Study Management
SM – 307.01

STANDARD OPERATING PROCEDURE FOR
Investigational Product Management

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I. INTRODUCTION AND PURPOSE

This standard operating procedure (SOP) describes the processes Georgia CORE monitors at the investigator sites for the receipt, storage, dispensing, reconciliation and return or authorized destruction of the investigational drug (study drug).

2. SCOPE

This SOP applies to all procedures related to all clinical studies subject to investigational new drug (IND) regulations for drugs and biologics or those eligible for investigational new drug (IND) exemption during all investigational phases of development. It describes the steps monitored by Georgia CORE from the time the investigational product is received on-site until it is either returned to the designated location in the protocol or destroyed on-site.

3. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 312.50	General responsibilities of sponsors
21 CFR 312.56	Review of ongoing investigations
21 CFR 312.57	Recordkeeping and record retention
21 CFR 312.59	Disposition of unused supply of investigational drug
21 CFR 312.60	General responsibilities of investigators
21 CFR312.61	Control of the investigational drug
21 CFR 312.62	Investigator recordkeeping and record retention
21 CFR 312.68	Inspection of investigator's records and reports
21 CFR 312.69	Handling of controlled substances
27 October 2016	Pharmaceutical Management Branch (PMB) : Investigational Drug Accountability Training Videos, and accountability record forms, transfer form and return forms/local destruction forms
01 March 2014	NCI Guidelines for Auditing Clinical Trials for the NCI National Clinical Trials Network for the (NCTN) Program, Community Clinical Oncology Program (CCOP)/NCI Community Oncology Research Program (NCORP) and Research Bases
January 1988	Guidelines for the Monitoring of Clinical Investigations
September 1993	FDA Internal Compliance Program Guidance Manual 7348.811: Clinical Investigators
October 2009	Guidance for Industry Investigator Responsibilities---Protecting the Rights, Safety, and Welfare of Study Subjects
May 1997	International Conference on Harmonization; Good Clinical Practice: Consolidated Guideline

4. REFERENCES TO OTHER APPLICABLE SOPs

GA-102	Sponsor Responsibility and Delegation of Responsibility
SS-204	Site Initiation Visit
SM-303	Documentation and Records Retention
SM-304	Routine Monitoring Visits
SM-305	Closeout Visits
DM-501	Data Management

5. ATTACHMENT

A. Sample Investigational Product Accountability Log
B. Sample Study Subject Investigational Product Dispensing Log
C. Website location for CTEP-PMB Training and Accountability Forms

6. RESPONSIBILITY

This SOP applies to those members of Georgia CORE involved in monitoring the sites' management of the investigational product. This includes the following:

- President and CEO
- Georgia CORE staff and consultants

7. DEFINITIONS

The following definitions from the International Conference on Harmonization, Good Clinical Practice: Consolidated Guideline, apply to this SOP.

Blinding/Masking: A procedure in which one or more parties to the trial are kept unaware of the treatment assignment(s). Single blinding usually refers to the subject(s) being unaware, and double blinding usually refers to the subject(s), investigator(s), monitor, and, in some cases, data analyst(s) being unaware of the treatment assignment(s).

Investigational Product: 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.

Randomization: The process of assigning trial subjects to treatment or control groups using an element of chance to determine the assignments in order to reduce bias.

Source Documents: Original documents, data, and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate and complete, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files, and records kept at the pharmacy, at the laboratories, and at medico-technical departments involved in the clinical trial).

8. PROCESS OVERVIEW

A. Receipt and inventorying of the investigational product
B. Storage of the investigational product
C. Dispensing of the investigational product
D. Return/destruction of the investigational product

9. PROCEDURES

A. Receipt and inventorying of investigational product

• Research Staff/Consultant	Confirm that investigational product is shipped to a site only after initiation visit training and applicable regulatory requirements, including IRB approval and contract, have been fulfilled by the site(s). Check that upon receipt of the investigational product, the site staff has inventoried the shipment, ensuring that the information on the packing slips matches exactly with what has been sent to the site, including • Amount • Lot numbers • IP study assignment numbers (if applicable) • Quantity per carrier/container (if easily verified) • Maintenance of temperature stability (if applicable) Determine if the site promptly brought any discrepancies to the attention of the supplier of the investigational product. Review with the site staff to check the investigational product to confirm it is packaged properly and the labels and/or labeling provide the information that is required by the applicable regulations. The information required on the investigational product label or in accompanying labeling may include but is not limited to the following: • Study name and number • Drug name (unless blinded)

	• Dosage and formulation • Lot number • Sponsor name and place of business • FDA required statement: "Caution: New Drug – Limited by US law to investigational use." (if applicable) • Subject numbers and/or visit numbers • Special instructions regarding dosage or storage • Expiration date • Quantity in container • Any other information required in the applicable investigational product labeling regulations. Check that the site documented the receipt of the investigational product on the Investigational Product Accountability Log. (Attachment A, Sample Investigational Product Accountability Log or the applicable CTEP-PMB form) Check that if a form was included in the shipment to acknowledge receipt, that the network site staff obtained the appropriate signature and forwarded the form to the appropriate address. Check that the site retained a copy for the regulatory files. Check that the site has supplies required for the blinding of the investigational product. (if applicable) Review with the Investigator and site staff that if the investigational product is blinded, the blind will not be broken except in the case of an emergency or a protocol-defined situation. In addition, review that the protocol should be consulted for explicit directions about breaking the blind for the investigational product.

B. Storage

• Research Staff/Consultant	Check that the investigational product is stored in a secure environment with access limited to essential personnel, according to the storage requirements detailed in the protocol or supplied in a supplementary document. Check that the investigational product is stored at the appropriate temperature and that the site staff is maintaining a storage area temperature log, if appropriate. Check that the site staff is following any special requirements for controlled substances required by the protocol in addition to those specified by the regulations. Check with the site staff that the randomization code, if applicable,

	has been received.

C. Dispensing of investigational product

• Research Staff/Consultant	During routine monitoring visits and the study closeout visit, verify that the investigational product documentation has been accurate and complete throughout the study. Check that each time the investigational product is dispensed, the investigational product accountability form is completed (Attachment A). Documentation will include: • Amount (and lot number, if appropriate) dispensed, • Initials of individual dispensing investigational product, • Subject's number, • Subject's initials, • Date (and time, if appropriate) of dispensing, • Date (and time if appropriate) of investigational product return, • Amount of investigational product returned. Check that this form is maintained with the investigational product during the course of the study and included in the regulatory file at the conclusion of the study. Check that the site staff is maintaining a Study Subject Investigational Product Dispensing Form (Attachment B) on each subject including: • Visit number • Date • Lot number • Amount dispensed • Amount returned • Amount lost Check that after the study subject returns all used containers/units, if required by the protocol, that the site returns the containers/units to the location designated in the protocol. Also check that if any containers/units are missing, the reasons are documented by the site staff. Check that the site staff notes any discrepancies between amounts used by subjects and amounts expected to be returned and documents the reasons.
• Designee	Check that the site's investigational product supplies are adequate and within an appropriate expiration date. Review with the site staff that they are to alert the supplier when additional supplies will be required.

• Designee	Review with the Investigator and site staff that if emergency breaking of the investigational product blind is medically necessary, all circumstances are documented appropriately in the study file, including the exact manner in which the code was broken and the rationale. Review with the Investigator and site staff that if the blind is broken, they are to notify the Investigator who initiated the study (if applicable), the IRB and Georgia CORE.

D. Return/destruction of investigational product

• Designee	Check that at the conclusion of the study, all documentation regarding receipt, storage, dispensing, and return of used containers is complete and accurate. Review with the site staff that they must prepare the investigational product and containers for return shipment to the supplier as noted in the protocol.
• Designee	Review with the site staff that the destruction of investigational product at the site, upon written authorization from Georgia CORE, may be undertaken so long as such procedures are permitted by the site's OSHA and biohazard materials policies. Review with the site staff that they must provide the Georgia CORE with written documentation of the destruction of the investigational product. Check that the site has maintained a copy in the regulatory files and sent a copy to Georgia CORE.

10. HISTORY OF CHANGES

Version Number	Section Number	Modification	Approval Date
307.00	All	Original Version	
307.01	9A	Added several steps for checking information on packing slips on investigational products (Bullets 3 & 5)	09 March 2012
307.01	All	No changes necessary	01 June 2014
307.01	3, 5C, 9A	Changes include CTEP-PMB information for NCTN trials	17 March 2017

Attachment A

SAMPLE INVESTIGATIONAL PRODUCT ACCOUNTABILITY LOG

Protocol #: _____ Protocol title: _____

_____

_____

Name of Investigational product received: _____

Investigational product received

Bottles ___ Blister packs _____ Capsules _____
Ampules _____ Patches_____ Other (describe)_____

Date of receipt: __/__/__ Received by: _____

Amount: _____ Lot number: _____
Amount: _____ Lot number: _____

Investigational product dispensing record:

Date	Subject #/ initials	Number dispensed	Number used	Number returned	OK? Y/N	Lot #	Dispensed by (Initials)	Comments

For investigational product not returned or accounted for, complete the following:

Date	Subject #/ initials	Recorder's Initials	Reason

Date that all investigational product was returned to _____ (location designated in protocol) Date __/__/__
Signature of person completing this form: _____ Date __/__/__

Attachment B

SAMPLE STUDY SUBJECT INVESTIGATIONAL PRODUCT DISPENSING LOG

Investigator:	Site:
Protocol Number/Title:	
Investigational Product Name:	Dose Form/Strength:
Subject's Initials:	Subject's Study Number:

Visit #	Date	Lot #	Quantity dispensed	Quantity used	Number returned unused	Dispensed by	Comments

Review/Approval (Signature):

_____ _____
Investigator's Name (please print) Signature Date

_____ _____
Investigator's Name (please print) Signature Date

Attachment C

CTEP PMB Investigational Drug Information/Management

Investigational Drug Accountability Training Videos for CTEP NCTN trials:
https://ctep.cancer.gov/branches/pmb/drug_training_videos.htm

Investigational Drug Forms: Accountability, Return, Destruction, Transfer
https://ctep.cancer.gov/forms/

Agent Management Information/Policies
https://ctep.cancer.gov/branches/pmb/agent_management.htm