This document provides guidance on investigational drug accountability for study drugs. Investigational new drug is defined as a drug or biological drug that is used in a clinical investigation. Investigational new drugs are referred to as “study drugs” in this guidance document.

1. Recordkeeping

1.1 The investigational pharmacist shall maintain adequate records related to the study drug. In addition to this section, subsequent sections identify specific record keeping responsibilities.

1.2 A study binder will be created for all investigational drug studies. The binder will include specific dispensing instructions, randomized log, drug accountability form, record of drug dispensing, drug invoice, drug return forms and labels, study protocol, IB or copy of package insert, copy of blank consent form and copy of current IRB approval notice.

1.3 Records must be accessible to the study investigator. Under certain circumstances, the clinical investigator may be masked to specific data in the records, for example, in a blinded study.

1.4 Upon request from any properly authorized officer or employee of FDA, at reasonable times, permit such officer or employee to have access to, and copy and verify any records or reports made by the investigator pursuant to 312.62

1.5 Records shall be maintained as required by applicable federal requirements and for a minimum of three years following study completion.

1.5.1 DHHS regulations require that, “…records relating to research which is conducted shall be retained for at least 3 years after completion of the research.” 45 CFR 46.1115(b)

1.5.2 For Investigational New Drug (IND) research, the FDA requires that sponsors and investigators retain “records and reports required by this part for 2 years after a marketing application is approved for the drug; or if an application is not approved for drug, until 2 years after shipment and delivery of the drug for investigational use is discontinued and the FDA so notified.”

1.5.3 For Investigational Device Exemption (IDE) research, the FDA requires the investigator or sponsor to maintain the records “for a period of 2 years after the latter of the following two dates: The date on which the investigation is terminated of completed, or the date that the records are no longer required for purposes of supporting a premarket approval application or a notice of completion of a product development protocol.”
1.5.4 For sponsored projects, online platforms and/or phone systems may be provided and used for drug accountability. The system must comply with 21 CFR 11 if it is to be considered equivalent to paper records. Secure access must be maintained and any PIN provided by the sponsor cannot be shared. If the PIN is compromised, the sponsor must take steps to secure access (e.g. reissue PI) and any such incidents are to be reported to the IRB via an Unanticipated Problem Involving Risks to Subjects or Others (UPIRSO) form for review.

2. Receipt and Inventory of Study Drug

The designated investigational pharmacist will:
2.1 Upon receipt of the investigational drug, inventory the shipment ensuring that the information on the packing slip matches exactly with what has been sent to the site, including the amount, lot numbers and quantity, and document the inventory.
2.2 Promptly bring any discrepancies, breakage or evidence of tampering to the attention of the study investigator who will report to the Sponsor.
2.3 Retain a copy of the shipping inventory, packing slips, and documentation of inventory in the study’s records.
2.4 If the investigational pharmacist is unavailable to accept delivery, a pharmacist / pharmacy employee accepts delivery, assures proper storage and drug accountability, or records the information for the investigational pharmacist to record inventory at later time on the drug log.
2.5 Any excursions from storage procedures must be reported to the study investigator who is responsible for reporting the information to the sponsor and possibly the IRB.

3. Study Drug Labeling

3.1 Study drugs for sponsored companies are pre-labeled and the labels are not to be defaced or changed without written permission of the sponsor; it is recommended that an additional label be placed to include the MSU study staff contact name/number, but only if the sponsor agrees.
3.2 Labeling may include a statement “For investigational use only.”
3.3 For investigational drugs subject to 21 CFR 312.6, all labeling requirements must be followed.
3.3.1 The immediate package must bear a label with the statement "Caution: New Drug--Limited by Federal (or United States) law to investigational use."
3.3.2 The label or labeling of an investigational new drug shall not bear any statement that is false or misleading in any particular and shall not represent that the investigational new drug is safe or effective for the purposes for which it is being investigated.

4. Storage of the Study Drug

4.1 Study drugs must be stored in a secure environment according to the storage requirements detailed in the protocol or supplied by the Sponsor.
4.2 The drugs must be kept locked in a locked secure area. The study drugs must be stored at the appropriate temperature and a storage area temperature log when applicable must be obtained and monitored.

4.3 The drugs must be accessible only to an absolute minimum number of specifically authorized people. The 1572 can determine who those individuals are to be.

4.4 Written procedures must be available describing the actions to be taken in the event of temperature excursions outside the labeled storage conditions. All excursions outside the labeled storage conditions must be appropriately investigated and reported to investigator the investigator and sponsor.

5. **Dispensing of Study Drug**

5.1 The investigational pharmacist shall dispense or administer the study drug only to subjects entered into the study, under the direction of the PI or to individuals authorized to receive or dispense it.

5.2 The study drugs will not be dispensed or supplied to any person not authorized to receive it. The pharmacy must have a mechanism to identify who is authorized to receive the drug and must verify when dispensing the drug.

5.3 Each time a study drug is dispensed; there must be documentation in the sponsor provided log as to the amount dispensed, to whom it is dispensed, and the date and signature or initials of the person dispensing the drug.

5.4 Subjects should be advised to follow the study protocol and as appropriate to protocol return all used and unused containers/units to the site of original dispensing if required.

5.5 Any discrepancies between the amounts used by the subjects and the amount returned should be documented.

6. **Return/Destruction of Study Drug**

6.1 Assure that unused supplies of the study drug are returned to the sponsor in accordance with sponsor requirements.

6.2 Obtain authorization from the sponsor if unused supplies of the study drug will be disposed of at the conclusion of the study and assure that the disposition does not expose humans to risks from the drugs.

6.3 Maintain records of the return or disposition of the unused study drug, including the unused study drug amount, lot numbers and quantity, method of return or disposition, and any documentation related to shipment or destruction.

6.4 At the conclusion of the study ensure that all documentation regarding receipt, storage, dispensing, return of used containers, and accountability is complete and accurate.

7. **Controlled Substance**

7.1 If the investigational drug is subject to the Controlled Substances Act, adequate precautions, including storage of the investigational drug in a securely locked, substantially constructed cabinet, or other securely locked, substantially constructed
enclosure, access to which is limited, must be taken to prevent theft or diversion of the substance into illegal channels of distribution.

7.2 If the drug is a controlled substance or subject to any other laws those additional requirements must be followed.

8. Training

8.1 The investigational pharmacist and any other individual authorized to handle the investigational product must be qualified through appropriate training and experience.

8.2 Individuals who are considered engaged in research and/or a clinical investigation with human subjects must also complete any relevant human subject research protection training. See HRPP Manual Section 11-1-A, Education: Investigators and Research Staff for specific requirements.