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Guidance regarding Drug Management

when the PI manages the drug

Purpose:

This Guidance document was created by the Investigational Product Review Committee (IPRC) to assist Principal Investigators (PI) in the prevention of diversion and mismanagement of study drug(s) used in human subject research conducted under the auspices of the University of Colorado Denver. It describes the management and documentation for drug(s) that are used in a human study and managed through the PI at the University of Colorado at Anschutz Medical Campus or free-standing University locations. This document applies only to single site studies as it does not cover procedures for managing study drugs in multiple locations. This document does not include processes and procedures to be followed when study drugs are compounded.

Procedure:

1. The PI will maintain responsibility for accountability of all drugs being used in a study and in accordance with hospital policy.
2. The PI may delegate some drug management activities to other study personnel to help and ensure proper drug management.
3. All study personnel managing study drugs must be CU employees, unless otherwise approved.
4. The PI must have adequately sized, limited access storage location that was inspected and approved by the Investigational Product Review Committee (IPRC).
    a. The PI is responsible for establishing a process that ensures limited access to the approved storage location.
    b. The PI is responsible for ensuring that appropriate storage conditions/equipment can be made available to store the drug(s) according to the product specifications.
    c. The PI is responsible for having appropriate equipment that is current on its calibration to track the storage temperature and other conditions (such as humidity) as necessary.
5. The PI will be responsible for submitting all documents that are relevant to the management of the study drug(s) to the Human Subject Research Portal (HSRP). This includes protocol, investigator's brochure, package inserts, pharmacy manual, and completed Investigational Product Management Plan (IPMP).
    a. Check the appropriate study sites on the Protocol Assessment Form (PAF).

b. Check "No" to the question whether the compounding and/or local management of the investigational drug/biological is being managed by a pharmacy on the AMC campus or a UCHealth pharmacy on the PAF.
c. If drug management is planned to change after the study started, an amendment needs to be submitted to the HSRP to assess if a revision to the Investigational Product Management Plan is required.

6. The PI is responsible for developing forms and policies to document the chain of custody of the study drug from time of receipt to the time when the drug will be dispensed to the study subject.
    a. For investigator-initiated studies, the PI is responsible for developing the randomization schedule (if applicable), study drug inventory logs and subject drug accountability logs. The attached templates may be used..
    b. For studies that are initiated externally, templates provided by the sponsor or a coordinating center may be used if available. Otherwise use the attached templates.
7. The PI is responsible for management of drug used in the study with activities including but not limited to; inspecting any product received for damage, documenting the match against any accompanying shipping forms and any discrepancies, completing all shipment tracking forms and inventory logs, quarantining any damaged packages or products that experienced excursions beyond the acceptable range in temperature or other conditions during shipment, and contacting the manufacturer/sponsor for instructions on the quarantined products.
8. The PI is responsible for establishing processes for tracking and documenting drug storage conditions, and alerts for excursions beyond the allowed ranges.
9. The PI is responsible for storing drug(s) for different studies, and unused and returned products for each study separate from each other.
10. The PI is responsible for creating and attaching additional labeling to the containers of study drug(s) that are self-administered at home.
    a. The additional labeling must include COMIRB#, PI name, CU Denver, and a 24 hour emergency phone # (cannot be 911).
    b. If not already otherwise on the study drug label, the additional label must also have fields for subject name (preferred) or initials, and for dispensed date.
    c. If not already otherwise on the label, the statement "**Caution: new Drug – Limited by Federal law to investigational use."** must be on the label for studies under an IND. The statement **"For Research Use Only**" is sufficient for studies that are not under an IND.

11. Any drug(s) for which the storage is managed by the study team must also be dispensed and/or administered by the study team to the study subject.
    a. UCHealth staff, including CTRC nurses, are not permitted to dispense or administer any drugs that were not managed by a UCHealth pharmacy.
    b. "UCHealth pharmacy" includes only the Investigational Drug Services (IDS), Cancer Center pharmacy, and Infections Disease Group pharmacy (IDGP).
12. If study drug is managed and stored outside of a UCHealth hospital or HOPD (Hospital outpatient departments) but dispensed or administered in a UCHealth hospital or HOPD:
    a. the study drug must be dispensed and administered to the study participant with direct oversight by a licensed independent practitioner (LIP). This task cannot be delegated to any other individual that is not an LIP;
    b. the dispensing of the study drug must be initiated by an order; and
    c. the administration of the study drug must be documented in EPIC.
    d. Please note that the clinics located within the Anschutz Outpatient Pavilion (AOP) are HOPDs of UCHealth Denver Metro.
13. The PI is responsible for education of the research staff regarding the use of the drug(s) being used in the study including the following:
    a. Instructions on completing all drug-related forms completely and accurately
    b. Directions for the use of the study drug(s)
    c. Subject safety monitoring
    d. Staff safety while handling the drug (eg protective equipment for hazardous drugs)
14. The PI is responsible for establishing procedures that ensure that transport of the drug(s) to different locations is appropriate for the agent being transported.
15. The PI will ensure that the participant's informed consent has been obtained prior to the performance of study procedures and placement / use of the study drug.
16. The PI is responsible for ordering the study drug(s) from the sponsor or drug manufacturer.
17. The PI is responsible for entering the drug disposition/administration to study subjects in a research note in the electronic medical record system (EPIC) per hospital policies (if connected to EPIC) or in the study subject's medical records.
18. The PI is responsible for documenting all relevant information in the medical record including the dose, number of days prescribed and date of next visit.
19. The PI is responsible for documentation and reporting of adverse drug events in accordance with SOP, sponsor or FDA requirements as applicable.
20. The PI is responsible for ensuring the relevant information is documented on the case report form.

21. The PI is responsible for notifying the person(s) who accepted the delegated duty of drug management when a study is complete or terminated to arrange for the return or disposition of any of the remaining drug supply.

Record Keeping and Record Retention

1. The PI must maintain adequate records showing the receipt, shipment or other disposition of the study drug.
    a. Documentation will be done using either the sponsor-provided inventory logs, or forms equivalent to the attached Study Drug Inventory Log.
    b. For multi-site studies, these records must include the name of the investigator to whom the drug is shipped and date, quantity and batch or code mark of each such shipment as appropriate.
2. The PI is required to maintain adequate records of the disposition of the drug, including dates, quantity and use by subjects.
    a. Documentation will be done using either the sponsor-provided drug accountability logs, or forms equivalent to the attached Subject Drug Accountability record.
3. The PI is required to maintain the records documenting the storage conditions and chain of custody.
4. Investigators are required to prepare and maintain adequate case histories that record all observations and other data pertinent to the investigation on each individual administered the study drug or employed as a control in an investigation. Case histories include the case report forms and supporting data including, for example, the signed and dated consent forms and medical records including, progress notes of the physicians, the individual's hospital record and the nurses' notes. **The case history must document that consent was obtained prior to participation in the study.**
5. These records shall be retained in accordance with IRB approval and CU Record Retention Policy. FDA and other monitoring agencies may review these records at any time.

Disposition of unused supply of investigational drug

1. If the investigation is terminated, suspended, discontinued or completed, the PI or the person(s) who accepted the delegated duty of drug management shall dispose of all unused supply of drug(s) according to the approved IPMP. Any changes to the approved process must be reviewed and approved by the Investigational Product Review Committee (IPRC).

Forms associated with this guidance:

1. Delegation log
2. Training log
3. Study Drug Inventory Log
4. Subject Drug Accountability Log

Applicable Regulations and Guidelines

ICH GCP	E6 Good Clinical Practice: Section 5.12, 5.13, 5.14
21 CFR 312	312.57 (Record Keeping and Record Retention), 312.58 Inspection of Sponsor's Records and Reports), 312.59 Disposition of unused supply of Investigational Drug), 312.60 (General Responsibilities of Investigators), 312.61 (Control of the Investigational Drug), 312.62 (Investigator Recordkeeping and Record Retention)
UCD Human Research Protection Program	Investigator Responsibilities for the Protection of Human Subjects