INSTITUTIONAL POLICY & PROCEDURE
Date of Original P&P: 01/15/2014
Revision No.: 1
Effective Date 05/18/2015

TITLE: Institutional Review Board Special Considerations
SC 512 Clinical Research Involving Investigational Drugs

ORIGINATOR: Institutional Official

APPROVAL: Institutional Official

POLICY STATEMENT: The use of an Investigational Drug and/or Biologic in research is subject to the United States Code of Federal Regulations Title 21 - Food & Drugs Part 312 - Investigational New Drug Application (IND). This policy defines the applicability of the Code of Federal Regulations and the procedures the Mercy Health IRB follows to determine whether an IND is needed for a clinical investigation; outlines the responsibilities of the investigator who holds the IND and establishes procedures for the proper control, storage, use and handling of investigational drugs.

GENERAL PROVISIONS:
In order to verify the validity of the IND, the Office of the IRB requires that a copy of the letter from the FDA with the IND assignment for the clinical investigation under review or a letter from the FDA stating that an IND is not needed, be submitted to the IRB with the new protocol application.

In accordance with FDA regulations 21 CFR 312.3, and Good Clinical Practice (GCP) guidelines, the requirements applicable to a sponsor-investigator under part 312 include both those of an investigator and a sponsor. The responsibilities include the following:

- Maintaining the Investigational New Drug application
- Obtaining Qualified Investigators and Monitors
- Providing Necessary Information and Training for Investigators
- Monitoring the Investigation
- Controlling the Investigational Agent
- Reporting Significant Adverse Events to FDA/Investigators
- Maintaining and Retaining Accurate Records
- Implementing and Maintaining Quality Assurance with Written Standard Operating Procedures (SOP’s)

When a Mercy Health Investigator is the sponsor of the Investigational New Drug (sponsor-investigator), the Mercy IRB requires the investigator to meet with the Medical Director from the Office of Research and Innovation to review his/her FDA responsibilities as a sponsor-investigator. The Research Medical Director is responsible for providing the Mercy Health Office of the IRB with documentation in writing that the review has taken place, and that the investigator understands his/her FDA Investigational New Drug application responsibilities. The Investigator must also follow other established pre-IRB submission review processes such as review by the Mercy Health Research Oversight Committee.

If the investigator indicates on their application that there is no Investigational New Drug number, the IRB will be responsible for determining whether an Investigational New Drug Application is required in accordance with the following criteria:
In accordance with FDA regulations 21 CFR 312.2 all clinical investigations that involve drugs (any use of a drug other than the use of a marketed drug in the course of medical practice must have an Investigational New Drug Application, unless the drug meets one of the exemptions from the requirement for an Investigational New Drug Application in 21 CFR 312.2(b). These categories are:

Exemption #1:
- The drug is lawfully marketed in the United States.
- The investigation is not intended to be reported to FDA as a well-controlled study in support of a new indication for use nor intended to be used to support any other significant change in the labeling for the drug.
- The investigation is not intended to support a significant change in the advertising for the product.
- The investigation does not involve a route of administration or dosage level or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product.
- The investigation is conducted in compliance with the requirements for institutional review set forth in part 56 and with the requirements for informed consent set forth in part 50.
- The investigation is conducted in compliance with the requirements of 21 CFR 312.7.
- The research does not involve an exception from informed consent under 21 CFR 50.24.

Exemption #2:
The research involves one of the following in vitro diagnostic biological product:
- Blood grouping serum;
- Reagent red blood cells; and
- Anti-human globulin.
- The in vitro diagnostic biological product is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure.
- The in vitro diagnostic biological product is shipped in compliance with 21 CFR 312.160.
- The research does not involve an exception from informed consent under 21 CFR 50.24.

Exemption #3:
- The drug is intended solely for tests in vitro or in laboratory research animals.
- The drug is shipped in compliance with 21 CFR 312.160.
- The research does not involve an exception from informed consent under 21 CFR 50.24.

Exemption #4:
- Use of a placebo.
- The research does not involve an exception from consent under 21 CFR 50.24.

In accordance with FDA regulations 21 CFR 312 and Mercy Health policies, the Sponsors and/or Investigators are responsible for the proper ordering, handling, storage and disposition of investigational drugs in clinical trials at Mercy Health. The Principal Investigator may delegate a portion of this responsibility to the Mercy Health Investigational Drug Service. In order to do so, the PI must contact the IDS serve at 616-685-6100 while in the research planning stages prior to IRB submission.
Principal Investigator must ensure the following takes place:

1. Prescribing

Prescribing an investigational drug must be done by an investigator listed on the IRB approved protocol. The authorized prescriber must be licensed and be credentialed through Mercy Health.

2. Procurement

Procurement of an investigational drug must be done by the Principal Investigator or Investigational Drug Service Representative according to the terms of the executed agreement and only after the protocol has been approved by the IRB.

3. Receipt

Investigational drugs may only be received by the Principal Investigator or designated study personnel at a Mercy Health business address (the address listed on the 1572).

Upon receipt of the investigational drug, the Principal Investigator or a designated Investigational Drug Service staff member will inventory the shipment to ensure that the information on the packing slip matches with what has been shipped, including lot numbers and quantity.

Packing slips and documentation of inventory must be maintained with the study records.

4. Storage/Labeling

Investigational drugs used in conjunction with a research protocol must be kept in a locked and secured area.

Additional labeling for inpatient Investigational Drugs shall be in compliance with Mercy Health policies. Any other information pertinent to administration of the Investigational Drug may also be included on the label (e.g. expiration date).

Labeling for outpatient Investigational Drugs must include: participant identifier, a description of the IP, Instructions for Use/Administration, Lot#, Expiration Date, Prescribing Physician, and the following statement: For Investigational Use Only as outlined in the Operations Manual for the Investigational Drug Service.

Access to investigational drugs must be limited to personnel designated by the Principal Investigator.

5. Dispensing

- The investigational drug may not be given to anyone not enrolled in the study.
- The Principal Investigator must not supply the investigational drug to any person not authorized.
- Dispensing of the study drug must be done by an authorized prescriber listed on the IRB approved protocol.
- For accountability purposes an investigational drug accountability log(s) must be kept for all investigational drug studies. Documentation of the following elements should be recorded for each drug used:
  - Date Received
  - Date Returned
  - Date Dispensed
  - Investigator Name
Institutional Policy & Procedure

- A description of the IP (i.e. name of study drug, protocol id #, drug dose, form, strength)
- Participant Identifier (i.e. Research participant ID, name, initials or a combo of these)
- Quantity Dispensed
- Dose Form and Strength
- Quantity Received
- Balance Forward
- Balance
- Manufacturer
- Lot #
- Recorders Initials
- Name of Institution
- Protocol Number
- Agent Name
- Protocol Title
- Dispensing Area
- Site Number

Personnel may not remove any drug(s) from the standard drug inventory and substitute them for an investigational drug, even if the drug, under study, is approved and used in practice.

6. Maintaining a Drug Accountability Log:

- Investigational drug logs must be maintained with the study’s regulatory records for the period of time required by the federal regulations or terms of the agreement, whichever is longer.
- The full names, titles/positions, signatures and/or initials of all Mercy Health personnel responsible for maintaining or documenting in the log(s) must be indicated on either a cover sheet or in the log itself.
- The Principal investigator or designated Investigational Drug Service personnel must regularly review the drug logs to ensure that there is an adequate amount of drugs available to conduct the study procedures.
- Drug records must show the receipt, shipment, or other disposition of the investigational drug in compliance with Mercy Health Saint Mary's Operations Manual, Investigational Drug Service.
- The disposition of the drug, including dates, quantity and use by research subjects must be recorded.

7. Disposition

7.1. Upon conclusion or termination of the clinical investigation, or by the sponsor’s request, the principal investigator shall return to the sponsor any remaining supply of the investigational drug or otherwise dispose of the drug as the sponsor directs. The investigational drug should not be disposed of by the principal investigator or study personnel without obtaining advanced written permission from the sponsor.

7.2. Documentation of why, when, and the personnel involved is required.

DEFINITIONS:

Research: As defined by Department of Health and Human Services (DHHS), any systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

Under FDA regulations activities are “research” when they involve:

a. Use of a drug other than the use of an approved drug in the course of medical practice (21 CFR 312.3 (b)).
b. Use of a medical device other than the use of an approved (means approved by the FDA for marketing) medical device in the course of medical practice (Food, Drug and Cosmetic Act 530 (g)(3)(a)(i)).

Investigational New Drug: A new drug or biological drug that is used in a clinical investigation. The term also includes a biological product that is used in vitro for diagnostic purposes. The terms "investigational drug" and "investigational new drug" are deemed to be synonymous for purposes of this part. 21CFR 312.3

Drug Dispensation: The term dispense means the final association of a drug with a particular patient pursuant to the prescription, drug order, or other lawful order of a prescriber and the professional judgment of and the responsibility for: interpreting, preparing, compounding, labeling, and packaging a specific drug.

Drug Used in Clinical Investigation: Any drug, biological, botanical or other substance used specifically for a clinical investigation as described in the investigational protocol.

Investigational Drug Service (IDS): Refers to the Mercy Health pharmacy responsible for the storage and dispensation of investigational drugs.

Sponsor: Means a person who takes responsibility for and initiates a clinical investigation. The sponsor may be an individual or pharmaceutical company, governmental agency, academic institution, private organization, or other organization. The sponsor does not actually conduct the investigation unless the sponsor is a sponsor-investigator.

Sponsor-Investigator: Means an individual who both initiates and conducts an investigation, and under whose immediate direction the investigational drug is administered or dispensed. The term does not include any person other than an individual. The obligations of a sponsor-investigator include both those of a sponsor and those of an investigator.

REFERENCE:
21 CFR 50
21 CFR 60
21 CFR 312
Guidance for Industry E6: Good Clinical Practice, Consolidated Guidance
Mercy Health Pharmacy Policy INST. 12/102 Formerly MSP 119 & Rx 560/441

ATTACHMENTS:
SC 512-A Worksheet for the Review of Clinical Trial Involving an Investigational Drug or Biologic

PROCEDURE: All Mercy Health Campuses

<table>
<thead>
<tr>
<th>Responsibility</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>IRB Specialist/IRB Coordinator</td>
<td>1. Review the newly submitted IRB application for initial review and determine if an investigational drug is part of the clinical trial. 2. Ensure the submission package has all of the needed documentation required for review of an IRB application for initial review that involves an investigational drug.</td>
</tr>
</tbody>
</table>

Version Date 05/18/2015
3. Notify the IRB Chairperson of the newly submitted IRB application for initial review and inform them the study includes the use of an investigational drug.
4. Provide primary and secondary reviewers with appropriate protocol review worksheets.
5. Upload completed worksheets into the IRB Manager system when they are returned.
6. Provide the completed forms to the Investigator for review and response.
7. Issue correspondence letters as assigned by the IRB Chairperson.

IRB Chairperson

1. Review the initial application package and assign appropriate reviewers.
2. Ensure all reviewers' findings have been addressed and prepare to discuss reviewer findings with the IRB Committee.

Investigators

1. Submit all IRB required documentation
2. Accept responsibilities for the clinical trial and control of the investigational drug. Certain responsibilities for control of the drug may be designated to the Investigational Drug Service.

Investigational Pharmacist

1. Manage Investigational Drug as designated by the Principal Investigator, study sponsor and as outlined in the Investigational Drug Service Manual

Medical Director of Office of Research and Innovation

1. Meet with the PI who holds the IND and discuss expectations and responsibilities.
2. Provide the Office of the IRB with written notification of completion of the required meeting.

IRB Members

1. Review the proposed study and ensure the study plan is adequate enough to ensure the general responsibilities of investigators; control of the investigational drug, record keeping, record retention and required reporting are adequate for the type of investigational drug or biologic the investigator is proposing to use.

CONCURRENT CONSENTS:

Institutional Official

Version Date 05/18/2015