POLICIES AND PROCEDURES MANUAL

Section: MISCELLANEOUS ORGIZNATIONAL FUNCTIONS (MI)
Subject: Investigational Devices
Number: MI29

Attachments:
- Attachment 1 Definitions
- Attachment 2 Acronyms
- Attachment 3 Shelf/Container Labels
- Attachment 4 Individual Device Labels

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Investigational Devices

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POLICY
It is the policy of The Nebraska Medical Center (TNMC), the University of Nebraska Medical Center (UNMC), and Bellevue Medical Center (BMC) to effectively manage and control the receipt, storage, dispensation, and return of investigational devices pursuant to federal regulations, contractual obligations, and business controls, to ensure the integrity of research practices and the safety of our patients.

This policy applies to any device, investigational or not, that has been submitted to the IRB in an application for review and approval and that meets one or more of the following criteria:
- has not been approved by the Food and Drug Administration (FDA),
- has been approved by the FDA but is being used for purposes other than those stipulated by the FDA,
- is a commercially marketed device, but is being used in a trial for research purposes,
- is being used for Humanitarian purposes [as a Humanitarian Use Device (HUD)],
- has received a Humanitarian Device Exemption (HDE),
- has received an Investigational Device Exemption (IDE),
- has received a Compassionate Use (CU) designation,
- has received an In-Vitro Diagnostic (IVD) designation or,
- has been approved for distribution and use; but, data must continue to be collected for submission to the FDA.

PURPOSE
To assure regulatory and operational compliance in efficient management and security of receiving, storing, dispensing, returning/destroying, and billing of investigational devices.

PROCEDURE – SIGNIFICANT RISK DEVICES
The procedures below are divided into seven (7) sections:
A. Overview

1. Prior to the use of any device(s) submitted to IRB on an application for review and approval, the Principal Investigator (PI) or Primary Physician (for IDE/IVD/HDE/CU) must receive confirmation of:
   • approval by the Institutional Review Board (IRB),
   • execution of a Clinical Trial Agreement (CTA), if applicable,
   • assignment of a billing account number (WBS# / CC#) for charges, when appropriate,
   • review and approval by the Investigational Device Review Committee (IDRC), and
   • documentation of Medicare billing determination (Medicare Parts A&B) for IDE Devices by the Device Manufacturer and Study is listed on the CMS.gov IDE approval website [https://www.cms.gov/Medicare/Coverage/IDE/Approved-IDE-Studies.html]

2. Study Personnel must use a consistent process for receipt and distribution of the devices submitted to IRB on an application for review and approval designated for use in a clinical trial or research. The process must include a communication component allowing for the efficient and timely notification to:
   • The clinical area(s) affected regarding plans for the study and the need for an investigational device inventory,
   • The clinical area where the procedure, for a patient who needs to use the investigational device, is being scheduled (i.e., area where the device will be surgically implanted or used during a procedure)
   • The clinical departments providing personnel involved in the procedure/testing, for a patient who needs to use the investigational device, (i.e. radiology, respiratory therapy, perfusion, etc.)
   • The PI, stating that the devices have been received and are available for use, and
   • The Compliance Sr Analyst (CSA), Compliance for central compliance coordination and oversight.

3. The Ancillary departments must maintain documentation of the specific use of each device by individual study subjects consistent with federal regulations, contractual requirements, and hospital policies.

4. The PI / designee is responsible for:
   • documenting the return of the unused investigational devices to the sponsor, or
   • destruction of the investigational device, with written authorization from the sponsor at the completion of the clinical trial, research, or IDE/IVD/HDE/CU project.

5. All records tracking the investigational devices must be maintained with the inventory and must fully account for the distribution and use of each device.

B. Administrative Procedures

1. IRB submission and approval
   • The PI must submit an application and receive written approval from the UNMC/TNMC IRB for any clinical trial or research involving an investigational device.
   • Once the PI receives written approval from the UNMC/TNMC IRB, They must notify any clinical department(s) involved in the trial prior to any clinical activity related to the trial or any use of the investigational device(s).

2. Sponsor budget finalized
   • The cost of using the device will be negotiated, by PI / designee.
   • When negotiating provision of the device, preferred options are:
     a) Sponsor provides devices at no cost, or
     b) Sponsor ships devices on consignment.
     c) Exceptions considered on a case by case basis.
   • If the device and/or consumables must be purchased, the purchase agreement shall be reviewed by Nebraska Medicine Purchasing, Resource Control and ancillary department(s), if applicable.
   • If Nebraska Medicine is required to purchase the device or cover any of the cost related to the trial, prior approval by the Investigational Device Review Committee (IDRC) and appropriate TNMC authorization is required in writing prior to finalization of the clinical trial agreement.
3. Contract, with attached study budget, completion
   - The PI / designee must provide a negotiated study budget
   - The PI must verify contract execution with Contract Specialist
   - The IRB will not approve the study start without a signed contract

4. Account Set up
   - Prior to the study’s start date, the PI / designee must verify that a funding account(s) has been established to facilitate accurate research billing for the study.
   - NM Departments that may assign account numbers to support the study are:
     a) NM Grant accounting (contact Sr. Grant Accountant)
     The number must be provided to the Sr. Grant Analyst for entry into Workday grant module
   - UNMC Departments that may assign account numbers to support the study are:
     a) UNMC Sponsored Programs Administration who will assign WBS number for Sponsor supplied funding, and/or
     b) Department Administrator who will establish a cost center (CC#) for departmental funding approved and provided to support the study, and/or
     c) The Director of Clinical Operations who administers the funding awarded by the Clinical Translational Research (CTR) Support Fund. The number assigned will be an MHX account number.
     The number(s) must be provided to the Clinical Research Manager in the Clinical Research Center to be entered into the Clinical Trials Management System (CTMS) application and/or entered on the Clinical Trial Master Matrix (CTMM) page in the Automated Matrix workbook to facilitate appropriate and compliant billing

5. Medicare review and decision documentation (IDEs only)
   - The PI / designee must complete the “Medicare Qualification – Device” page in the Automated Matrix Workbook and forward to the CSA, Compliance, for completion of the CMS Billing Determination Request packet
   - The PI / designee must provide documentation to the CSA, Compliance as requested. Documentation may include, but is not limited to:
     a) FDA device approvals, or limited use approvals (un-redacted)
     b) 2-3 supporting peer reviewed articles
     c) Sponsor Protocol
     d) Investigators Brochure
     e) A copy of the CMS approval letter, if applicable
   - Prior to clinical activity, the CSA, Compliance must verify approval from the Medicare Administrative Contractor (MAC) Medical Director to avoid rejection of claims
   - Upon receipt of response documentation, the CSA, Compliance will:
     a) Compare the determination to the Protocol and the informed consent to ensure that the documentation accurately reflects the billing determination
     b) Distribute copies of determination letter(s) (Parts A&B) to:
       ▪ Nebraska Medicine compliance / Billing Departments
       ▪ UNMC/TNMC IRB and
       ▪ place a copy of the correspondence on the NHSsecure drive in the Clinical Trials Folders/Physician’s sub-folder

6. The Protocol must be reviewed by the Investigational Device Review Committee (IDRC). The IDRC is an ad hoc review committee comprised of representatives from UNMC, Nebraska Medicine, Bellevue Medical Center, and ancillary department(s) that provide the services to review the study requirements. The protocol is reviewed by the CSA to determine whether an abbreviated review (AR) or a Full Board review (FB) process will be required and initiate the process required by the committee.
   - The PI or designee must provide the following information:
     a) General study overview
     b) Specific services requested
     c) Cost, if any, to the ancillary department, along with the availability of grant funding to cover those costs
d) Logistical considerations, including inventory of device(s), confirmation of billing account number(s), services that are considered investigational, impact on workload when adding research patients to conventional care patient workload.

The PI or designee must contact the Biomedical Instrumentation Department regarding all electrical devices powered by either external (facility’s power supply) or internal (battery) sources prior to first use of the devices on ensure that the use of the device is consistent with existing standards.

- If the device involves laser therapy, the PI must obtain written approval from the Laser Safety Officer for the use of the device.
- If the device will be used for diagnostic / therapeutic radiation or involves the use of radioactive pharmaceuticals, the PI must obtain approval from the Radiation Safety Subcommittee for the use of the device.
- Devices to be used for patient care must be handled consistently with policy for cleaning, disinfection, and sterilization of patient care items. Hospital Department of Infection Control & Epidemiology can be consulted for assistance in evaluating proper cleaning and disinfection/sterilization.
- The PI must notify the CSA when prerequisites are completed and approval is granted to proceed with the trial in the ancillary department(s) including necessary approvals for use of the device in clinical areas from Biomedical Engineering, Radiation Safety, Laser Safety, and Infection Control & Epidemiology, etc. as appropriate.

C. Device Receipt

1. Investigational Devices are ordered or received from the Sponsor, as determined by the Sponsor and the research protocol.

*Note: Devices shall not be taken from hospital/clinic stock for research purposes (exceptions require written authorization prior to dispense and use).*

- The PI must request Sponsor notification of shipment of investigational devices.
- Upon receipt of the investigational device shipment, inventory the shipment to ensure the information on the packing slips match exactly what has been received by the site.
- Promptly notify Sponsor of any discrepancies identified
- If Sponsor includes a separate “acknowledgement of receipt” form in the shipment:
  a) obtain the appropriate signatures and date
  b) copy form and packaging slips for study records, and
  d) forward the original form to the Sponsor / CRO.
- If the Sponsor does not provide “acknowledgement of receipt” forms, the packaging slip should be signed and dated with the date of receipt at the site. Packaging slips should be filed in the study records and if requested, a copy may be faxed to the sponsor.
- Devices must be tagged, individually, with a tag [attachment 4] to indicate investigational status.
- Ensure any supplies required for the blinding of the investigational device are available, if appropriate.
- Ensure the randomization code has been received, if appropriate.

2. Receiving dock personnel will generate a purchase order (PO) to document the receipt and distribution of investigational devices to the appropriate department.

3. The PI is responsible for notifying the clinical department(s) of any device(s) not directly received by the receiving dock personnel. Additionally, the PI is responsible for all documentation required by the Sponsor. Required information includes, but is not limited to, the following items:

- Sponsor name
- Study/Protocol Title
- PI Name
- Type of Device received
- Quantity received
- Date of Receipt
- Batch number or code mark of each individual device (unique identifier for each device)
- Name of personnel receiving device(s) (associated with the unique identifier of the device)
- Implantation date
D. Device Storage
1. All devices shall be stored in the appropriate ancillary department in a secure, centralized location with limited access, separate from other devices. The storage container should be clearly labeled as containing an investigational device (Tagged) [attachment 3]. Off-site storage is prohibited.
2. Store the devices according to the storage requirements detailed in the protocol or supplied by the sponsor in a supplementary document. If climate control is required, ensure the investigational device is stored at the appropriate temperature and temperature checks are documented in a storage area temperature log.

Note: If special storage parameters are required (i.e., climate controlled or special storage containers), it is preferred that the sponsor provide the storage vessel/container that meets the specified parameters.

4. At all times, each department must maintain a perpetual inventory log of stored devices by study.
5. Investigational devices should generally not be received on site, nor should they be stored in patient care areas, prior to IRB approval for the study.

E. Device Use / Dispensing
1. Ensure that all key research personnel involved in investigational device accountability are:
   • Appropriately listed on the “Delegation of Authority Log” in the study documentation
   • Listed on the IRB application
   • Performing activities appropriate to their job categories and licensures. For example, a Research Nurse Clinician may distribute an investigational device while a Research Assistant may not.
2. The ancillary department will record the use/dispensing of each investigational device. The record shall include the following information, as appropriate, (Sponsors may require additional information)
   • Date device dispensed
   • Time (if appropriate)
   • Quantity used
   • Device serial number (S/N), if applicable
   • Verify that the Investigational device is within the appropriate expiration date, if appropriate
   • Name of person (printed and Signature) using device (i.e., implanting, applying, etc.)
   • Subject number / initials of research subject recipient of device

Note: The PI will be ultimately responsible for obtaining the legally effective informed consent of the research subject's/Legal Authorized Representative (LAR) which is documented on an IRB approved informed consent form (ICF).

   • Verify and document quantity of investigational device(s) returned to storage, if appropriate.
3. PI / designee is responsible for ensuring accurate inventory and notifying study monitor or Sponsor when additional inventory is needed.
4. PI / designee is responsible for informing Sponsor and IRB if emergency breaking of the investigational device blind is medically necessary. PI / designee will follow the procedures outlined in the protocol and document all circumstances appropriately.

F. Device Return / Destruction
1. The ancillary department and the PI / designee are jointly responsible for returning all unused devices to the Sponsor upon the completion of the clinical trial, unless the Sponsor authorizes otherwise.
2. Investigational devices are returned at the Sponsor’s expense, unless otherwise stipulated in the CTA.
3. When returning any investigational devices, the PI/designee will include documentation with the device shipment, as appropriate. The documentation will include, but is not limited to, the following information:
   • Sponsor Name
   • Study / Protocol Name
   • PI Name
   • Type of device received
   • Date received
   • Batch number, unique identifier, or code mark of each individual device
   • Date of return
   • Name of person returning device (printed and Signature)
• Return Goods Authorization (RGA) number

4. The PI / designee is responsible for tracking all information necessary to report back to the Sponsor related to the Investigational device(s). This may be accomplished by separately recording all necessary information or obtaining copies of the ancillary department’s inventory logs. The Ancillary department also will need to make this information available for Resource Control, if necessary, to make arrangements for the return of unused devices.

5. If the Investigational devices have been designated for destruction in lieu of return shipment (in writing by Sponsor) the PI / designee may destroy the devices as designated by Sponsor and in accordance with Occupational Safety and Health Administration (OSHA) requirements. Destruction of investigational devices should be documented and verified by two qualified personnel (Key study personnel / Biomedical Instrumentation personnel). Documentation should be retained in the study record and a copy sent to the Sponsor.

G. Device Billing

1. Devices provided by sponsor at no charge shall be provided to study participants at no charge.

2. Devices provided on consignment or purchased for use in a study will follow the billing requirements for claim submission as outlined in the “Medicare Claims Processing Manual 100-04”, Chapter 32, sections 68 and 69.

REGULATIONS AND GUIDELINES

21 CFR 50.23(e) Exceptions from General Requirement
21 CFR 812 Investigational Device Exemptions (IDE)
21 CFR 814 Premarket Approval of Medical Devices
21 CFR Part 820 Quality Systems Regulations
21 CFR 820.30 Subpart C – Design Controls of the Quality System Regulation
21 CFR 892 Radiological Devices

FDA Guidance on IDE Policy and Procedures
FDA Guidance for HDE Holders, Institutional Review Boards (IRBs), Clinical Investigators, and FDA Staff – Humanitarian Device Exemption (HDE) Regulation: Questions and Answers

Medicare Claims Processing Manual 100-04, Chapter 32 sections 68 and 69

REFERENCES – PARTNER POLICY / PROCEDURES

Nebraska Medicine
EC01 Medical Equipment
EC02 Non-Hospital Owned Medical Equipment
EC03 Electrical and Electronic Safety
EC44 Reporting Medical Device Malfunction
FN18 Contracting Management Policy
FN22 Consignment Inventory
FN23 UNMC & UNMC-P Contract Management
MI06 Vendor Policy
MI19 Research Billing Process
MP-ME05 Medical Equipment Management Plan
CSA-004 SOP - Investigational Device Exemptions (IDE) – Identification, Notification, and Special Requests

UNMC
8008 Clinical Trial Professional and Technical Fee Billing Policy
Clinical Trial Professional and Technical Fee Billing Procedures

IRB Policies
Section 6: FDA Regulated Research/Drugs & Devices
6.2 Research Involving Investigational and Marketed Devices
6.3 Humanitarian Use Device (HUD)
6.4 Emergency Use of a Test Article
**STAFF ACCOUNTABILITY**

IRB Executive Chair, Assistant Vice Chancellor for Regulatory Affairs (05/27/2014, 12/30/2020)
Associate Vice Chancellor for Clinical Research, Institutional Official (05/23/2014, 12/30/2020)
Director, Business Operations (05/27/2014, 12/30/2020)
Director, Sponsored Programs Administration (05/27/2014, 12/30/2020)
Manager, Clinical Research Center (05/27/2014, 12/30/2020)
Director, Compliance, Accreditation & Regulatory Services (05/23/2014, 12/30/2020)

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| Signed | s |: G. L. Videtich       | Signed | s |: Christopher J. Kratochvil, M.D.  
| Title: Compliance Sr. Analyst | Assistant Vice Chancellor for Regulatory Affairs, Institutional Official; Associate Vice Chancellor for Clinical Research and Vice President of Research  
| Department: Compliance | Title: Research |