NIDCR PHARMACY GUIDELINES AND INSTRUCTIONS FOR NIDCR-SPONSORED CLINICAL TRIALS

INTRODUCTION

The National Institute of Dental and Craniofacial Research (NIDCR) at the National Institutes of Health (NIH) is responsible for ensuring compliance with domestic and international quality standards governing the receipt, use, storage, and disposition of study products in NIDCR-sponsored trials. NIDCR must not only ensure that clinical sites are proceeding in accordance with the International Conference on Harmonization (ICH) guidelines and all other applicable standards, but that investigators establish and maintain records clearly documenting accountability of study product. The following guidance helps the sponsor/Principal Investigator to manage appropriate handling of study products and to comply with applicable state and federal regulations and institutional policies and procedures.

INVENTORY CONTROL AND MANAGEMENT

The Investigator or designated individual is responsible for ordering, receiving, tracking inventory, dispensing, and returning study products properly, and, where necessary, for labeling of study product according to protocol guidelines prior to dispensing.

- The ordering of study products from the supplier, distributor or manufacturer may be conducted by the Investigator, study coordinator, or research pharmacist.
- Arrangements must be made between the product supplier and the study site to determine the most appropriate time and place for study product delivery.
- Upon receipt of study product, the Investigator or designee must ensure that the information on the packing slip matches the study product received.
- At a minimum, the recipient should verify the following:
    a) Product identification
    b) Amount of product received
    c) Lot numbers
    d) Expiration dates
    e) Physical product is in good condition
    f) Maintenance of proper storage conditions
- Evidence of breakage, compromised storage, or product tampering should be reported to the supplier immediately. The study product should be quarantined and maintained under the correct storage conditions until further instructions are given.

- Copies of shipping inventories and packing slips are to be maintained along with other study records.
- Study products should not be dispensed until they are properly inventoried and the quality is verified.

INVENTORY AND ACCOUNTABILITY

- All study products supplied for a protocol must be accounted for and tracked in a manual or electronic accountability log. Accountability of the study product must be documented from the time of initial receipt, through dispensation and final disposal of study product. The accountability log should indicate the amounts received from the supplier.
- Each time a study product is dispensed to a subject, the occurrence should be documented in the accountability log. The accountability log should indicate the amounts dispensed to the subject and returned/destroyed/disposed per the protocol. A balance of remaining study product should be documented on the log.
- Quality assurance and accountability may be performed each time a study product is dispensed.
- Prior to dispensing study product to a subject, enrollment must be confirmed.

STUDY PRODUCT TRANSPORT AND DELIVERY

- Study products that have been shipped for a protocol must be packaged in containers that maintain the proper storage conditions during transport, as per the protocol.
- Chain of custody documentation should be maintained for the transport, handling, and receipt of study products, as per the protocol.

ENVIRONMENTAL CONTROL

- Proper storage conditions should address the temperature, light, moisture, ventilation, and sanitation needs of the study product, as per the protocol.
- Where appropriate, proper environmental control should address maintenance of conditions such as temperature and light control from the pharmacy to the dispensing area.
- If storage conditions have been compromised (i.e., temperature excursions from the allowable range), or if there is any suspicion that the study product has not been stored properly:
    a) Quarantine study product.

b) Maintain the study product under the correct storage conditions until further notice.

c) Contact the Investigator immediately, providing the protocol number, the protocol name, description of the degree of temperature/storage violation, and the length of storage violation time.

d) Document the occurrence.

STUDY PRODUCT DISPENSING

- Prescribers must be licensed clinicians allowed to prescribe in the site jurisdiction.
- A mechanism must be established to ensure that study products are dispensed only upon the order of the Investigator or the licensed clinician directly responsible to the Investigator, as stated on Form FDA 1572 (IND studies) or the Investigator agreement (non-IND studies). Form FDA 1572 is a binding and legal document, whereby in completing and signing the form the IoR has certified that the study product will be administered only to subjects under his/her personal supervision or under the supervision of sub-investigators responsible to him/her.
- The Investigator and pharmacy must have a proper communication plan to notify the research pharmacist of authorized prescribers for an investigational trial (this is often a copy of the 1572 for a specific study).

ESSENTIAL INFORMATION ON STUDY AGENTS

- The pharmacist should ensure that there is a current IRB-approved version of the protocol on file for reference and that the protocol is followed when dispensing the protocol-specific drug.
- The research pharmacist should receive and have on file all bulletins, clarifications, or letters of amendment for each protocol.
- When final study product preparation occurs at the study site pharmacy, labeling of the study product will be as described in the protocol.

INVESTIGATOR'S BROCHURE AND PRODUCT PACKAGE INSERT

- A copy of the study-specific Investigator's Brochure, or the most current product package insert containing information as supplied by the manufacturer, should be distributed to the pharmacy along with the most current version of the protocol. The Investigator's Brochure or product package insert should be retained by the pharmacy for reference when dispensing.
- The Investigator Brochure should provide guidance on the potency and stability of the study product.

- In general, study product orders should include:
    a) Protocol number
    b) Date of the order
    c) Subject identification number
    d) Randomization number if available
    e) Subject height and weight, if applicable
    f) Study product prescribed (if study is blinded, the study product will be labeled accordingly)
    g) Quantity or instructions to indicate appropriate amount to be dispensed
    h) Route of administration
    i) Prescriber's signature

STUDY PRODUCT RETURN

- The investigator or designee should ensure that the study product is returned properly, including:
    - Return study product to the properly designated location or individual
    - Maintain study product accountability logs to note the amount returned, lot numbers, expiration dates, and condition of product
    - Study product is stored and shipped under the conditions suitable to the product