SOP 502A: CATEGORIES OF RESEARCH – DRUGS

1. POLICY

The IRB shall review all human participant research involving investigational drug studies. Investigational drug studies typically pose greater than minimal risk and therefore require convened IRB review.

The category of research covered by this policy involves methodology that requires additional considerations or for which there are federally mandated determinations that IRBs are required to make and document.

All investigational drugs or agents used in human participant research shall be stored, handled, and dispensed in accordance with University policy and state and federal laws and regulations. If an investigational pharmacy is not utilized for dispensing the investigational drugs and agents, the investigator shall assure that dispensing is in accordance with University policy and state and federal laws and regulations.

Specific Policy

1.1 Clinical Research Involving Investigational Drugs

The review of most studies involving investigational drugs requires convened IRB review. Additional review by other University committees may be required.

1.1.1 Determination of a Valid Investigational New Drug (IND)

When research involves the use of a drug other than a marketed drug in the course of medical practice, the drug shall have an IND unless the protocol meets one of the following FDA exemptions from the requirement to have an IND. The IND goes into effect 30 days after the FDA receives the IND, unless the sponsor receives earlier notice from the FDA. The IRB requires investigators to provide documentation of the IND number for the investigational drug when submitting new research projects for investigator-initiated or industry-sponsored research by submitting a letter from the FDA, a letter from the sponsor, or a commercial protocol with the IND number.

Exemption 1 (all must be true)

- The drug product 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.
- If the drug that is undergoing investigation is lawfully marketed as a prescription drug product, 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 21 CFR 50 and 56.
The investigation is conducted in compliance with the requirements of 21 CFR 312.7.

Exemption 2
A clinical investigation is for an *in vitro* diagnostic biological product that involves one or more of the following:

- Blood grouping serum.
- Reagent red blood cells.
- Anti-human globulin.
- The diagnostic test is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure.
- The diagnostic test is shipped in compliance with 21 CFR 312.160.

Exemption 4
A clinical investigation involving use of a placebo if the investigation does not otherwise require submission of an IND.

1.1.2 **Investigator Responsibilities for Investigational Drug Dispensing and Accountability**
An investigator shall administer the investigational drug only to participants under the investigator’s personal supervision or under the supervision of a Sub- investigator responsible to the investigator.

The investigator shall not supply the investigational drug to any person not authorized to receive it.

The investigator shall maintain adequate records of the disposition of the investigational drug, including usage, dates, quantity received, and use by the participants.

If the research is terminated, suspended, discontinued, or completed, the investigator shall return the unused supply of the investigational drug to the sponsor or otherwise provide for the disposition of the unused investigational drug consistent with the terms of the underlying research agreement.

The initial research project submission shall include the location where the drug will be stored and who will dispense it (i.e., the hospital pharmacy, the out-patient pharmacy, the investigator's office). If the investigational drug is subject to the Controlled Substances Act, the investigator shall take adequate precautions to prevent theft or diversion of the investigational drug. This includes storage of the investigational drug in a secure, well-constructed cabinet or other securely locked, well-constructed enclosure with limited access. The pharmacist member or designee of the IRB shall review the plan to store and dispense drug for adequacy.

Investigators shall have access to training in investigational drug storage, dispensing, and accountability in the Good Clinical Practice course in CITI. Investigators are responsible for making themselves familiar with and complying with all requirements of the Oklahoma Bureau of Narcotics and Dangerous Drugs, the Drug Enforcement
Agency, and any other agencies having jurisdiction over the investigational drug or the investigator’s license to use it.

For VA Research: The investigator shall inform the VA pharmacy service that IRB and Research and Development Committee (R&D) approval has been obtained through the use of VA Form 10-1223. The investigator shall provide the pharmacy with the currently approved protocol, a signed copy of the VA Form 10-1086 to document each participant’s consent to participate in the research project, documentation of IRB approval (including continuing review approval, if applicable) or other relevant approvals, a copy of VA Form 10-9012, if applicable, copies of sponsor-related correspondence specific to the appropriate drugs, and copies of all correspondence addressed to the investigator from the FDA specific to the investigational drug(s). The investigator shall inform the Chief, Pharmacy Service, and the R&D Committee, when the research has been terminated, suspended, or closed. The investigator shall comply with all dispensing requirements and with all documentation requirements and make relevant records accessible to the investigational drug pharmacist upon request.

1.1.3 Investigational Use of Marketed Drugs

Investigational use is the use of an approved drug in the context of a clinical study protocol. When the principal intent is to expand the drug’s safety or efficacy, an IND application may be required. However, according to 21 CFR 312.2, the clinical investigation of a marketed drug may not require submission of an IND if all five of the following conditions are met:

(A) it is not intended to be reported to FDA in support of a new indication for use or to support any other significant change in the labeling for the drug;

(B) it is not intended to support a significant change in the advertising for the product;

(C) it does not involve a route of administration or dosage level, use in a research project population, or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product;

(D) it is conducted in compliance with the requirements for IRB review and informed consent [21 CFR parts 56 and 50, respectively];

(E) it is conducted in compliance with the requirements concerning the promotion and sale of drugs [21 CFR 312.7]; and it does not intend to invoke 21 CFR 50.24.

All investigator-initiated research in which a drug is being used for its approved indication may not require submission of an IND application to the FDA. The FDA may grant an exemption or may assign an IND number. When the investigator holds the IND, additional reporting responsibilities are required of the investigator. These reporting requirements include an annual report to the FDA.

The investigator considers whether or not an IND is indicated when s/he fills out the IND sub-form. The IRB considers whether or not an IND is indicated when reviewing the IND sub-form the investigator provides. In the event of a disagreement, the investigator will be requested to submit the study for IND review with the FDA, which will have final say.

1.1.4 Investigational Drug Protocols

An investigational new drug is a drug that is used in a clinical investigation and that has not been approved by the FDA to be marketed or that has not been approved by the FDA for the indication(s) the investigator will study.
The IRB shall carefully scrutinize the following for all investigational drug studies:

A. Scientific soundness – research validity and value.

B. Research project design for the research project population, trial phase, and mechanism for data analysis and surveillance.

C. Risk/benefit analysis and review of the procedure for obtaining informed consent.

D. Investigator qualifications – investigator experience and resources to carry out the protocol.

E. Conflicts of interest that must be addressed.

F. Confidentiality safeguards – how information will be handled.

G. Data and safety monitoring – the level of monitoring for the level of risk.

H. Participants must be advised in the informed consent and HIPAA form that the FDA may access their medical records as they pertain to the research project.

1.1.5 International Investigational Drug Research

For FDA-regulated research involving an investigational drug conducted outside of the United States, an IND is not required provided the research is conducted under the Declaration of Helsinki (1989) and Good Clinical Practice guidelines. If, however, the investigation is intended to be reported to the FDA as a well-controlled study in support of a new indication for use, intended to be used to support any other significant change in the labeling for the drug or intended to support a significant change in the advertising for the product, then an IND would be required under FDA regulations.

2. SCOPE

This SOP applies to all research studies involving investigational drugs submitted to the IRB.

3. RESPONSIBILITY

3.1 The HRPP Director or IRB designee is responsible for maintaining up-to-date review tools for review of this type of research.

3.2 The IRB Chair or IRB designee is responsible for providing IRB members adequate submission review training and ongoing guidance and for selecting one Primary and one Secondary reviewer with the relevant expertise to perform reviews and make necessary recommendations on approval decisions by the IRB. If the IRB Chair or IRB designee cannot select Primary and Secondary reviewers with the relevant expertise, the IRB Chair or IRB designee defers the review to another IRB with Primary and Secondary reviewers with the relevant expertise or obtains consultation for that expertise.

3.3 The IRB Reviewer is responsible for conducting appropriate review of research planned for these categories in consultation with appropriate experts and resources.

3.4 Communication with the FDA is the responsibility of the IRB, the sponsor, and the sponsor-investigator as appropriate.

4. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46
21 CFR 50, 56
5. REFERENCES TO OTHER APPLICABLE SOPS

None

6. ATTACHMENTS

- 203-A HSC Reviewer Checklist
- 203-A-1 NC Reviewer Checklist
- 603A-C VA Form 10-9012 Investigational Drug Information Record

7. PROCESS OVERVIEW

7.1 The investigator submits a new study application and uploads all applicable documents into the IRB electronic information system.

7.2 The submission is received in the IRB Office and processed (see SOP 301: Research Submission Requirements and SOP 403: Initial Review – Criteria for IRB Approval). The submissions with all applicable documents are made available to all IRB members.

7.3 The IRB Administrator conducts a pre-review of the submission and verifies all necessary documents are received as required, including documentation of a valid IND, investigator’s brochure or drug package insert. The IRB Administrator also verifies if additional University committee review or information is required. The IRB Administrator communicates with the investigator and/or research staff to obtain any addition information and/or reviews. If the research project is investigator-initiated, the investigator shall forward to the IRB a copy of all communications with the FDA regarding the IND.

7.4 The IRB Administrator assigns the submission either to the appropriate Board agenda or to the IRB Chair/IRB designee.

- 7.4.1 If to an IRB agenda, the process follows SOP #403: Initial Review – Criteria for IRB Approval
- 7.4.2 If to the IRB Chair / IRB Designee, the process follows SOP #402: Expedited Review

7.5 If an IND is required, final IRB approval shall not be granted until the IND process is complete and the necessary documents are received.

7.6 Following review of the submission, the IRB Administrator updates the outcome of the IRB review then communicates the outcome and any stipulations to the investigator. The IRB Administrator posts the final IRB approval to the next appropriate IRB agenda.

7.7 Enrollment into the research project may not commence until all required University committees have completed their review and the research contract is signed, if applicable.

APPROVED BY: _______________________________ DATE: 01/06/2020

NEXT ESTABLISHED REVIEW DATE: AUGUST 2020