I. **Procedure Statement**

To describe the procedures for managing investigational products and devices in clinical trials, including receipt, storage, dispensing, administration and accountability after approval of the product has been secured by MU Health.

II. **Definitions**

1. **Biologic**: Biological products include a wide range of products such as vaccines, blood and blood components, allergenics, somatic cells, gene therapy, tissues, and recombinant therapeutic proteins.

2. **Combination Product**: Combination products include: (1) A product comprised of two or more regulated components, i.e., drug/device, biologic/device, drug/biologic, or drug/device/biologic, that are physically, chemically, or otherwise combined or mixed and produced as a single entity, (2) Two or more separate products packaged together in a single package or as a unit and comprised of drug and device products, device and biological products, or biological and drug products, (3) A drug, device, or biological product packaged separately that according to its investigational plan or proposed labeling is intended for use only with an approved individually specified drug, device, or biological product where both are required to achieve the intended use, indication, or effect and where upon approval of the proposed product the labeling of the approved product would need to be changed, e.g., to reflect a change in intended use, dosage form, strength, route of administration, or significant change in dose, or (4) Any investigational drug, device, or biological product packaged separately that according to its proposed labeling is for use only with another individually specified investigational drug, device, or biological product where both are required to achieve the intended use, indication, or effect.

3. **Investigational Device (ID)** is a device, including a transitional device which is the object of an investigation.

4. **Investigational Product (IP)** is a pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorization when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use.
5. Investigational New Drug Application (IND) is a request for authorization from the Food and Drug Administration (FDA) to administer an investigational drug or biological product to humans.

6. Investigational device exemption (IDE) allows the investigational device to be used in a clinical study in order to collect safety and effectiveness data.

III. Procedure/Content/Scope

This SOP will apply to all clinical trials research within MU Health including the School of Medicine, School of Health Professions, School of Nursing, and MU Healthcare. This SOP will cover the processes and procedures to follow with respect to investigational products including drugs, biologics, vaccines, devices, and combination products. The investigator should ensure that the IP or ID is used only in accordance with the approved protocol. Depending on the respective sponsor’s policy, an IP may include study-specific concurrent medication/treatment such as the comparator drug/placebo and rescue medication.

1. Responsibility:
   a. The Principal Investigator is responsible and accountable for the following:
      i. Storage
      ii. Distribution
      iii. Inventory
      iv. Documentation
   b. The Principal Investigator may delegate responsibility, yet not accountability, to qualified study personnel to performing the following relative to IPs:
      i. Inventory
      ii. Storage
      iii. Dispense
      iv. Return/repair/destruction of IP or ID
      v. Documentation
   b. Prior to the start of the study, the principal investigator or his/her delegate should ensure appropriate FDA notification/approval/clearance of the IP has been received for the applicable study activity.
   c. Specific to device studies: prior to the start of the study, the Principal Investigator shall ensure that the ID has been approved for research use by the MU Value Analysis Team (VAT).

2. Receipt of IP/ID into the research unit:
   a. The Principal Investigator or his/her delegate shall do the following:
      i. While determining feasibility: perform a final check on the required IP or ID storage conditions to ensure the IP or ID can be stored as per requirements set forth by the sponsor/or as designated by the protocol.
Title: Core Standard Operating Procedure for Investigational Products and Devices

ii. Seek confirmation from the sponsor /clinical research organization (CRO) regarding the anticipated date of the IP or ID delivery and the quantity of the IP or ID to be delivered.

iii. Once the IP or ID is delivered, the designated study site staff should check for any inconsistencies in the shape, form and appearance of the IP or ID, the environment that the IP or ID is stored in upon delivery, and the total quantity of the IP or ID that have been delivered.

iv. Upon delivery of the IP or ID, sign the receipt slip/delivery notice and send to the sponsor/CRO.

v. File all shipping records and/or signed receipt slips/delivery notices in the investigator site file.

vi. Update the quantity on protocol specific drug accountability log.

3. Storage of IP/ID within the research unit:
   a. The Principal Investigator or his/her delegate shall do the following:
      i. Ensure the IP or ID is stored immediately according to the conditions stated in the protocol and that the location is secure and limited to research personnel, or:
         1. Ensure the storage premises shall be in an area that is designated for IP or ID only and should not be stored with non-clinical trial medications, biologics, or devices. The premises should be secured with limited access.
      ii. Record the storage temperature once every working day on a temperature log.
      iii. Ensure the randomization code has been received, and properly documented, if applicable.
      iv. Store unused IP or ID for return to the sponsor/CRO.
      v. Store in a secure location, separate from active inventory.
      vi. When discrepancies or violations of the storage condition are detected, report such problems to the sponsor/CRO.

4. Dispensing/administration of IP or ID:
   a. The Principal Investigator or his/her delegate shall do the following:
      i. Review sponsor or CRO provided SOPs/procedures regarding protocol requirements for dispensing/administering applicable IP or ID.
      ii. Follow protocol requirements regarding IP and medication administration. When protocol specifically allows, abide by hospital-specific procedures for medication administration.
      iii. For randomized studies, follow the study randomization procedures in allocating the assigned IP or ID to the trial subject.
      iv. Investigator or designated research staff will check the expiration date prior to use or dispensation of the IP or ID.
      v. Follow sponsor/protocol-defined procedures to track identifiers for the IP or ID in blinded studies. Ensure each subject received the correct IP or ID and document the expiration date.
vi. For open-label studies, dispense the correct IP or ID and/or the correct dosage to each subject and document the expiration date.

vii. When administering intravenous IP, arrange for proper facility location/room ahead of time.

viii. For self-administered IP or ID, provide instructions to the subject on how to use the IP or ID.

ix. Give the subject instructions of how to complete a diary, if applicable.

x. Instruct the subject to return any unused or remaining IP at the next visit or in accordance with protocol.

xi. Count the IP when the subject returns unused or remaining IP.

xii. Document all IP dispense/administration and return activity on the protocol specific drug accountability log, which shall include as applicable, yet is not limited to:

1. Subject and IP identifier,
2. batch number,
3. date and time of IP preparation,
4. expiration date(s),
5. quantities dispensed/administered, returned and/or destroyed,
6. administration start times and completion times,
7. initials or signature of the qualified study personnel member who performed the specific activity

xiii. Report to the sponsor any IP or ID discrepancies, abnormalities or defects.

xiv. Follow MU’s unanticipated problems procedures for adverse events/protocol deviations related to IP or ID.

5. Request for IP or ID resupply:
   a. The Principal Investigator or his/her delegate shall do the following:
      i. Routinely monitor products that are not automatically resupplied for adequate availability of on-site IP or ID.
      ii. Ensure expiration dates are noted and monitored on a regular basis.
      iii. When resupplies are needed, make a request to the sponsor per sponsor’s resupply instructions
      iv. After resupply arrives, follow receipt of IP or ID procedures outlined above

6. Return/Reconciliation of IP or ID:
   a. The Principal Investigator or his/her delegate shall do the following:
      i. Ensure that the reconciliation process has been discussed and agreed upon with the sponsor.
      ii. Ensure the accountability has been checked by the study monitor before reconciliation of the IP or ID.
      iii. Follow the study standard operating procedures for returning the IP or ID to the sponsor or local destruction of IP or ID, if protocol specified.
      iv. For the return of IP or ID to the sponsor, document the following on the trial specific reconciliation log:
Title: Core Standard Operating Procedure for Investigational Products and Devices

i. Description of what was returned  
ii. Quantity  
iii. Date/time of transfer of the IP or ID to the sponsor’s designated personnel (as applicable)  
iv. Initial or signature and date of qualified study personnel coordinating the transfer  
v. Keep and file shipping documentation (as applicable)  

v. For disposal/destruction of IP or ID locally, document the following on the trial specific reconciliation log:  
i. Specific IP or ID disposed/destroyed  
ii. Quantity  
iii. Date/time of transfer of the IP or ID to the disposal/destruction company  
iv. Initial or signature and date of the qualified study personnel coordinating the transfer  

vi. For an IP or ID to be disposed/deestroyed locally, the study site staff should comply with all applicable local laws and regulations. The following information on local disposal/destruction of an IP should be recorded on a reconciliation of IP log:  
i. The IP or ID disposed/destroyed (use IP or ID identifier if applicable;)  
ii. The quantity of the IP or ID disposed/destroyed;  
iii. The date and time of transfer of the IP or ID to the disposal/destruction company; and  
iv. The initial/signature and date of the study site staff responsible for the transfer.  

vii. The study team may liaise with the sponsor for arrangements of retrieval of the used IP(s) by the study monitor or local destruction of the IP(s) when the storage facility is full.  

viii. The reconciliation of IP log(s) should be regularly maintained and updated in the investigator site file.  

IV. REFERENCES:  

1. MU Health policies related to Investigational Device Exemptions and VAT.  
3. Combination Products: http://www.fda.gov/combinationproducts/aboutcombinationproducts/ucm118332.htm  
4. IND:http://www.fda.gov/biologicsbloodvaccines/developmentapprovalprocess/investigationalnewdrugindordeviceexemptionideprocess/default.htm  