SOP 502B: CATEGORIES OF RESEARCH - BIOLOGICS

1. POLICY

The IRB shall review all human research involving biologics. These studies pose greater than minimal risk and therefore require convened IRB review.

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

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

Specific Policy

1.1 Clinical Research Involving Biologics

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

1.1.1 Determination of a Valid IND

When research involves the use of a biologic other than a marketed biologic in the course of medical practice, the biologic shall have an IND unless the protocol meets one of the following FDA exemptions from the requirement to have an IND.

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 3
A clinical investigation involving use of a placebo if the investigation does not otherwise require submission of an IND
The IRB requires investigators to provide documentation of the IND number when submitting new projects to the IRB 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.

1.1.2 Investigator Responsibilities for Biologic Dispensing and Accountability

The investigator shall administer the biologic 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 biologic to any person not authorized to receive it.

The investigator shall maintain adequate records of the disposition of the biologic, including dates, quantity, and use by the participants.

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

All investigational biologics shall be stored in the pharmacy or other location designated.

The IRB shall approve the plan submitted by the investigator to the IRB for storing, dispensing, and disposing of the investigational biologic, which shall be consistent with the underlying research agreement.

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 biologic drug or the investigator’s license to use it.

1.1.3 For VA Research:

VA human research involving biologic drugs, as regulated by the Food, Drug, and Cosmetic Act, must be conducted in accordance with all applicable VA and other Federal requirements including, but not limited to VHA Directive 1200.05, VHA Handbook 1108.04, and FDA regulations. This applies to investigator conduct and IRB approval of biologic drug research projects, as well as to storage and security procedures for biologic drugs. The investigator must:

(A) Provide the VA Pharmacy Service or Research Investigational Pharmacy information on each research participant receiving a biologic drug through the electronic medical record (CPRS) or other locally approved means. Documentation is to include allergies, toxicities, or adverse drug events related to the biologic drug, or the potential for interaction with other drugs, foods, or dietary supplements, i.e., herbals, nutriceuticals (see VHA Handbook 1108.04).
(B) Ensure the local VA Pharmacy Service or Research Service Investigational Pharmacy receives:

(a) Documentation of initial and subsequent IRB approvals, and any other relevant approvals;

(b) Documentation of R&D Committee approval;

(c) A copy of VA Form 10-9012, Investigational Drug Information Record, when applicable;

(d) A copy of the current approved protocol;

(e) A copy of the informed consent documents for each research participant with all appropriate signatures;

(f) Documentation of the IRB continuing review approval;

(g) Copy of current or updated Delegation of Authority form;

(h) Copies of sponsor-related correspondence specific to the drug(s) as appropriate; and

(i) Copies of all correspondence addressed to the investigator from the FDA (and other involved authorities) specific to the biologic drug(s) as appropriate.

(C) Inform the Chief of the Pharmacy Service, the research pharmacy when applicable, and the IRB in writing when a research project involving biologic drugs has been suspended, terminated, or closed.

(D) Comply with all dispensing requirements.

(E) Comply with all documentation requirements and make relevant records accessible to the investigational drug pharmacist when requested (VHA Handbook 1108.04).

(F) Comply with all VHA pharmacy requirements regarding receiving, dispensing, storing, and record keeping for investigational and/or biologic drugs.

1.1.4 Investigational Use of Marketed Biologics

All investigator-initiated research in which a biologic is being used for other than its approved indication requires submission of an Investigational New Drug (IND) application to the FDA. The FDA may grant an exemption or may assign an IND number. When the investigator holds the IND, additional FDA reporting responsibilities are required of the investigator.

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.

The IRB requires investigators to provide documentation of the IND number when submitting new research projects to the IRB for investigator-initiated or industry-sponsored research.

1.1.5 Investigational Biologic Research Projects

An investigational new biologic is a new product or biologic that is used in a clinical investigation and that has not been approved by the FDA to be marketed.

The IRB shall review the following for all studies involving the use of biologics:

A. Scientific soundness – research validity and value.
B. Research project design to the research 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 research project.
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. Research participants must be advised in the informed consent documents and HIPAA form that the FDA may access their medical records as they pertain to the research project.

1.1.6 Gene Transfer
The Institutional Biosafety Committee, prior to IRB approval, must approve all gene transfer research projects. All gene transfer research projects require review by the convened IRB.

2. SCOPE
This SOP applies to all biologics research projects regarding biologics 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 biologics 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 regarding biologics research 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
   21 CFR 312.2(b), 312.7
   OHRP Guidance Document, IRB Guidebook

5. REFERENCES TO OTHER APPLICABLE SOPS
   SOP 301: Research Submission Requirements
   SOP 402: Expedited Review
   SOP 403: Initial Review – Criteria for IRB Approval
6. ATTACHMENTS
   203-A HSC Reviewer Checklist

7. PROCESS OVERVIEW
   7.1 The investigator or investigator staff 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 and an 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 additional 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 IRB Chair/IRB Designee, the process follows SOP 402: Expedited Review
   7.5 If IBC review is required, final IRB approval shall not be granted until documentation of IBC approval has been received.
   7.6 Following review of the submission, the IRB Administrator updates the outcome of the IRB review and 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: 09/03/2019

NEXT ESTABLISHED REVIEW DATE: AUGUST 2020