEDULING

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PM 304
STUDY-RELATED (NON-STANDARD OF CARE) PROCEDURES

1. PURPOSE

Sometimes during the course of clinical trial participation a participant will need to have a procedure done which would not be done if the participant were not on the clinical trial. Such procedures are not considered standard of care and should not be billed to the participant's insurance provided. Instead, these so called "for research only procedures" should be billed directly to the study's Bulk Account.

2. PROCEDURES

The research bulk account should be set-up during the final stage of the regulatory process, please see http://www.ucdmc.ucdavis.edu/medresearch/medsp/includes/Bulk_%20Acct1097.doc for guidelines regarding requesting a bulk account.

Obtain a bulk account card. If your department does not have an embosser, request a bulk account card from the Admissions Department in the main hospital. Fax a request with the participant's name, medical record number, DOB, Principal Investigator, study name and bulk account number to 734-0550; they will generate a card that will need to be picked up by the CRC or designee. Do not give this card to the participant.

A. Lab/PK Draws

   i. Complete the Department of Pathology Checklist for Research and fax to 734-7371. This will prompt Pathology Client Services to generate protocol specific Lab Requisitions with the appropriate Bulk Account number.

   ii. Give the lab request to the patient or directly to the lab.

B. Radiology Exams (e.g., x-rays, CT scans, MUGA scans)

   i. Research protocols utilizing Radiology must be reviewed by the Radiology Research Committee before procedures can be scheduled.

   ii. Obtain a pink "Radiology Examination Request (Research)" form
   ii.
   iii. Stamp the form using the patient's bulk account card.

   iv. Complete the information requested on the form.

   v. Schedule the exam through the normal channels.

C. Miscellaneous Diagnostic Exams (e.g., Echocardiograms, PFTs, EKGs, PET imaging)

   i. Complete the standard procedure requisition paperwork being sure to stamp each requisition with the patient's bulk account card.

   ii. Schedule the exam through the normal channels.

iii. On the day of the scheduled exam, the CRC should go to where the exam is being performed with the bulk account card so that all of the patient's paperwork can be stamped. This step helps ensure the exam is appropriately billed.

D. Surgical Procedures

i. Research protocols utilizing the operating rooms must have an Operating Room Resource Review Approval letter on file before surgical time can be scheduled.

ii. Complete the standard procedure requisition paperwork being sure to stamp each requisition with the patient's bulk account card.

iii. Schedule the procedure through the normal channels.

iv. On the day of the scheduled procedure, the CRC should go to where the procedure is being performed with the bulk account card so the participant's paperwork can be stamped. This step helps ensure the procedure is appropriately billed.

3. SCOPE

This SOP specifies the guidelines for requesting lab draws, radiology exams, miscellaneous diagnostic exams and surgical procedures which will be billed to a study bulk account.

4. RESPONSIBILITY

The CRC is responsible for ensuring all non-standard of care procedures are billed to the study's bulk account rather than the participant's insurance provider.

5. APPLICABLE REGULATIONS AND GUIDELINES

UCDHS Policy and Procedure 1815

PM 304
STUDY-RELATED PROCEDURES

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PM 305
PARTICIPANT RESEARCH RECORD

1. PURPOSE

A research record should be maintained for all participants enrolled in UCDHS clinical trials. The purpose of the research record is to ensure that the data necessary for a participant's management while on a clinical trial be available at all times. The research record also serves as a place to file any study specific forms that cannot be contained within the participant's hospital chart. Research Records are considered Protected Health Information and are to be stored in a secure, locked location where unauthorized persons cannot obtain access.

2. PROCEDURES

A. Content

1. The content of a participant research record may vary considerably between studies. In general, the research record should contain all information used to verify eligibility (both for enrollment and treatment) and document treatment, response and toxicity. The following is a list of items which, at a minimum, should be included in the research record:

    - Progress notes detailing the consenting process, study visits and all other procedures/exams/evaluations, and changes in concurrent medications
    - Signed Informed Consent Form (ICF) and HIPAA Release
    - Baseline history and physical
    - List of current medications
    - Clinic progress notes
    - Lab results, pathology results and operative reports
    - Diagnostic test results
    - Protocol treatment orders
    - Adverse event list, if applicable
    - Serious adverse event documentation, if applicable

B. Results from Outside Hospitals

1. In addition to being filed in the participant's research record, a copy of any diagnostic test results (e.g., lab, pathology, CT scan, etc.) obtained from an outside hospital should be sent to medical records for inclusion into the participant's hospital chart. This is done to ensure that in case of an emergency/inpatient hospitalization, the treating physicians have all available information that might affect patient care.

3. SCOPE

This SOP specifies the guidelines for participant research records.

4. RESPONSIBILITY

The CRC is responsible for assembling the participant research record and ensuring that it contains all necessary protocol documentation.

5. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 312.62 Investigator Recordkeeping and Record Retention
21 CFR 312.68 Inspection of Investigator's Records and Reports
ICH GCP Consolidated Guideline
UCDHS Policy and Procedure 2306
UCDHS Policy and Procedure 2902

PM 305
PARTICIPANT RESEARCH RECORD

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PM 306
SPECIMEN MANAGEMENT

1. PURPOSE

Many clinical trials involve the collection of blood, urine, or tissue specimens for pharmacokinetic (PK) or pharmacodynamic (PD) testing. Specimens collected for PK or PD research purposes are used to study the mechanism by which the drug acts.

2. PROCEDURE

A. Specimen Processing

For specific information regarding laboratory procedures, including workbench preparation and use of the centrifuge, see SOP AM 105.

Depending on the protocol, specimen processing requirements will vary. *Please see the protocol for study-specific specimen processing and shipping requirements.*

i. Labeling specimens

Each specimen must be labeled with the following information:

- Participant initials
- Study number
- Patient study ID
- Date and time specimen was drawn
- Initials of lab personnel drawing the specimen

ii. Specimen transmittal forms

A specimen transmittal form should be completed if required by protocol.

B. Smear Preparations

i. Obtain two clean slides.

ii. Place a small drop of blood near the labeled end of the one of the slides using a 1mL pipette. Do not place the drop right at the edge of the slide.

iii. Working quickly, place this slide on the workbench. Pick up the second slide which will be used as a “spreader “ slide.

iv. Place the “spreader” slide slightly in front of the drop of blood. There should be an approximately 25 degree angle between the two slides.

v. Draw the “spreader “ slide toward the drop of blood. As soon as it touches the blood, the blood will spread to the edges of the “spreader” slide.

vi. Keeping the “spreader “ slide at the same angle and its edge firmly against the horizontal slide BUT without pushing down, push the “spreader” slide rapidly down the length of the horizontal slide without stopping.

vii. Allow the smear to dry in the ambient air, in an absolutely horizontal position (do not place wet slides at an angle to dry).

C. Central Lab Submissions

Many industry sponsored protocols require research specimens be shipped to a central lab for processing. *Please see the study specific protocol for guidelines on central lab processing.*

D. Specimen Shipment

i. Training

All personnel involved with shipping specimens are required to take the “Shipment of Dangerous Goods” training course. This course is offered quarterly by the UC Davis School of Medicine Safety Coordinator. A certificate is issued when the course has been successfully completed. The certificate is valid for two years.

ii. Preparing a specimen for shipment

a. All specimens shipped should be packed in approved boxes with adequate packing materials and room for dry ice, if necessary.

b. All boxes should include a piece of absorbent material. *Please refer to the study specific protocol for shipping requirements.*

iii. Ambient temperature shipping

a. Specimens shipped at ambient temperature, or room temperature, do not need dry ice.
b. Specimens should be processed as soon as possible and shipped overnight to the recipient specified in the protocol.

iv. Dry ice shipping

a. Frozen specimens must be shipped on dry ice.
b. Dry ice can be obtained in the main hospital, Davis Tower basement, room 0771.
c. A dry ice label must be attached to the outside of the box with the approximate weight of dry ice written on the label.

3. SCOPE

This SOP specifies the guidelines for specimen and PK management for participants enrolled in UCDHS clinical trials.

4. RESPONSIBILITY

The Clinical Research Coordinator (CRC) is responsible for ensuring specimens and PKs are processed as indicated in the protocol. The CRC, Research Nurse, or research lab support staff may manage specimen and PK processing, depending on specific protocol requirements.

5. APPLICABLE REGULATIONS AND GUIDELINES

UCDHS Policy and Procedure 3090

PM 306
SPECIMEN MANAGEMENT

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PM 307
UNANTICIPATED ADVERSE EVENTS

1. PURPOSE

Unanticipated risks are sometimes discovered during the course of research. Information that may impact the risk/benefit ratio should be promptly reported to, and reviewed by, the UC Davis Institutional Review Board (IRB) Administration to ensure adequate protection of the welfare of the participants. Based on such information, the IRB may need to reconsider its approval of the study, require a modification to the study, or revise the continuing review timetable. The IRB is also responsible for ensuring that reports of unanticipated problems involving risks to research participants or others are reported to the FDA. Usually, this reporting is accomplished through the investigator to the sponsor to the FDA. It is the responsibility of the Principal Investigator (PI) to notify the IRB of a Serious Adverse Event (SAE) or injury to participants while on a clinical trial.

2. PROCEDURES

A. Recognition

i. Events occurring at another site using the treatment will be in the form of a letter describing the event or from Med-Watch

ii. Information regarding an event for a UC Davis research participant may be gathered from a physician's progress note, nursing note, diagnostic test, ancillary service and/or from the patient or family member.

iii. After gathering details about the event, determinations must be made about the severity of the event and whether the event is related to the treatment (see Applicable Regulations and Guidelines below). This should be recorded by the individual responsible for the care of the participant and used as source documentation.

iv. The Principal Investigator will make the determination of the relationship of the event to the treatment.

B. General Reporting

i. Principal Investigators are required to report all adverse events and/or injuries that occur at UC Davis for patients enrolled in their research studies.

ii. Serious, unanticipated and related adverse events occurring at UCD or a protocol open at UCD, must be reported on the Serious Adverse Event/Injury Report Form to the IRB no later than five working days after first awareness of the event.

iii. Anticipated or unrelated serious adverse events, must be reported to the IRB at the yearly renewal, as well as at the close of a study, in a tabular or chart form.

iv. Mild to severe adverse events, must be reported to the IRB at the yearly renewal, as well as at the close of a study, in a tabular or chart form.

v. Any adverse event must be reported to the IRB within five days if all three of the following criteria are met:

A. The event or problem is unanticipated; **and**
B. The event or problem is related or possibly related to the research (An adverse event is 'related to the research procedures' if in the opinion of the principal investigator, it was more likely than not that the event affects the rights and welfare of current participants); **and**
C. The event or problem suggests that the research places participants or others at a greater risk of harm than was previously known or recognized.

External Events

Events occurring at studies conducted at other institutions should only be reported to the IRB when the PI has determined that the events meet the criteria for reporting as described above unless required by the sponsor.

vi. Any adverse event occurring on a protocol that is closed to enrollment and patients are no longer receiving active treatment regardless of severe, expectation or attribution DOES NOT need to be reported to the IRB.

vii. Deaths do not require any special reporting beyond what is outlined above.

Investigators will be asked to provide their opinion as to whether any proposed changes need to be made in the description of the study or the consent forms(s). Investigators will also be required to make these assessments for the severity of the event and relationship to the study drug.

B. Sponsor Reporting

i. Please refer to the guidelines in the study-specific protocol for reporting.

C. IRB Reporting

All adverse events shall be reported to the UC Davis IRB Administration in the following manner (also refer to http://research.ucdavis.edu//documentDisplay.cfm?id=400,pdf):

The Report of Unanticipated Problems Involving Risk to Participants or Others Form is used to transmit pertinent information about the event to the IRB. Only serious or severe events (as defined by the protocol) need to be reported. The report must be submitted NO LATER THAN 5 WORKING DAYS after first awareness of the event.

- Serious, unexpected, **and** related events occurring at UCD, or at other sites performing the same research, must be reported on The Report of Unanticipated

Problems Involving Risk to Participants or Others Form, no later than five working days after first awareness of the event.

- Signature of the Principal Investigator will need to be obtained before IRB submission. If the Principal Investigator is unavailable to sign the document, a preliminary report may be submitted in order to meet the submission deadlines. A letter to the IRB will explain that a final report of the event will follow upon the return of the PI.
-
- This notice of reporting SAE requirements to the IRB does not affect the investigator reporting requirements of adverse events to the FDA, CCRC, and/or the study sponsor. If there is a question concerning adverse event reporting requirements, please review the applicable Federal Regulations below.

- Other hospital reporting requirements must be observed. For specific UCDHS requirements, refer to the Hospital Policies & Procedures Manual.

- Deaths do not require any special reporting beyond what is outlined above

IRB review of the serious adverse event / injury form:

In addition to completing the form, investigators should provide their opinion as to whether any proposed changes in the Description of Study or the consent form(s) are warranted as a result of the adverse event. If changes are warranted, the revised documents must be attached to the Report of Unanticipated Problems Involving Risk to Participants or Others Form. Completion of the Modification/Amendment Form is not necessary in these instances.

3. SCOPE

This SOP specifies the guidelines for adverse event recognition and reporting for all UCDHS clinical trials.

4. RESPONSIBILITY

The PI and Clinical Research Coordinator are responsible for reporting all serious or unexpected adverse events immediately according to protocol) to the Sponsor and applicable government agencies. The PI or designated study personnel will also report all serious and unexpected adverse events to the IRB within 5 working days.

5. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 312.32	IND Safety Reports
21 CFR 56.108	IRB Functions and Operations
21 CFR 56.115	IRB Records

B. Definitions

i. Adverse Event - A medical event occurring during a clinical study that can represent a new symptom experienced by a study subject or an exacerbation or worsening of an existing condition.

ii. Serious Adverse Event - (FDA 21 CFR 312.32) Any adverse drug experience occurring at any dose that results in any of the following outcomes:

a. Death: Report if the patient's death is suspected as being a direct outcome of the adverse event.

b. Life-Threatening: Report if the patient was at substantial risk of dying at the time of the adverse event or it is suspected that the use or continued use of the product would result in the patient's death.
Example: Bone marrow suppression

c. Hospitalization (initial or prolonged): Report if admission to the hospital or prolongation of a hospital stay resulted because of the adverse event.
Example: Bleeding causing or prolonging hospitalization.

d. Disability: Report if the adverse event resulted in a significant, persistent, or permanent change, impairment, damage or disruption in the patient's body function/structure, physical activities or quality of life.
Examples: Peripheral neuropathy

e. Congenital Anomaly: Report if there are suspicions that exposure to a medical product prior to conception or during pregnancy resulted in an adverse outcome in the child.
Example: Malformation in the offspring caused by thalidomide.

f. Requires Intervention to Prevent Permanent Impairment or Damage: Report if you suspect that the use of a medical product may result in a condition that required medical or surgical intervention to preclude permanent impairment or damage to a patient.
Examples: Burns from radiation equipment requiring drug therapy.

g. Important Medical Event: Events which may not result in death, be life-threatening or require hospitalization but based upon appropriate medical judgment may jeopardize the patient or subject and may require medical or surgical intervention to prevent death or hospitalization.
Examples: Convulsions or allergic reaction not requiring hospitalization.

iii. Unexpected Adverse Event – (21 CFR 312.32)

a. Studies Conducted Under an Investigational New Drug (IND): Any AE; the specificity or severity of which is not consistent with the current Investigator Brochure or product labeling.

b. Studies Conducted Under The New Drug Approval (NDA): Any AE not listed in the current labeling or is different from current labeling because of greater severity or specificity. This includes an event that may be symptomatically and pathophysiologically related to an event listed, but differs from the event because of greater severity or specificity. An AE that results in death is unexpected unless the labeling indicates a possible fatal outcome.

C. Intensity

- Mild: Symptom(s) barely noticeable to subject or does not make subject uncomfortable; does not influence performance or functioning; prescription drug not ordinarily needed for relief of symptom(s) but may be given because of personality of subject.

- Moderate: Symptom(s) of a sufficient severity to make subject uncomfortable; performance of daily activities is influenced; subject is able to continue in study; treatment for symptom(s) may be needed.

- Severe: Symptom(s) cause severe discomfort; symptoms incapacitation or significant impact on subject's daily life; severity may cause cessation of treatment with study drug; treatment for symptom(s) may be given and/or subject is hospitalized.

D. Relationship of the Adverse Event to the Study

- Not Related - Any reaction that does not follow a reasonable temporal sequence from administration of study drug and that is likely to have been produced by the subject's clinical state or other modes of therapy administered to the subject.

- Unlikely Related - Any reaction that does not follow a reasonable temporal sequence from administration of the study drug or that is likely to have been produced by the subject's clinical state or other modes of therapy administered to the subject.

- Likely Related - A reaction that follows a reasonable temporal sequence from administration of study drug or that follows a known response pattern to the suspected drug and that could not be reasonably explained by the known characteristics of the subject's clinical state or other modes of therapy administered to the subject.

- Definitely Related - A reaction that follows a reasonable temporal sequence from administration of study drug and that follows a known response pattern to the suspected drug and that recurs with rechallenge, and/or is improved by stopping the drug or reducing the dose.

PM 307
UNANTICIPATED ADVERSE EVENT REPORTING

SOP: PM 307 Version No: 1 Effective Date: 5/10/2007	PARTICIPANT 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

PM 308
DATA MANAGEMENT

1. PURPOSE

This standard operating procedure (SOP) describes the processes followed 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:

a. Quality control
b. Data query resolution
c. Record retention and archiving

2. PROCEDURES

A. Collection of clinical research data

i. The Principal Investigator (PI), subinvestigator, research manager, research nurse/coordinator, and support staff are responsible for collecting data as outlined by the protocol.

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 (some sponsors will require blue ink). 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 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/coordinator • 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.

3. 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.

4. RESPONSIBILITY

This SOP applies to members of the research team involved in data collection, transcription to CRFs, and the management of the data. This includes the Principal Investigator, subinvestigator, research manager, research nurse/coordinator, study pharmacist, and support staff.

5. 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
ICH GCP	IConsolidated Guideline

1. Definitions

The following definitions from the International Conference on Harmonisation, Good Clinical Practice: Consolidated Guideline, apply to this SOP.

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 trial subject.

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

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 a trial, and the actions taken.

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

Quality Assurance (QA): All those planned and systematic actions that are established to ensure that the trial is performed and the data are generated, documented (recorded), and reported in compliance with GCP and the applicable regulatory requirement(s).

Source Data: All information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial 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).

PM 308
DATA MANAGEMENT

SOP: PM 308 Version No: 1 Effective Date: 5/10/2007	PARTICIPANT MANAGEMENT	Supercedes version: N/A

Originated by: CTSC SOP Advisory Panel

Modified by:

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