The Right Prescription for Working with Investigational Drug Service at BMC

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What is Investigational Drug Services?

- IDS is a division of pharmacy, with an appointed investigational pharmacist, specializing in the handling, storage, labeling, and distribution of investigational agents in accordance with the most current regulatory requirements maintained by the FDA, Joint Commission, ICH, and GCP Guidelines.
Do *ALL* study drugs need to be stored and dispensed by BMC Pharmacy?

**YES**

*All* medications used in Investigational Protocols at BMC must be stored, labeled, and dispensed by BMC IDS Pharmacy. (JCAHO Medication Management Standard 7.40)

Investigational drugs must be in a securely locked, substantially constructed enclosure, with limited access to prevent theft or diversion of the substance. (CFR 312.69)
What does BMC IDS need from the Research team to get started?

- A current copy of the study Protocol, all Protocol amendments, drug brochures, IRB Approval letter, and 1572 (if an IND study)
- Study drugs
- IDS Charge Form
- Protocol activation meeting
- Lead time in advance of proposed study startup to prepare for study and get procedures written and in place
Does a protocol with study drug need to be reviewed by BMC Pharmacy?

Yes. All studies involving drugs to be used as part of a research study must be reviewed for feasibility by the BMC IDS Manager or Director of Pharmacy and signed *prior* to IRB review.

-IRB approval alone is not sufficient to activate dispensing of investigational medication from the IDS.
How do I obtain study drugs from BMC IDS Pharmacy?

- For any *outpatient* study medication, a Study Drug Request Form must be faxed to IDS Pharmacy
- A Study Drug Request Form must be signed by either a primary investigator or a sub-investigator (CFR 312.61)
- Last page of informed consent form if first dispensing
- Call BMC IDS Pharmacy if a subject is waiting at clinic
- Written expiration/retest date on the study material (GCP 5.14.5)

- Written sponsor/manufacturer memo on expiration/retest date
- Certificate of analysis per GMP
- Regulatory affairs agency (FDA) memo to a sponsor
How are the drugs handled for Inpatient protocols?

- For *inpatient* study medication, an order must be put in via SCM. Once the order has been verified, study drug will be placed inside the Pyxis under “Investigational Study Drug”.
- Parenteral study medications are prepared according to the specific protocol. All parenteral study drugs are given a 24 hour expiration unless otherwise designated by the manufacturer.
What if someone enrolled in an outpatient study is admitted to BMC?

- Once admitted, IDS Pharmacy is contacted by research team.
- If PI wants to continue the study drug during hospitalization, an order is placed into SCM and the drug is loaded into the Pyxis machine on that floor.
- PI’s consent of continuation must be documented in ‘Additional Information’ in SCM
Mr. Smith was admitted to BMC E6N. He is taking an experimental study drug from a BMC protocol in a stroke prevention trial.

- **What should the covering physician do?**
  - Research team should be contacted by physician to see if it is ok to continue study drug and to ensure safety and rule out any contraindications based on the patient’s current condition.
  - *Upon request*, IDS pharmacy will provide information about the study medication as well as contact information of the Principal Investigator and research team.
  - The physician should see if patient can bring in their own study medication.

***If research team is on a pager, please respond to your pager. BMC IDS Pharmacy cannot verify the scm order without research team doctor’s approval***
Who should be contacted if a patient is admitted who is currently enrolled in a non-BMC study?

- Shall be handled in accordance with the “Patient’s Own Medication” policy
- Ordering physician must consult with the outside investigator and get their permission to continue therapy while subject is inpatient at BMC
- Order is entered into SCM as a nonformulary medication
  - Note in the additional instructions field the primary investigator contact and their approval
  - Ordering physician shall provide documentation on identity of the study medication and appropriateness of use
How does a physician put an order into SCM for an investigational study drug?

- Select “Investigational Study Drug”
- This selection will require the physician to enter the study drug name, dosage strength, dosage, BMC Protocol #, Protocol Title, name of PI, and note of approval by PI or sub-investigator
- Additional Instructions
  - Details of the study to communicate to BMC nursing staff
Investigational Drug Storage & Handling

- Stored according to Controlled Substances Act (CFR 312.69)
- Acceptable storage conditions, temperature, storage times, reconstitution requirements (if applicable) should be determined by the sponsor for all investigational products (GCP 5.13.2)
- Packaging of study drugs to prevent contamination and deterioration during transport and storage (GCP 5.13.3)
- Address adequate and safe receipt, handling, storage, dispensing, retrieval of unused product from subject, return of unused drugs (GCP 5.14.3)
Investigational Drug Storage & Handling

- Storage of study drugs under appropriate conditions of temperature, humidity, and light so that the identity, strength, quality, and purity of the study drugs are not affected (FDA 211.142)
- The study drugs should be stored according to regulatory requirements (GCP 4.6.4)
- The study drugs should be used only according to the protocol (GCP 4.6.5)
Drug Accountability

- Records of the study drug’s delivery, inventory, use by each subject, and return/disposition of unused drugs must be kept (GCP 4.6.3)
  - Drug accountability records:
    - Shipping/Receipt logs
    - Perpetual inventory
    - Lot numbers/Kit numbers/Expiration dates
    - Patient-specific dispensing logs
    - Record of final drug disposition (e.g. destruction or return to sponsor)
Investigational Drug Disposal

(BMC Policy #8.41)

- Before returning medication to IDS Pharmacy, SC shall count and document on the bottle and any other required documents per sponsor.
- Once drugs are returned to the pharmacy by the study coordinator, they are double checked and logged in the accountability record. If there is any discrepancy, SC will be contacted.
- Investigational drugs are then stored under the PI’s name until the study monitor visits to return them to the sponsor.
- If determined in the protocol that the drug can be disposed of by IDS staff, it is done so per BMC policy.
  - Placed in marked biohazard bins to be incinerated
  - All patient information removed on boxes
Returned Drug Process

- An investigator is required to maintain adequate records of the disposition of the drug, including dates, quantity, and use by subjects. If investigation is over, the investigator shall return the unused supplies of drug to the sponsor or otherwise provide for disposition of the unused supplies of the drug under CFR 312.59. (CFR 312.62a)

- Drug study records must be kept for a duration of 2 years following the date a marketing application is approved for the drug for the indication being investigated or 2 years after the investigation is discontinued. (CFR 312.62c)
Site Monitor Visit Notification

Adequate notification shall be given when study monitors/auditors/inspectors visit so appointments can be scheduled and appropriate study documents made ready.
Utilizing IDS Services

- When using BMC IDS for an upcoming study, be sure to contact us before the study budget is approved. Failing to do this may result in unexpected study costs that could have been included in the study budget if considered early in the negotiations with the sponsor.

- As the management of some studies are more complicated than others, contact IDS for a fee schedule.
What is an IND and when is it needed?

- The Investigational New Drug application is a request for Food and Drug Administration (FDA) authorization to administer an investigational drug to humans.
  - IND also referred to as Form 1571
- IND is required when the investigational drug is a completely new chemical or if it is intended to support a:
  - New indication
  - Change in the approved route of administration or dosage level
  - Change in the approved patient population
  - Significant change in the promotion of an approved drug
- Vitamins, herbal products, and other supplements from the health store?
The 3 Types of IND Applications

- **Investigator IND**
  - Submitted by a physician to propose studying an unapproved drug, or an approved product for a new indication/patient population.

- **Emergency Use IND**
  - Allows the FDA to authorize use of an experimental drug in an emergency situation that does not allow time for submission of an IND (in accordance with 21CFR, Sec.312.23 or Sec.312.34). Also used for patients who do not meet criteria of an existing study protocol or if an approved study protocol does not exist.

- **Treatment IND**
  - Submitted for experimental drugs showing promise in clinical testing for serious or immediately life-threatening conditions while the final clinical work is conducted and the FDA review takes place.
  - Are not intended for single patient use.
What are the 3 broad areas the IND application must have?

- Animal Pharmacology and Toxicology Studies
  - Preclinical data to permit an assessment as to whether the product is reasonably safe for initial testing in humans. Also included are any previous experience with the drug in humans (often foreign use).

- Manufacturing Information
  - Information about the composition, manufacturer, stability, and controls used for manufacturing the drug substance and product to ensure the company can product and supply consistent batches of the drug.

- Clinical Protocols and Investigator Information
  - Detailed protocols for proposed clinical studies to assess whether trials will expose subjects to unnecessary risks. Also included is information on the qualifications of the clinical investigators.
How soon can the trial be started after the IND is submitted?

Once the IND is submitted, the sponsor must wait 30 calendar days before initiating any clinical trials. During this time, FDA has an opportunity to review the IND for safety to assure that research subjects will not be subjected to unreasonable risk.
What are the contents of the IND application (FDA 1571)?

- See handout
  - Items 1-20
- FDA Form 1571 Section 12
  - Form FDA 1571
  - Table of Contents
  - Introductory Statement
  - General Investigational plan
  - Investigator’s brochure
  - Protocol(s)*
  - Chemistry, manufacturing, and control data
  - Pharmacology and toxicology data
  - Previous human experience
  - Any additional information
What is a 1572 form?

- The 1572 is the statement of the investigator that he/she will abide by the federal guidelines set forth in the Code of Federal Regulations for the use of drugs in an investigational setting.
  
  - Any study operating under an IND requires a 1572
All BMC IDS policies and procedures can be found at [http://www.internal.bmc.org](http://www.internal.bmc.org) under the Pharmacy department.

- Policy 8.40 – Investigational Drug Service
- Policy 8.41 – Investigational Drug Disposal
- Policy 3.31 - Investigational Drug Storage
IDS Charge Sheet Information

- See handout
- The following fields shall be filled out:
  - Financial Manager Name and Phone Number
  - Name of funding agency
  - BUMC or BMC Account Number
  - Signature of PI
Contact Information

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