PURPOSE

This policy describes the management of investigational or study agents used for clinical research at Beaumont Health (BH). The policy is designed to protect human participants in research at Beaumont by assuring drug security, safety, and accountability.

SCOPE

This policy applies to all clinical studies involving investigational and/or study agents at BH. It also applies to key research personnel and pharmacists involved in handling investigational or study agents.

RESPONSIBILITY

The Department of Pharmaceutical Services will maintain control of all investigational and study agents used in the conduct of Beaumont human participant research. The Investigational Drug Service (IDS), physically located on the Royal Oak campus, maintains administrative control over all sites within Beaumont. The IDS may delegate direct investigational or study agent handling procedures to local Beaumont employees (e.g., Beaumont Troy, Department of Pharmaceutical Services) but will retain oversight of all processes.

Pharmacist management duties include (but are not limited to) receipt, storage, and dispensing of investigational or study agents, accountability, inventory control, randomization, packaging, labeling, providing matching placebo, compounding, meeting with study sponsors/monitors, creating Investigational Study Data sheets and educating key research personnel and hospital staff. For inpatient studies, the pharmacist is responsible for creating the order protocol request for the investigational or study agent in the EPIC medical records system.

Key research personnel responsibility for investigational and study agent management includes obtaining agent from the IDS pharmacist, providing to participants in accordance with the Institutional Review Board (IRB) approved protocol under direction of the Principal Investigator (PI), and when required, collecting drug diaries, empty packaging and/or unused investigational or study agents from participants.

BACKGROUND

Food and Drug Administration (FDA) regulations, Joint Commission hospital accreditation standards (MM.06.01.05) and Association for the Accreditation of Human Research Protection Programs (AAHRPP) accreditation standards for human research protection programs require a uniform and centralized plan for management of investigational and study agents.

DEFINITIONS

Investigational agent refers to any agent which has not received Food and Drug Administration (FDA) approval or which was previously approved and is being evaluated for a new and different indication in humans.

Study agent refers to any agent which is either: 1) FDA approved and is being used under protocol for human research, possibly as a control or outside of the FDA approved labeling; or 2) is not regulated by the FDA (such as vitamins or herbal supplements).

PROCEDURES

The PI will provide the pharmacist with the study protocol and Investigator's Brochure (if applicable). The PI will also provide the pharmacist with all

documents necessary for ordering initial and subsequent supplies of agents (if available). The PI will instruct the sponsor or agent supplier to ship the agent in care of the IDS (or another location as determined by study requirements and approved by the IDS). The pharmacist (or designee) and/or sponsor will set minimum inventory levels. These levels will be maintained via an agent reorder program which may be manual or automatic depending on the protocol. If problems develop in obtaining the agent, the PI will be notified via the research nurse clinician or clinical research manager.

As part of the IRB submission process, the PI will authorize and delegate management of the study agents/treatments, including any investigational agents, per the confines of the approved protocol, to the Investigational Drug Service. Management includes (but is not limited to) the receipt, storage, dose calculations/adjustments, preparation, dispensing, accountability, destruction and/or return of all sponsor-supplied investigational and study drug(s).

Investigational or study agent requests are made by designated key personnel to the pharmacist. Requests ***must*** be made in a written format, such as email. Telephone medication requests ***are not*** permitted, in order to eliminate errors associated with misinterpreted verbal or telephone communications. The IDS pharmacist will establish the required written format for each study (e.g. email or physical study-specific request form) and establish a study-specific request process flow. The IDS pharmacist will communicate these requirements to the clinical research manager and involved key personnel before enrollment of the first participant. All agents dispensed by the pharmacist will be labeled; labeling will include the participant's name and study ID, unless prohibited by the study design.

Positive identification of research participants must occur before involving potential or actual participants in research activities, consistent with Joint Commission "National Patient Safety Goals". Before providing an investigational/study agent, specimen collection or other services, the positive identification is repeated, using at least two participant identifiers and verifying against documentation present on the investigational/study agent packaging (as available), the research record, and the participant's verbalization. Research-specific identifiers, such as participant ID or randomization numbers or kit numbers, are verified.

All investigational or study agent will be delivered to the IDS, or another location as determined by study requirements. All original packing slips (also known as shipping invoices/records) will be maintained by the pharmacy unless otherwise determined by the IDS. The pharmacist will record receipt of each investigational or study agent shipment. Packing slips and accompanying information should be included in the pharmacy study file. Packing slips should, at a minimum, include the name and quantity of the agent, date of acceptance, and signature of individual receiving the agent. Other information found on the packing slip may include lot number(s), expiration date(s), and PI name. Properly identified agents will have shipping records reconciled to the shipping contents. Discrepancies will be resolved by contacting the agent supplier and/or study sponsor/ monitor and providing them with a report of contents damaged during shipping or missing upon delivery. Investigational

Agent Accountability Records (IAARs) or equivalent will have an entry for each drug shipment received.

Investigational and/or study agents will be securely kept in the IDS office or a satellite location (e.g. Troy Pharmacy). Each area will be uniquely designated specifically for these agents and kept separate from other non-investigational and non-study agents.

IAARs may contain the following information: agent name, strength, unit size, study title, IRB number, PI name, participant ID, manufacturer's lot number, date received/dispensed, units and doses dispensed, stock balance, and dispensing pharmacist's (or designee's) initials. Most sponsored trials will provide a study specific IAAR. The National Cancer Institute (NCI) sponsored trials use a uniform accountability record (available on their website) for most of their studies. Beaumont sponsored trials will use a template for agent accountability which may be modified to suit study requirements. Agent accountability records may be maintained on an agent basis, a participant-specific basis, or a combination of both. Participant-specific records may also be maintained by the PI/research nurse clinician/study coordinator. These records will reflect agent supplied to and returned by the study participant as well as participant compliance.

The IDS pharmacist will meet with study monitors/sponsors throughout the study providing access to investigational and study agent records.

Final reconciliation of investigational and/or study agent accountability records will be completed by the pharmacist upon notification of a study closeout by the PI, clinical research manager, research nurse clinician, or study coordinator. A closeout audit by the sponsor monitor will be arranged. At that time, detailed agent accountability records will be reconciled with shipping receipts and a physical inventory of all remaining study drug. Copies of IAARs will be provided to the monitor/sponsor. Upon reconciliation of all agent records by the monitor, investigational/study agent may be returned with documentation signed by both the Pharmacist and monitor. With written direction from the sponsor and in accordance with the Department of Pharmaceutical Services policies, investigational or study agents may be destroyed on-site. Pharmacy-related study records may be returned to the PI for inclusion in their investigator file or maintained in the IDS office at the closure of the study. Either the original documents or copies will be maintained in the IDS office.

Key research personnel involved in investigational or study agent studies will be:

- appropriately listed on the "Delegation of Authority Log" in the regulatory binder;
- listed on the IRB key personnel roster;
- perform activities appropriate to their job categories and licensures. (refer to research personnel WJQs).

Key research personnel will work closely with the pharmacist to ensure agent is available for participants in accordance with the protocol. The pharmacist will dispense the appropriate agent for each participant. The agent will then

either be hand delivered to the appropriate key personnel in the research department or clinical area or one of the appropriate key personnel will retrieve the agent from the pharmacy, consistent with Investigational Drug Service Policy Transporting of an Investigational or Study Agent for Inpatient Use or to an On-Campus Location. After use by study participants, key personnel will ensure return of all used and unused agent container/units to the Pharmacist. Participants taking agents after leaving the facility (e.g. at home) will be instructed to return all unused agents and empty packaging from used agents to the appropriate key personnel. If any agent containers/units are missing, key personnel will document and report to the PI, Pharmacist and/or sponsor as appropriate.

For blinded studies, if the knowledge of the treatment arm is medically necessary, key research personnel and the IDS pharmacist will follow procedures outlined in the protocol for unblinding, informing the PI and sponsor, and documenting circumstances appropriately.

Request Exception to Pharmacy Drug Storage Requirement

If the PI believes storage of investigational or study agent in the Pharmacy is impractical, he or she may request an exception explaining the extenuating circumstances. The IDS Pharmacist will consider an exception on a case-by-case basis only in very unusual circumstances. To grant an exception, the IDS must insure proper agent storage, inventory, handling and preparation conditions are met. Regular audits must also be conducted minimally, on a semi-annual basis. Deficiencies noted on audit may result in withdrawal of exception approval.

APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 312
International Conference on Harmonization; Good Clinical Practice: Consolidated Guideline, May 1997
Joint Commission Standard MM.06.01.05
Joint Commission 2015 National Patient Safety Goals

REFERENCES TO OTHER APPLICABLE SOPs

Research Administration Policy *Responsibilities of the Principal Investigator*
IRB Policy *Investigational New Drug Research*
Clinical Research Policy *Responsibilities of the Research Team*
Clinical Research Policy *Study Close Out*
Corporate Patient Care Policy 322, *Patient Identification*

☐ Original ☒ Revision or Review

Research Institute Compliance Committee Review Date: _____

Corporate Administration Approval:_____ Date: _____
V.P. of Research or Chief Medical Officer

Research Institute Board Approval:_____ Date: _____

Research Administration Approval:_____ Date: _____

Administrative Director