UC Riverside, School of Medicine Policies and Procedures
Policy Title: Investigational Drug, Storage, Dispensing and Return
Policy Number: 950-12-001

Responsible Officer:	Senior Associate Dean, Research
Responsible Office:	Biomedical Sciences, Clinical Research
Origination Date:	14 April 2021
Date of Revision:	
Scope:	SOP for Investigational Drug

I. Policy Summary

To ensure that the Principal Investigator (PI) and all research team members assisting in the conduct of clinical research are informed about their obligations and responsibilities as they pertain to Good Clinical Practices (GCP), the investigational plan, applicable regulations, guidance's, and institutional policies. This Standard Operating Procedure (SOP) applies to the written procedures followed by all members of a clinical research team involved in the conduct of human subjects' research at University of California Riverside Health (UCR Health), hereafter called the investigational site. These detailed instructions promote compliance in conducting clinical research.

II. Definitions

Please refer to the SOP Glossary document for detailed definitions of commonly used clinical research terminology.

III. Policy Text

A describes the process for the receipt, storage, dispensing, reconciliation and return or authorized destruction of an investigational product (IP; e.g., drug). Attachment templates include:

A. Master Drug Accountability Log
B. Subject Drug Accountability Log
C. Subject Drug Diary
D. Study Drug Transport and Chain of Command Form

IV. Responsibilities

UCR Health-School of Medicine – Research Office (UCR Research Office) develops, implements, and maintains SOPs. The need to write a new or revise an existing SOP is based upon changes to federal regulations, guidelines, institutional policies, or procedures. These documents will be provided to departments and research teams conducting human subjects' research. Departments or research teams may develop additional research SOPs or a Research Procedure Addendum (RPA) to expand on an existing SOP, however this need should be limited. The PI is ultimately accountable for all clinical research activities and is responsible for the appropriate delegation of tasks to individuals with adequate training and education to perform such tasks. It is the responsibility of all members

of the clinical research team involved in supervising, managing, or conducting study-related activities to follow the SOPs. The clinical research team may include but is not limited to the following members:

Research Team Members

Principal Investigator (PI)	Sub-Investigator (Sub-I)
Clinical Research Coordinator (CRC)	Clinical Graduate Student Research (CGSR)
Clinical Research Manager (CRM)	Clinical Research Assistant (CRA)
Other Research Staff as appropriate	Administrative and Support Staff

V. Procedures

The PI will personally conduct or supervise the clinical research study to ensure that the investigation is conducted according to the signed investigator statement, the investigational plan, GCP and applicable regulations to protect the rights, safety and welfare of subjects under the Investigator's care and for the control of drugs under investigation.

The PI may delegate some or all of the Investigator's duties for managing investigational product accountability at the investigational site to an appropriate pharmacist or another appropriate individual who is under the supervision of the Investigator. The PI and delegated research team members will maintain a list of appropriately qualified staff members that have been delegated significant clinical research study-related duties. Additionally, delegated research team members engaged in the management of investigational product should be listed as key personnel with the IRB.

The PI and delegated research team members will be qualified by education, training, and experience to assume responsibility for the proper conduct of the study, will meet all the qualifications specified by the applicable regulatory and sponsor requirements, and will provide evidence of such qualifications through up to-date curriculum vitae and/or other relevant documentation requested by the sponsor, the IRB, and/or the regulatory authorities.

The PI and delegated research team members will:

A. Ensure that the investigational product is used in accordance with the IRB approved protocol.

B. Have continuous documented training on handling and dispensing of investigational products. Explain the correct use of the investigational product to each subject and will check, at intervals appropriate for the clinical research study, that each subject is following the instructions properly.

C. In a randomized, double-blinded clinical research study, follow the study's randomization procedures, if any, and ensure that the randomization assignment is broken only in accordance with the protocol. (If the clinical research study is double-blinded, the investigator will promptly document and explain to the sponsor any premature unblinding of the investigational product such as accidental unblinding or unblinding due to a serious adverse event.)

D. If emergency breaking of the study drug blind is medically necessary, the delegated research team member will document the reasons for breaking the blind and contact the study sponsor and other required regulatory authorities immediately.

Study Drug

A. Receipt and Inventory

Upon receipt of study drugs, a delegated research team member will review the shipment to ensure the information on the packing slips matches exactly what has been received at the site. This includes verifying the content, amount of study drug, lot numbers, expiration dates, supplies required for blinding the drug (if applicable) and that randomization assignment (if applicable) have been received. All information is to be tracked on a Master Drug Accountability Log (See Attachment A: Master Drug Accountability Log).

If the sponsor includes a form to acknowledge receipt, the delegated research team member will obtain the appropriate signature and forward the form to the sponsor and retain a copy for the regulatory files. If any errors are identified, the delegated research team member will promptly document the errors and contact the sponsor regarding the discrepancies. Copies of all invoices, drug dispensing and disposition records, randomization codes, and any other drug activity forms will be stored securely at the investigational site.

B. Safe Handling and Compounding

Study drug will be handled per the IP package insert, Investigator's Brochure (IB), protocol, or Investigational Drug Service (IDS) guidelines. Specific precautions should be considered when handling hazardous drugs.

C. Storage

The study drugs will be stored in a secure environment that is lockable, separate from routine drug stock, with limited access for only delegated research team members. The site will ensure that the study drugs are stored according to the storage requirements detailed in the protocol or supplied by the sponsor. This includes ensuring the study drug is stored at the appropriate temperature and a temperature log will be maintained, if required.

All refrigerators used for study drug storage will be plugged into outlets with back-up power where available. If the study agent is temperature sensitive, measures will be taken to capture the temperature continuously or at least daily. In the event that a temperature deviation is identified, the sponsor will be notified, and the affected drugs will not be dispensed until further instruction is received from the sponsor. No food, drink, or specimens will be stored in the same location as study drug.

The PI and delegated research team members will follow any special requirements for controlled substances required by the Controlled Substances Act at this investigational site in addition to those specified by the study drug

regulations and institutional policies. The PI should contact IDS for consultation for specific guidance and training on controlled substances for research prior to study implementation.

D. Dispensing of Study Drug

Prior to dispensing study drug, the delegated research team members will ensure that study drug supplies are adequate and within an appropriate expiration date. If additional supplies are needed, the monitor or study sponsor will be contacted to request additional study drug. The Master Drug Accountability Log should be updated any time study drug inventory changes.

The PI is responsible for ensuring that study drug is appropriately dispensed and/or administered per protocol by delegated research team members. The delegated research team members will ensure that each time a study medication is dispensed, the Subject Drug Accountability Log is completed (See Attachment B: Subject Drug Accountability Log).

Documentation should include:

1. Amount dispensed
2. Lot number (if applicable)
3. Name of individual dispensing study drug
4. Subject's number
5. Subject's initials
6. Date (and time, if appropriate) of dispensing
7. Date (and time, if appropriate) and amount of study drug returned

If errors are made on the accountability form, there should be a single line through the error, with the initials of the person correcting the error and the date corrected. When recording the date, the month, day, and year will be recorded. For short stability agents, the preparation time and date as well as the dose time will be documented, if required by the sponsor. If study drug is wasted in error during preparation by the research team, this will be documented as a separate entry on the drug accountability form with reason for the error.

The delegated research team members will ensure that the correct study drug is used from the appropriate study supply and documented on the appropriate study drug accountability form. Study drug may not be used across protocols, and commercial drug may not be used in place of study drug.

It is recommended to provide diaries for administration of study medication at home to properly document use. The diary must be IRB approved, if applicable. When the diary is returned to the site, the research team member will review the data for completeness. Source documentation should reflect but is not limited to amount of medication dispensed, kit number(s) dispensed, administration instructions, and subject education (See Attachment C: Subject Drug Diary).

Discrepancies in the amount dispensed to the subject, used by the subject, or amount expected to be returned by the subject will be documented along with the reason for the discrepancies.
After the study drug has been dispensed, all containers and unused study drug should be returned by the subject to the site. The delegated research team member will document the date of return, drug name, lot number, quantity of unused study drug, and reason for missed doses, noncompliance or missing study drug.

E. Labeling of Study Drugs

All investigational drugs dispensed shall bear on the label "Investigational Drug: Limited by Federal Law to Investigational Use." Additional labeling information to be included: subject name or initials, MRN or study sequence number, date, study number, study drug name, directions for use, quantity, and name of PI and initials of dispensing staff. Investigational drug labels should not be obscured in any way.

F. Mailing of Study Drug to Subjects

Study products may be mailed within the state of California; however, all efforts will be made to avoid mailing study drug to subjects. If arrangements cannot be made, mailing of study drug to subjects within the state of California is allowable as long as it is permitted per protocol, the sponsor and PI have given written authorization, and the mailing method is traceable (e.g., UPS or FedEx). Copies of shipping labels and permission from the sponsor and PI will be maintained in the subject's research record. If mailing across state lines, IDS must be contacted and provide approval.

G. Return/Destruction of Study Drug

At the conclusion of the study, the delegated research team member will ensure that all documentation regarding receipt, storage, dispensing, and return of used containers and unused study drug is complete, accurate, and ready for review for the termination visit.

Delegated research team members may appropriately destroy study drug at the site with written authorization and approval from the sponsor to do so. Destruction of study drug must follow institutional policies and procedures required by OSHA and biohazard materials policies. IDS will assist with study drug destruction, as needed. The delegated research team members will provide the sponsor with written documentation of the destruction of the study drug and maintain a copy for the regulatory files.

VI. Forms/Instructions

VII. Applicable Regulations, Guidance's and Policies

Regulation/ Guidance/Policy Title

21 CFR 50 Protection of Human Subjects

21 CFR 312 Investigational New Drug Application
45 CFR 46 Protection of Human Subjects
45 CFR 160 HIPPA Privacy Rule
45 CFR 164 Subparts A and E HIPPA Privacy Rule
UCR IRB Research Participant Resources
UCR Research Integrity Research Integrity
ICH GCP Guideline for Good Clinical Practices: E6 Integrated Addendum
FDA Guidance for Industry Information Sheet Guidance for Clinical Investigators
FDA Compliance Program Guidance Manual Drug Administration Compliance Program
FDA Frequently Asked Questions Frequently Asked Questions – Statement of Investigator (Form FDA 1572) | FDA

VIII. Revision History

Approvals:

COMPLIANCE COMMITTEE (04/28/2020)

Paul Hackman Digitally signed by Paul Hackman Date: 2021.05.14 14:40:47 -07'00' — 05/14/2021

PAUL HACKMAN, J.D., L.LM. — DATE
CHIEF COMPLIANCE AND PRIVACY OFFICER,
SCHOOL OF MEDICINE

Deborah Deas, MD, MPH Digitally signed by Deborah Deas, MD, MPH Date: 2021.05.20 11:44:00 -07'00'

DEBORAH DEAS, M.D., M.P.H — DATE
VICE CHANCELLOR, HEALTH SCIENCES
DEAN, SCHOOL OF MEDICINE

UCR HEALTH

Master Drug Accountability Log

Documentation and tracking investigational Drug receipt and dispensation

Principal Investigator:_____ Protocol#_____
Protocol Title:_____Sponsor: _____
_____

RECEIPT				DISPENSE		RETURN		DESTRUCTION/RETURN to Sponsor	
From Label		Date Received	Initials	Date Dispensed to Subject	Initials	Date Returned to Site	Initials	Date	Initials
Kit/lot #	Expiration								

UCR HEALTH

Subject Drug Accountability Log
Documentation and tracking investigational Drug receipt and dispensation

Study Start Date or Date Document Implemented:_____
Study End date or Date Document Discontinued: _____

Attachment B

Principal Investigator:_____ Protocol#_____
Protocol Title:_____
_____

Subject Initials	Subject ID	Drug Kit #	Visit	Date Dispensed (DD/MMM/YYYY)	Dispensed By (initials)	Date Returned (DD/MMM/YYYY)	Site Personal Signature	CRA/Monitor Signature

STUDY DRUG DIARY TEMPLATE (One Drug) - Modify the diary to meet the specific needs of the study. Remember to delete all instructions, i.e., blue text - these statements are provided for guidance only.

Study Participant
Self-Administration
Study Drug Diary
Dana-Farber/Harvard Cancer Center

Participant Identifier: _____
Protocol # : Insert DFCI IRB protocol number
Your MD _____ Phone _____
Your Coordinator _____ Phone _____

OTHER MEDICATIONS TAKEN

If you take a daily medication (prescribed or otherwise), please use one line per drug and indicate the start and stop dates under the "Date(s) Taken" section (i.e., 6/2/09 - 6/5/09).

Drug Name	Dose	Dates Taken	Reason Taken

Study Participant Initials _____ Date _____

FOR STUDY TEAM USE ONLY	
Staff Initials:	
Date Dispensed:	Date Returned:
# pills/caps/tabs dispensed:	# pills/caps/tabs returned:
# pills/caps/tabs that should have been taken:	
Discrepancy Notes:	

STUDY DRUG INSTRUCTIONS:

Study Drug: Insert drug name
How Much: Your dose is enter the amount and units.
How Often: You will take each dose ….
When: You should take your dose ….

SPECIAL INSTRUCTIONS:

List any special drug instructions. When appropriate, include: (i) exclusionary food or beverage item; (ii) storage requirements; (iii) mixing instructions; (iv) what to do with late, missed or vomited doses; (v) information related to safety concerns; and (vi) a statement that drug must be kept in original container.

End with a reminder to bring any unused study drug, all empty containers, and diary to the next clinic visit.

DOSING LOG

Insert study drug name
For each AM dose take: # pills/capsules/tablets
For each PM dose take: # pills/capsules/tablets

Please indicate the date, time, amount taken and any comments.

	Date	Amount Taken		Comments
		AM dose	PM dose	
Ex:	6/1/2009	8 am - 1	7:30 pm - 1	vomited PM pill
Day 1				
Day 2				
Day 3				
Day 4				
Day 5				
Day 6				
Day 7				
Day 8				
Day 9				
Day 10				
Day 11				
Day 12				
Day 13				
Day 14				
Day 15				
Day 16				
Day 17				
Day 18				
Day 19				
Day 20				
Day 21				
Day 22				
Day 23				
Day 24				
Day 25				
Day 26				
Day 27				

SYMPTOMS/SIDE EFFECTS

Please record any side effects experienced during this cycle. Include the date the particular symptom started and when it ended. Please evaluate the severity of the symptom according to the following scale:

Mild: Awareness of sign or symptom; easily tolerated and did not affect ability to perform normal daily activities. Symptom did not require medication or therapeutic intervention.

Moderate: Significant discomfort which interfered with ability to perform normal daily activities. Symptom was easily resolved with at home medication or simple therapeutic intervention.

Severe: Marked discomfort with an inability to carry out normal daily activities. Symptom required new medication and/or therapeutic intervention in order to resolve.

Please Note: The severity should reflect the most severe level experienced during the time period.

Symptom	Start Date	End Date	Severity