



Clinical Manual

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Section:

Approved by: Nursing Congress; Operations Council

Subject:

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Values: Safety, Excellence, Efficiency

Investigational Drug Service

Policy:

The pharmacy is responsible for ensuring that procedures are developed and implemented for the control and usage of medications in clinical research at Upstate Medical University in order to ensure the safety of research subjects in conjunction with the Upstate Institutional Review Board for the Protection of Human Subjects (IRBPHS).

Procedure for Research Medications:

1. Investigational drugs are defined as:
 - a. Medications which are not FDA approved.
 - b. Medications being researched for non-FDA approved uses (off-label use of an FDA approved medication)
 - c. Medications from a different institution that are not FDA approved.
 - d. Medications being used by a patient from another country where the medication has not been approved by the FDA for use in the US.
 - e. Note: In addition to investigational drugs, as defined above, All medications administered to research subjects per study protocol (regardless of FDA status) are considered medications being used for research and require to be listed on the *Pharmacy Worksheet*.
2. Investigational drugs are to be used under the direct supervision of the Principal Investigator and/or the patient's attending.
3. When nurses are called upon to administer investigational drugs, basic information shall be available to them concerning dosage, strength, actions, uses, and symptoms of toxicity. The Principal Investigator is responsible for arranging an in-service for the nursing staff prior to initiating a study.
4. Orders for investigational drugs will follow the routine procedures for the writing of all drug orders. In addition to orders written in the medical record (including areas that use CPOE), an Investigational Drug Prescription, signed by the principal investigator or co-investigator(s), will be required. Protocol identification and randomization information is required to be included in the "Special Instructions" section of the prescription.
5. Investigational Drug Prescriptions may be faxed to the pharmacy. The hard copy must be forwarded to the Pharmacy as soon as possible.
6. Investigational drugs shall be stored in the pharmacy in a designated space separate from regular pharmacy stock and clearly labeled "For Investigational Use". All medications and supplies for outpatient studies done in clinics or off-site should be stored in the department of pharmacy. If logistically impossible, a secure, temperature monitored, location is to be chosen by the principal investigator. All dispensing must meet the intent of the standards listed in this document.

Safety

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Innovation

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a. The department of pharmacy shall conduct compliance rounds to off-site locations to ensure compliance with federal, state, local and JCAHO regulations. Compliance rounds will be performed, at minimum, annually.

7. The Pharmacy is established as a central unit where information on investigational drugs is maintained and made available to authorized personnel during shifts when the IRB is not available.

8. Patients must sign an IRB approved stamped consent form before an investigational drug can be administered. It is the responsibility of the principal investigator to ensure that consent is obtained prior to prescribing investigational agents.

a. For medications that are not being directly researched at University Hospital, a patient must consent to continue usage of their medication while here at University Hospital.

1. A copy of the full protocol, IRB approval letter, and any drug data sheet (or Investigator Brochures) must be provided to the Pharmacy by the investigator or his staff, and maintained on file in the Pharmacy. Any amendments must also be provided to the Pharmacy by the investigator. ALL study documentation including shipping receipts, faxed correspondence, and drug accountability forms will be kept in the pharmacy study file.
2. A multidisciplinary meeting of pharmacists, physicians, nurses, and/or other staff will be held to discuss the extent of Pharmacy services required by the protocol. "Pharmacy Worksheet: The Use of Medications or Biological Agents in Clinical Research Studies" shall be completed to assist in the IRB determining the pharmacy services required for a study.
3. The principal investigator or authorized members of the research team are responsible for educating subjects and monitoring therapy (including adverse drug event reporting).
4. In studies requiring return drug documentation, any suspected subject adherence problems will be brought to the attention of the investigator's research staff. At the discretion of the investigator, a pharmacist will be available to assist in counseling to improve subject adherence.
5. The Investigational Pharmacist will provide the pharmacy staff with specific written guidelines for each study, so any pharmacist will be able to fill the Investigational Drug Prescription. The pharmacy guidelines will include the following: a brief description of the study, what information is necessary on the Investigational Drug Prescription, how to enroll patients, location of the drug, description of how the drug is supplied, computer entry, directions for use, amount to dispense, inventory sheets, what to do with tear-off labels, emergency unblinding, side effects, drug preparation for IV meds, sterile products worksheets, drug ordering and acknowledgment information, Principal Investigator/Study Contact people including telephone #'s, and any other protocol specific information.
6. Compensation (fees) for pharmacy services are defined on the University Hospital Department of Pharmacy website. Fees are solely to compensate for the costs of providing services.
7. All pharmacy guidelines for studies will be kept in binders in the investigational dispensing area. The binder will include (as needed) subject logs, study directions, randomization sheets, inventory sheets, drug dispensing logs, pediatric dosing worksheets, sterile products worksheets, drug re-order forms, and any other documentation specific to a particular protocol.
8. Prescriptions for research medications will be stored in the binder specific to that protocol.
9. Prescriptions will be set up by the pharmacy staff and checked by a Pharmacist. An "Investigational Drug" auxiliary label will be affixed to every prescription label.
10. A perpetual inventory will be kept and a physical inventory conducted for all studies. Perpetual inventory sheets will include (as needed) drug name, strength, and dosage form, study name, protocol #, Investigator's name, lot#, expiration date, and par level (when necessary).
11. Expiration dates for all study medications will be checked.
12. Current recommendations for study documentation include:
 - b. Initials - always include THREE initials unless subject doesn't have a middle name. ** Do not use FULL names on original company accountability forms unless required by the protocol.
 - c. Ink Color - use BLACK, not blue.
 - d. Cross outs - no scribbles - draw one line through error, then date and initial. No white-out is to be used.
 - e. Both pharmacist and technician initials must be documented on ALL accountability forms.
 - f. Documentation format must be consistent with that study's accountability forms (i.e.; if form requests blisterpacks, document as blisterpacks, not # of tablets).
 - g. Always verify subject name/patient # /treatment # with information on enrollment sheet.

- h. Complete information requested on tear off labels and drug boxes (i.e.; subject #, subject initials, and treatment #).
13. A copy of the signatures and initials of all pharmacists and technicians involved in filling investigational prescriptions will be kept on file in the pharmacy for general documentation purposes.
14. Medications may be returned to pharmacy after usage by the subject if the protocol states to do so. Returned medications shall be stored in a separate protocol-specific area, and the quantity and date of return shall be recorded in the protocol binder, if required by protocol.
 - a. Returned (used) medications shall not be redispensed.
 - b. Medications that were “assigned” to a subject who was then disenrolled from the study may be “reassigned” if the protocol allows, the medication was never opened and never left the department of pharmacy.
15. Investigational drugs are disposed of according to institutional standard operating procedures, returned to the company sponsoring the study or by other means in accordance to study protocol.
16. Investigational controlled substances will be handled in the same manner as non-investigational controlled substances in accordance with federal and NYS law. If any discrepancy is found, an incident report will be completed and forwarded to the Director of Pharmacy and the Associate Director of Operations. If a shortage is discovered, a lost controlled substance form must be filed with the state.
17. The Regional Oncology Center (ROC) Pharmacy is part of the Department of Pharmacy, and shall be viewed as such.
18. Investigational controlled substances will only be repacked into blinding capsules by a pharmacist or under the direct supervision of a pharmacist. Repacked items will be logged into the pharmacy prepack book.

Procedure for Research Medication administration within University Hospital when a study has not yet received approval from the IRB:

1. Patient care instances addressed by this section of the policy include the non-elective admission of “local” patients (either temporary or permanent residents) on research studies, or the patient has re-located to this area and care is being transferred to a physician with Upstate admitting privileges, and the patient requires:
 - a. Admission to University Hospital but is previously enrolled on a research study using investigational agent(s), where the treating physician-investigator is not an Upstate employee.
 - b. The research study has been approved by an outside (non-Upstate) IRB, but the study has not yet gone through Upstate’s IRB process for approval.
 - c. Non-elective admissions for acute or supportive care, but not for the purpose of administering the investigational agent.
 - d. Admission for the purpose of administering an investigational study agent during hospitalization.
 - e. Determination by the attending physician and pharmacists that the investigational agent can be prepared and administered safely. However, in all instances, a full study protocol must be obtained by the University Hospital pharmacist and be provided to the pharmacy by the principal investigator or study group for reference.
2. It is the policy of the Upstate IRB that the investigational agent may be administered providing the above requirements or circumstances pertain.
 - a. In each event, it is the University Hospital admitting physician’s responsibility to notify the IRB within one week of the occurrence.
 - b. If care of the patient is being transferred to a University Hospital physician (i.e.; due to patient geographic relocation), the Upstate faculty member must submit an application and protocol for the study to the IRB for review within four weeks of his/her knowledge of the patient’s transfer. The investigational agent may continue to be administered while undergoing local, Upstate IRB review.
 - c. For patients admitted to University Hospital receiving investigational drugs from another source, it is the responsibility of the pharmacist filling the patients admitting orders to contact the source to obtain information about the drug including side effect profile and toxicity information.
3. The department of pharmacy shall obtain the medication and store it in a secure location separate from commercially available supplies. Medication will be dispensed daily by pharmacy. The medication shall not be stored in the clinic or nursing unit unless logistically necessary.
4. Record keeping of these medications shall be consistent with the procedures of all other research medications.

Safety	Excellence	Respect	Innovation	Compassion	Efficiency
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Procedure for storage of repackaged controlled substances for research:

1. Bulk containers of investigational controlled substances will be kept in the automated dispensing cabinet in the narcotics vault.
2. The following information will be included on the label attached to the medication container:
 - a. Drug/Strength/Form
 - b. Study Name/Protocol #
 - c. Quantity
 - d. Lot #
 - e. Expiration date
 - f. Date repacked
 - g. Pharmacist signature
3. Full controlled substance medication containers will be placed into a plastic bag and heat sealed prior to being placed into Pyxis narcotic vault. A label with the sealing pharmacist's signature and date will be placed over the heat seal.
4. Partial controlled substance medication containers will be labeled with a sticker showing the current quantity, the date and the initial of the pharmacist counting. A new sticker will be placed on the container each time the container is used for dispensing. The container will be placed into a plastic bag and heat-sealed prior to being placed into Pyxis narcotic vault. A label with the sealing pharmacist's signature and date will be placed over the heat seal.
5. A perpetual inventory sheet will be kept for each investigational controlled substance. This sheet will be kept in the investigational binder along with all other protocol specific instructions for that particular study.
6. The count on the medication container in the sealed plastic bag will be considered the count.
7. The person conducting the inventory will verify the sealed bag has not been tampered with.
8. If any discrepancy is found, an incident report must be completed and forwarded to the Director of Pharmacy and the Associate Director of Operations. If a shortage is discovered, a lost controlled substance form must be filed with the State.

Procedure for Transportation of research medication from the Department of Pharmacy:

The transportation of investigational study medication (i.e. vials, tablets, capsules) and study supplies (i.e. filters, infusion lines) from University Hospital Department of Pharmacy shall be handled by Department of Pharmacy personnel. Of note, the Regional Oncology Center (ROC) Pharmacy is part of the Department of Pharmacy, and shall be viewed as such in all aspects.

1. University Hospital Department of Pharmacy:
 - a. The pharmacy is locked at all times and has controlled access to authorized personnel only.
 - b. Personnel who have patient care responsibilities do not have access to the pharmacy.
2. Refrigerated or Frozen Investigational Study Medication:
 - a. Refrigerated or frozen investigational study medication is transported from University Hospital Department of Pharmacy to satellite pharmacies or the ROC pharmacy when medication is required for a study patient.
 - b. The required quantity of refrigerated or frozen medication is placed in a cooler/bag (containing refrigerated packs) in the University Hospital Department of Pharmacy and transported to the satellite pharmacy or ROC pharmacy.
 - c. It takes approximately 5 minutes to transport medication from the University Hospital Department of Pharmacy to the ROC pharmacy.
 - d. If refrigerated medication is not mixed immediately at the ROC pharmacy it is stored temporarily in a monitored refrigerator in the ROC pharmacy.
 - e. All unused investigational medication is returned to the University Hospital Department of Pharmacy when it is no longer required at the satellite pharmacy or the ROC pharmacy. Unused medication returned from satellite pharmacies will not be redispensed per sponsor requirements.
3. Ambient Investigational Study Medication or Supplies:
 - a. Ambient investigational study medication or supplies are transported from University Hospital Department of Pharmacy to satellite pharmacies or the ROC pharmacy when medication or supplies

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are required for a study patient.

- b. The required quantity of ambient medication or supplies are placed in a bag/box in the University Hospital Department of Pharmacy and transported to satellite pharmacies or the ROC pharmacy.
- c. It takes approximately 5 minutes to transport medication or supplies from the University Hospital main pharmacy to the ROC pharmacy.
- d. All unused investigational medication or supplies are returned to the University Hospital Department of Pharmacy when they are no longer required at the satellite pharmacy or the ROC pharmacy. Unused medication returned from satellite pharmacies will not be redispensed. If the protocol allows, unused supplies will be redispensed if they are unopened and not expired.

Procedure for the Disposal of research medication:

The disposal of drug supplies for research at University Hospital shall be handled by the department of pharmacy. All supplies for every research study shall be handled per the respective study protocol in the following manner:

- 1) Upon the end of a research study, the study protocol shall be reviewed to determine how to handle remaining study material. Study protocols often list the following methods:
 - a. The study sponsor will send a study monitor to retrieve all remaining study materials. If so, all materials will be stored in a segregated area in the pharmacy until the monitor is able to retrieve the materials.
 - b. The study sponsor will ask the site to ship back any remaining materials. If so, the study sponsor shall indicate how to ship materials back, give a specific address to send the materials, and provide a way-bill (prepaid Fedex, UPS or DHL) for the materials.
 - c. The study sponsor will indicate that the disposal of remaining materials on-site is acceptable. If so, a note to file for the study shall be written by the Investigational Drug Service coordinator and sent to the study PI or coordinator. This note to file shall indicate the study, all materials being handled, and their final disposition.
- 2) Study sponsors who indicate that disposal of study material on-site is acceptable shall have their material handled in the following manner:
 - a. A final inventory of study material shall be performed.
 - b. A study materials shall be placed in red sharps bins and sealed.
 - c. Environmental Services shall retrieve bins and send them out for destruction.
 - d. A note-to-file will be written listing all information pertaining to the disposal of study material.

Originating Department: Pharmacy

Contributing Department(s): Research Administration, Nursing

Reference(s): Website: <http://www.fda.gov/oc/ohrt/irbs/investigational.html>; JCAHO Guidelines; NYS Pharmacy Law;