

GUIDANCE: Investigational Drugs and Biologics

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1 PURPOSE

- 1.1 To establish guidance for the receipt, storage, handling, dispensing, accountability, returns and destruction (wasting) of investigational drugs and biologics used in Sharp HealthCare (SHC) Institutional Review Board (IRB) approved clinical trials protocols.
- 1.2 The guidance begins when an investigational drug is received at a Sharp HealthCare (SHC) facility.
- 1.3 The guidance ends when the investigational drug is wasted or returned to the study sponsor.
- 1.4 This guidance is to be reviewed and updated annually, or more often as needed, by SHC pharmacists and technicians who receive, store, handle, dispense or manage investigational drug accountability.

2 REVISIONS FROM PREVIOUS VERSION

- 2.1 None.

3 POLICY STATEMENT

- 3.1 Per SHC *POLICY: Investigational Drugs (43019.01)*

4 RESPONSIBILITIES

- 4.1 Principal Investigators, Sub investigators, Clinical Research Coordinators (CRCs), Investigator-Sponsors, Pharmacists, and Sponsor’s Study Monitors/Auditors carry out these procedures.

5 PROCEDURE

- 5.1 Drug Receipt, Storage and Documentation: Each clinical trial is to have designated site and/or pharmacy personnel manage investigational drugs. Those designated personnel are listed on the Protocol-Specific Site Delegation Log and the Protocol-Specific Site Training Log prior to executing any pharmacy protocol required functions, exceptions may apply in emergency situations. The sponsor provides the Site Delegation Log and Site Training Log which are maintained in the PI/research site regulatory binder.
 - 5.1.1 Pharmacy Binder: The investigational pharmacy personnel are responsible for creating a clinical trial protocol- specific pharmacy binder or electronic file which will contain the following:
 - 5.1.1.1 Patient Enrollment List: A master list is maintained for documenting patients enrolled in the clinical trial along with assigned patient number and/or randomization number. WORKSHEET: Pharmacy Patient Enrollment (HRP-326)
 - 5.1.1.2 Investigational Drug Summary using WORKSHEET: Investigational Drug Summary (HRP-351).
 - 5.1.1.3 Drug Accountability Forms: The investigational pharmacists may use sponsor-provided or SHC-created drug accountability forms (WORKSHEET: Master Drug Accountability Record [IV Meds] [HRP-327] and WORKSHEET: Master Drug Accountability [Oral Drugs] [HRP-328]). At the completion of the study, a copy is to be maintained in the protocol-specific pharmacy binder. To the extent permitted by the study design, this Drug Accountability Form shall contain the drug’s name, dosage form, strength, lot number, and expiration date. The Drug Accountability Form shall contain dated information regarding the disposition of drug (amounts received, transferred, wasted, dispensed, returned to sponsor or sent for destruction per *POLICY: Pharmaceutical Waste Management [18306.99]*).
 - 5.1.1.4 Study Protocol and Amendments: The protocol-specific pharmacy binder is to contain the most recent version of the clinical trial protocol only. Previous versions of the protocol and all amendments will be retrievable from the investigator/research site’s regulatory binder. An electronic version of the current version of the protocol may also be kept on file in the pharmacy database with an insert in the pharmacy binder identifying its location.

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- 5.1.1.5 Investigator’s Brochure (IB) and Amendments: The protocol-specific pharmacy binder is to contain the most recent version of the investigator brochure only. Previous versions of the investigator’s brochure (IB) and all amendments will be retrievable from the investigator/research site’s regulatory binder. An electronic version of the current investigator brochure may also be kept on file in the pharmacy database with an insert in the binder identifying its location.
- 5.1.1.6 Shipping and Receiving Invoices: All shipping and receiving invoices are to be retained in the protocol-specific pharmacy binder.
- 5.1.2 Receipt of Investigational Drug: Upon receipt of the investigational drug from the sponsor (e.g., pharmaceutical company), the investigational drug is to be logged onto the Drug Accountability Forms in accordance to protocol guidelines and 5.1.1.3 above.
- 5.1.3 Storage of Investigational Drug: Investigational drug is to be stored in a locked research storage area or cabinet within the pharmacy that is separate from non-investigational drugs. When the investigational drug is in the custody of the pharmacy, the pharmacy is to keep temperature logs and monitor on a daily or continual basis to ensure the investigational drug remains within temperature ranges specified on the package and by the clinical trial protocol. Use WORKSHEET: Investigational Pharmacy Temperature Log (HRP-323). Temperature logs are for use with multiple investigational drugs and are not kept in the protocol-specific Pharmacy Binder unless the sponsor requires copies to be maintained in the protocol specific pharmacy binder. Temperature logs are made available to sponsor monitors and auditors upon request.
 - 5.1.3.1 Storage of Investigational Drug at a non-SHC Facility: If an investigational drug is stored at a facility other than a SHC pharmacy but is to be dispensed through the SHC pharmacy, it is to be transported by designated research site staff and delivered to designated SHC pharmacy staff under the continuous control of the designated site study staff. When transporting investigational drug to or from another facility follow procedures outlined in 5.12 and 5.14 below.
 - 5.1.3.2 Excursions: If the investigational drug goes outside of the specified temperature range it is called an excursion. Temperature excursions are to be reported to the study sponsor and the drug retained in quarantine. The pharmacy is to follow the protocol specific procedures regarding temperature excursions accordingly. If follow-up documentation from the sponsor supports the drug is viable for use after the reported temperature excursion, then the drug may be pulled from quarantine and used for patient care.
- 5.2 Dispensing: Investigational drugs are to be dispensed to consented subjects enrolled in the clinical trial. Consent may be by the subject or their legally authorized representative (GUIDANCE: Legally Authorized Representatives (Surrogate Consent) [HRP-013]). The pharmacy is responsible for confirming a patient or legally authorized representative has signed the protocol-specific SHC IRB-approved Informed Consent Form (ICF) and verifies that a copy of the signed informed consent is in the patient’s chart before dispensing the first dose of the investigational drug. If the investigational drug is from another institution, refer to *POLICY: Patient’s Own Medication: Usage and Storage (43088.99)*.
- 5.3 Protocol-Specific Investigational Drug Education: The sponsor is responsible for providing protocol-specific investigational drug education to the PI, sub- investigators, clinical research coordinators (CRC), research site personnel, and SHC pharmacy personnel who prescribe, distribute, or administer the investigational drug.
- 5.4 Updated Information and Documents: The clinical research coordinator or designee is responsible for providing the pharmacy with a current copy of the protocol, including all revisions or amendments, and a current copy the Investigational Brochure (IB), and keeps the pharmacy informed of any new information that may affect patient safety or dispensing of the investigational drug.

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- 5.5 Investigational Drug Disposition: The CRC and/or the SHC pharmacist keeps adequate records of the disposition of the investigational drug/biologic, including dates of dispensing, quantity currently maintained for dispensing, and amount of the investigational drug dispensed to participants.
- 5.6 Investigational Drug Orders: The principal investigator or sub-investigator physician orders (prescribes) the investigational drug and has it assigned by the sponsor according to protocol guidelines (e.g., automated assignment system or other randomization process).
- 5.7 Order Verification: The pharmacist verifies the package number and order instructions to ensure accurate dispensing and labels the investigational drug packages according to protocol and pharmacy requirements.
- 5.8 Accountability, Returns, and Destruction: The clinical research coordinator and/or pharmacist maintain all drug accountability logs and accounts for all investigational drug dispensed, unused, used, and expired. If investigational drug and/or packaging are not returned by subjects who are outpatients, the CRC is to make all efforts to retrieve the package and/or investigational drug, including sending certified letters requesting the return of investigational drug to subjects who are lost to follow-up.
- 5.9 Clinical Trial Treatment Phase Termination: The principal investigator or designee notifies the pharmacy when the treatment phase of the clinical trial has been completed and when the study is terminated.
- 5.10 Sponsor Monitors and Auditors: The sponsor or their designee is to routinely monitor (audit) all clinical trials. The sponsor's monitor manages investigational drug returns or oversees wasting (destruction) according to sponsor protocol and/or SHC procedures (*POLICY: Pharmaceutical Waste Management [18306.99]*). The pharmacy is to log all returns and wasting in the WORKSHEET: Master Accountability Record (HRP-327 or HRP-328) unless otherwise specified. The sponsor monitor verifies and co-signs the WORKSHEET: Master Accountability Record (HRP-327 or (HRP-328) for confirmation of returned or destroyed investigational drug at the site to ensure complete accounting of all investigational drug.
- 5.11 Controlled Substances Act: If the investigational drug is subject to the Controlled Substances Act, the pharmacist, principal investigator, sub-investigators and CRC are to take adequate precautions to prevent theft or diversion of the substance into illegal channels of distribution.
- 5.12 Inter-facility Investigational Drug Transport: When an investigational drug is transported by courier or SHC employee from the pharmacy to a different site or entity before or after drug preparation, it is to be accompanied by an WORKSHEET: Investigational Drug Transport Log (HRP-325):
 - 5.12.1 The pharmacist or designee completes the information in the header and Investigational Drug Dispensation section of the Transport Log.
 - 5.12.2 A copy of the partially completed Transport Log is kept at the pharmacy and held until the pharmacy receives a faxed or scanned copy of the completed Transport Log. The clinical research coordinator is to keep the original completed Transport Log at the in the protocol- specific binders at the research site.
 - 5.12.3 Courier staff or the clinical research coordinator completes the Transport section of the Transport Log.
 - 5.12.4 Investigational Drugs requiring refrigeration during transport from the Sharp Memorial Investigational Pharmacy to the Grossmont Cancer Center or the Chula Vista Cancer Center will use an insulated cooler bag with a temperature monitoring device attached to each investigational drug unless otherwise specified by the sponsor:
 - 5.12.4.1 The temperature monitoring device is to be started at the time of preparation and placed on top of the investigational drug, which is then wrapped with gel-packs.
 - 5.12.4.2 The courier signs the Investigational Drug Transport Log at the time of pick-up.

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- 5.12.4.3 The SHC staff receiving the drug stops the temperature monitoring device and completes the information in the Transport Site section of the Investigational Transport Log.
- 5.12.4.4 If there is an alarm/alert indicating that the temperature in the drug transport cooler bag went outside of the protocol defined ranges (excursion), the pharmacist and clinical research coordinator are to be informed immediately and the drug is not to be administered to the patient until the dispensing pharmacist analyzes all alarm/alert data from the temperature monitoring device and communicates the excursion information to the protocol sponsor. The sponsor's medical monitor or designee reviews the temperature excursion data and determines if the drug is suitable for administration. If the drug is deemed not suitable for administration, the study coordinator coordinates with the pharmacy and patient for scheduling the next available investigational drug administration. If the sponsor's medical monitor or designee determines that the study drug was not compromised by the temperature excursion and is appropriate for administration, the research pharmacist contacts the study coordinator to release the drug for use. The sponsor is to provide written documentation that the drug is suitable for use. This documentation is to be stored in the Protocol Specific Pharmacy Binder with a copy stored in the research site's regulatory binder.
- 5.12.4.5 For oral drugs that do not require refrigeration during transport, no temperature monitoring device will be sent with the drug. However, the Investigational Drug Transport Log is to be utilized by the courier and the SHC staff with regards to times of pick up and times of receipt to build in accountability to retain the chain of custody.
- 5.13 **Emergency Use of Investigational Drug:** In the event of a one-time emergency use of an investigational device, drug, or biological product in a life-threatening situation physician/investigators are to follow guidelines according to the HRPP GUIDANCE: Emergency Use Review (HRP-023). FDA regulations allow for one emergency use of an IND without prospective IRB review. Any subsequent use of the IND shall undergo prospective IRB review and approval.
- 5.14 **Investigational Drug from Another Institution:** Investigational drugs from other institutions are to be managed according to the *POLICY: Patient's Own Medication: Usage and Storage (43088.99)*. The SHC physician or pharmacist is to obtain a copy of the non-SHC IRB approved clinical trial or protocol summary which is to be placed in the patient's medical record. An additional copy will be filed in the pharmacy. The SHC admitting physician or designee is to obtain a copy of the signed informed consent and places it in the patient's medical record. The SHC attending physician or designee contacts the principal investigator to assure that the patient is appropriately followed, and that all relative information is provided regarding the investigational drug, its effects, contraindications, drug interactions, etc.
- 5.15 **Emergency Breaking of a Blinded Investigational Drug in a Clinical Trial:** A study-specific mechanism shall be in place to allow a pharmacist or other designated health care provider, in a medical emergency during a randomized and blinded trial, to break the blinding code and reveal the identity of the investigational drug to other health care professionals as needed for the medical care of the patient. The sponsor is to provide the instructions for breaking the blind before any investigational drug is dispensed.
- 5.16 **Investigational Drug Adverse Reaction Reporting:** The principal investigator, CRC, or designee is to report adverse drug events according to the FDA and sponsor's requirements. Investigators or their designees report certain adverse events directly to the IRB using FORM: Unanticipated Problem or Event Report (HRP-214). The SHC staff documents adverse events according to *POLICY: Medication Safety Event Monitoring (48138.99)*. Refer to the *MANUAL: Investigator Guidance Manual (HRP-101)* for guidance on submission of a report on unanticipated problems or events.

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- 5.17 **Record Storage:** Store dispensing records for closed studies in a secure area that is readily retrievable until two years after the investigational drug receives FDA approval or until the sponsor notifies the investigator that investigational drug records are no longer needed. The sponsor or investigator may request that the dispensing records for closed studies be filed with the investigator's regulatory binders.
- 5.18 **Billing for Investigational Drug Dispensing and Drug Charges:** The pharmacist, pharmacy technician or their designee is responsible for entering agreed upon charges into the SHC billing system. This includes charges for all activities associated with investigational drug dispensing and protocol-required FDA approved medications not provided by the study sponsors.
- 5.19 **Annual Review of GUIDANCE and POLICY: Investigational Drugs.** This guidance *and POLICY: Investigational Drugs (43019.01)* are to be reviewed and this guidance updated (as needed) annually by October 1st each year by all SHC pharmacists and technicians involved with managing investigational and Biologics drugs or biologics. SHC pharmacists and technicians are to acknowledge annual review of the POLICY and this guidance by signing *WORKSHEET: Annual Investigational Drug Policy and Guidance Review Log (HRP-329)*.

6 MATERIALS

- 6.1 POLICY: Investigational Drugs (43019.01)
- 6.2 POLICY: Pharmaceutical Waste Management (18306.99)
- 6.3 POLICY: Patient's Own Medication: Usage and Storage (43088.99)
- 6.4 GUIDANCE: Legally Authorized Representative (Surrogate Consent) (HRP-013)
- 6.5 GUIDANCE: Emergency Use Review (HRP-023)
- 6.6 MANUAL: Investigator Guidance (HRP-101)
- 6.7 FORM: Unanticipated Problem or Event Report (HRP-214)
- 6.8 WORKSHEET: Investigational Pharmacy Temperature Log (HRP-323)
- 6.9 WORKSHEET: Investigational Drug Transport Log (HRP-325)
- 6.10 WORKSHEET: Patient Enrollment (HRP-326)
- 6.11 WORKSHEET: Master Drug Accountability Record (IV Meds - numbered vials) (HRP-327a)
- 6.12 WORKSHEET: Master Drug Accountability Record (IV Meds – non-numbered vials) (HRP-327b)
- 6.13 WORKSHEET: Master Drug Accountability Record (Oral Meds - numbered bottles) (HRP-328a)
- 6.14 WORKSHEET: Master Drug Accountability Record (Oral Meds – non-numbered bottles) (HRP-328b)
- 6.15 WORKSHEET: Annual Investigational Drug Policy and Guidance Review Log (HRP-329)
- 6.16 WORKSHEET: Investigational Drug Summary (HRP-351)

7 REFERENCES

- 7.1 (21 CFR 321.32(b))
- 7.2 21 CFR 312
- 7.3 21 CFR 601

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