1. PURPOSE
   1. The purpose of this policy is to ensure that all investigational drugs, agents and/or biologics used in human participants research are stored, handled, and dispensed in compliance with regulations or requirements of the FDA, JCAHO, ASHP, Federal and State Boards of Pharmacy, other applicable organizations and in accordance with applicable hospital, medical center, and University policies and guidelines.
2. REVISIONS FROM PREVIOUS VERSION
   1. None
3. POLICY
   1. The Pharmacy and Therapeutics Committee or Pharmacy and Therapeutics IRB liaison and the IRB must approve the investigator’s written request to manage test article storage, integrity, and accountability.
   2. The investigator’s responsibility to work with the Investigational Drug Service to ensure that the planned receipt, storage, handling, dispensing and return or destruction of the Investigational Agent is in compliance with Institutional, State, Federal (FDA), and JCAHO requirements.
   3. Storage of investigational drugs and biologics:
      1. Investigational agents should be stored in the Investigational Drug Service. If this is not possible, these agents may be stored in areas other than the Investigational Drug Service under the direct supervision of the principal Investigator and in accordance with the sponsor, if applicable. The Investigational Drug Service should be aware of the alternative storage site. Pharmacy monitoring may be incorporated into the IRB auditing process to ensure compliance.
      2. Controlled substances must be stored in the Department of Pharmacy.
      3. Sponsor-investigator IND studies must use the Investigational Drug Service.
   4. Dispensing of investigational drugs and biologics:
      1. Investigational agents should be dispensed through the Investigational Drug Service. Justification for requesting to deviate from this standard should be provided. Investigational Drug Service.
      2. If the Investigational Drug Service is not used to dispense investigational drugs and biologics, the Principal Investigator must ensure that dispensing is in accordance with Investigational Drug Service Policy.
         1. “Dispensing” may only done by licensed pharmacists, dentists, podiatrists and physicians; all other activities carried out by other licensed professionals (e.g., RN) are considered “distribution.”
         2. An investigational agent is “distributed” when it is provided to a subject in a pre-labeled container with subject-specific identification and does not require any manipulation (i.e., counting, packaging, transfer to another container, mixing, preparing, compounding).
         3. “Distribution” of investigational drugs and biologics must be carried out upon the order of an authorized prescriber.
      3. The Investigational Drug Service must prepare and dispense the following drugs and biologics:
         1. Controlled substances for all inpatients and outpatients.
         2. Drugs and biologics prescribed for inpatient use.
         3. Drugs and biologics prescribed for administration in the General Clinical Research Center.
         4. Hazardous drugs and biologics.
         5. Drugs and biologics requiring sterile admixture preparation.
         6. Drugs and biologics requiring compounding or repackaging.
         7. Drugs and biologics with specific sponsor requirements for control by a pharmacy.
      4. If the Investigational Drug Service is not used, the investigator must dispense the drug or biologic only to subjects under their personal supervision or under the supervision of a co-investigator responsible to the investigator.
      5. The investigator may not supply the investigational drug or biologic to any person not authorized to receive it.
   5. Records necessary to document test article accountability and integrity must be maintained, which include:
      1. Shipping invoices;
      2. Inventory and condition upon receipt;
      3. Storage conditions and temperature logs;
      4. Preparation/compounding logs;
      5. Packaging and labeling;
      6. Dispensing and return logs; and
      7. Final inventory and disposition.
   6. The Investigational Drug Service (UMMS or VA)
      1. As part of its role in ensuring proper labeling, storage, distribution, and control of all investigational drugs and biologics, the Investigational Drug Service will be available to assist investigators.
      2. The Investigational Drug Service must review and approve all Investigational Drug Data Sheets for all investigational drugs and biologics intended for administration to hospital inpatients.
      3. The Investigational Drug Service signs-off on the electronic application to ensure participation and agreement.
      4. Except for single-patient treatment protocols approved by the IRB in urgent situations, the Investigational Drug Service must prepare written dispensing instructions (“Preparation Guidelines”) for each protocol to be followed by pharmacy staff when dispensing investigational drugs and biologics. These instructions explain subject enrollment, test article preparation, dispensing, accountability and disposition.
      5. The Investigational Drug Service must distinguish investigational drugs and biologics from other drugs or biologics by the additional legend, “Caution – New Drug, Limited by Federal Law to Investigational Use”, or its equivalent.
      6. The Investigational Drug Service or the investigator must return all unused or expired investigational drugs and biologics in accordance with the sponsor’s requirements.
         1. The final disposition of used drugs and biologics, and subject drug and biologic, returns (outpatient studies) should be handled in accordance with the sponsor’s policies and procedures. If the site is authorized by the sponsor for on-site destruction, such activities will be documented, when applicable.
         2. Appropriate procedures also apply to those sites storing drugs and biologics outside the Investigational Drug Service. Information about these procedures should be described in the protocol and are subject to audit by the Investigational Drug Service and HRPP.
      7. The Investigational Drug Service must review Investigational Agent usage (i.e., inventory stock) on a routine basis and order new supplies from the sponsor, on behalf of the Principal Investigator.
      8. The Pharmacy and Therapeutics Committee Chairman must appoint a Pharmacy and Therapeutics-IRB liaison. The Pharmacy and Therapeutics Committee and/or Pharmacy and Therapeutics-IRB liaison will review the use of all investigational drug and biologic uses prior to final approval by the IRB. The use of FDA approved, non-formulary medications require Pharmacy and Therapeutics Committee approval. Use of FDA approved, formulary medications with Pharmacy and Therapeutics Committee approved restrictions and/or guidelines, use of FDA approved, formulary medications for off-label indications, and use of non FDA approved medications require approval by the a Pharmacy and Therapeutics-IRB liaison. At any time the Pharmacy and Therapeutics-IRB liaison may request the formal review of the Pharmacy and Therapeutics Committee.
      9. The Pharmacy and Therapeutics-IRB liaison must inform the Pharmacy and Therapeutics Committee about Investigational Agent use periodically at regularly scheduled meetings.
         1. The Assistant Director of Pharmacy Services, in conjunction with the Investigational Drug Service Coordinators/Pharmacists supplies the Pharmacy and Therapeutics Committee, Hospital Administration, and the Vice Dean for Research and Academic Affairs with an annual summary of Investigational Agent use, including but not limited to the number of research studies in progress, a listing of all drugs and biologics studied during the previous year and a summary of adverse experiences that lead to suspension or termination.
      10. All inpatient and outpatient research protocols involving investigational drugs and biologics, including radioactive agents used therapeutically or diagnostically, will receive review by the Investigational Drug Service representative for the assigned IRB panel. The Investigational Drug Service representative’s review for appropriateness will include an assessment of the source, purity, quality, method of preparation, and delivery. The nuclear pharmacist will be consulted on radioactive investigational drugs and biologics.
      11. The Investigational Drug Service will be responsible for implementing and monitoring the effectiveness of this policy for investigational drugs and biologics administered to subjects.
      12. Operational effectiveness may be periodically monitored by the Quality Improvement Team. The Quality Improvement Specialist will have access to documents pertaining to protocols reviewed by the Pharmacy and Therapeutics Committee.
      13. The IRB Pharmacy representative will have access to all relevant protocols within CICERO, provide a review of the proposed storage/dispensing plan for each study being reviewed, and alert the IRB to any specific concerns regarding special handling, preparation, or any other issues related to risk/benefit.
   7. The HRPO or the Investigational Drug Service must investigate potential mishandling of investigational drugs and biologics and promptly report findings to the IRB as required by the Reportable New Information submission form in CICERO[[1]](#footnote-1) Mishandling may include, but is not limited to, improper storage, dispensing, compounding, or distribution.
   8. Investigators conducting investigational drug and biologic research at the VAMHCS must follow applicable VA policies and procedures.
   9. Devices
      1. The Principal Investigator is responsible for the storage, dispensing, tracking and oversight of FDA-regulated devices in research in accordance with applicable institutional and Federal laws and regulations and in accordance with the instructions of the sponsor to the extent consistent with laws and regulations and institutional policies.
      2. The investigator must meet the following requirements in order to use an investigational device in research conducted under the jurisdiction of the UMB IRB:
         1. The investigational device must be used only by the Principal Investigator or under his/her direct supervision;
         2. The investigational device must be used only as approved by the FDA and as described in the currently approved IRB documents;
         3. The Principal Investigator must not supply the investigational device to any persons not authorized under the IDE;
         4. The Principal Investigator is responsible for the accountability, storage, dispensing, tracking, and oversight of the FDA-regulated devices in accordance with applicable institutional and Federal laws and regulations and for submitting a plan to the IRB for review and approval.
         5. The investigator is responsible to determine what institutional policies apply to the use of FDA-regulated devices and will adopt procedures to comply with those policies.
         6. If institutional policies do not provide for storage, dispensing, tracking and oversight of the device use, the investigator must establish procedures adequate for the study.
   10. Control and Distribution of Devices used in Research.
       1. Receipt and inventory of study device. This section applies to those study devices the investigator dispenses/administers to the study subject. The investigator is responsible for ensuring the following:
          1. Upon receipt of the study device, the shipment is inventoried by reviewing and documenting the type and quantity of device, the dates of receipt, and the batch number or code mark, and ensuring that the information on the packing slip matches what has been sent to the site, including the quantity and lot numbers.
          2. All discrepancies are promptly brought to the attention of the sponsor and/or supplier of the device(s).
          3. A copy of the shipping inventory, packing slips, and documentation of inventory are retained in the study files.
          4. An accountability log containing the names of all persons who received, used, or disposed each device is maintained.
       2. Study device labeling. The investigator is responsible for ensuring the following:
          1. Study devices from sponsor companies are pre-labeled. They should not be defaced, relabeled, or changed in any way without written permission of the sponsor. It is recommended that an additional label is included containing the study staff contact name and/or number, but only if the sponsor agrees.
          2. If the investigator is responsible for device labeling, the investigator should be aware of applicable FDA regulations. Examples of the information to appear on a label are: name of device, model number, serial number, and manufacturer.
          3. When a study device is designated as “Investigational” per FDA regulations, there should be a label with the following information:
             1. Name and place of business of the manufacturer, packer, or distributor.
             2. Quantity of contents if appropriate, and the following statement: “CAUTION- Investigational device. Limited by Federal (or United States) law to investigational use.”
          4. The label or other labeling shall describe all relevant contraindications, hazards, adverse effects, interfering substances, or devices, warnings, and precautions.
       3. Storage of the study device including devices that record data from automated instruments. The Principal Investigator must:
          1. Establish and maintain access controls for essential and appropriate research personnel;
          2. Develop procedures for verifying physical access;
          3. Store the study device in a secure environment to include locks on doors and controlled access;
          4. Establish equipment control both into and out of the research site;
          5. Develop Security Incident Procedures to report any privacy breaches;
          6. Assess any privacy risks anticipated and develop methods to avoid those risks;
          7. Develop data backup, storage, and emergency mode procedures, if applicable; and
          8. Store the study device at the appropriate temperature, and maintain a storage and temperature log, if appropriate.
       4. Dispensing of study device. The Principal Investigator is responsible for creating an access log to document each time the study device is dispensed/used, where it is dispensed/used, to whom it is dispensed/used, and the date and signature or initials of the person dispensing/using.
       5. Return/destruction of study device (as applicable to the specific device). The Principal Investigator is responsible for ensuring the following occurs in a timely manner:
          1. All documentation regarding receipt, storage, dispensing, return of used containers, and accountability is complete and accurate at the conclusion or termination of the study.
          2. Devices obtained from a sponsor for the specific purpose of a research study must be returned to the sponsor, with the reason why and the number of devices indicated.
             1. The same information must be detailed for devices that are repaired or otherwise disposed of.
             2. Only with the written authorization (i.e., in the protocol or other written correspondence) of the sponsor, and in compliance with Federal regulations and Institutional policies, may the investigator discard the device on site, or retain the device.
          3. Unused study devices that include individually identifiable health information must not be passed on to other investigators without IRB approval and an authorization from the study subject.
          4. Unused study devices without individually identifiable health information must not be passed on to other investigators, used for animal research, or dispensed to non-study patients unless written consent is obtained from the Sponsor/Provider of the device.
          5. Device study records must be kept for a period of two years after the latter of the two following dates:
             1. The date on which the investigation is terminated or completed; or
             2. The date that for the purposes of supporting a premarket approval application or a notice of completion of a product development protocol.
       6. Record retention. An investigator or sponsor may withdraw from the responsibility to maintain records for the period required above.
          1. The investigator may transfer custody of the records to any other person who will accept responsibility for them under 21 CFR 812.140, including the requirements of 21 CFR 812.145.
          2. Notice of a transfer shall be given to the FDA not later than ten working days after the transfer occurs.
       7. Research on FDA approved devices for FDA approved indications. The Principal Investigator is responsible for ensuring:
          1. Receipt, storage, dispensing, and return of the device is documented.
          2. The FDA approved label is adequate.
4. RESPONSIBILITIES
   1. The investigator and Investigational Drug Service are responsible for complying with this policy.
5. PROCEDURE
   1. None
6. MATERIALS
   1. CICERO
   2. CICERO FORM: Reportable New Information
7. REFERENCES
   1. None

1. This is CICERO FORM: Reportable New Information [↑](#footnote-ref-1)