Use of Investigational Drugs or Biologics

1.0 Purpose

The purpose of this policy is to define requirements and establish a procedure for Wright State University Institutional Review Board review and approval of clinical research that involves investigational drugs and biologics.

2.0 Scope

This policy also applies to research involving investigational drugs or biologics in which the Wright State Institutional Review Board (hereafter referred to as IRB) acts as an IRB of record for Wright State University, as well as, for an external Relying Institutions (e.g., Premier Health, Dayton VA Medical Center, etc.…). Investigators conducting drug/biologic research at Relying Institutions must also understand and comply with institutional-specific requirements (e.g., use of research pharmacy) and policies that are in addition to the requirements set forth in this policy.

3.0 Definitions

3.1 **Biological Product or Biologic** means a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, gene therapies, cellular therapies, or analogous product applicable to the prevention, treatment, or cure of a disease or condition of human beings. Biological products also include immunoglobulin products, monoclonal antibodies, products containing cells or microorganisms, nanoparticle technology and most proteins intended for therapeutic use.

3.2 **Clinical Investigation** means any experiment that involves a test article (i.e., drug, biologic, device) and one or more human subjects that either

- 3.2.1 Meets the requirements for prior submission to FDA under sections 505(i) or 520(g) of the Food, Drug, and Cosmetic Act: or
- 3.2.2 Need not meet the requirements for prior submission to FDA under the sections noted above, but the results of which are intended to be later submitted to or held of inspection by FDA as part of an application for a research or marketing permit.

3.3 **Investigational Drug** means a drug or biologic (i.e., not approved for marketing by FDA for indication under investigation) 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 policy.

3.4 **Investigational New Drug Application (IND)** means an application that permits an investigational drug that would otherwise be required to have pre-market approval by FDA to be legally shipped for a clinical investigation.

3.5 **Investigator** means the Project Director/Principal Investigator (PD/PI) and any other person, regardless of title or position, who is responsible for the design, conduct, or reporting of research, or proposing of research, including persons who are subcontractors, collaborators or consultants. At Wright State and its relying hospitals this definition includes, but is not limited to, the following roles: Principal investigator, co-investigators, research coordinators, research associates, collaborators and consultants, and may include research assistants and students as identified by the PD/PI depending on their specific roles and responsibilities.

3.6 **Sponsor** means a person who initiates, but who does not actually conduct, the investigation, that is, the investigational device is administered, dispensed, or used under the immediate direction of another individual. A person other than an individual that uses one or more of its own employees to conduct an investigation that it has initiated is a sponsor, not a sponsor-investigator, and the employees are investigators.

3.7 **Sponsor-Investigator** means an individual who both initiates (i.e., obtains an IND or IDE) and conducts an investigation and under whose immediate direction the investigational drug or biologic is administered, dispensed, or used. The obligations of a sponsor-investigator under this policy include those of an investigator and those of a sponsor.

4.0 Policy

This policy defines the applicability of the federal regulations and the procedures the IRB follows to determine whether an IND is needed for an investigation; outlines the responsibilities of the investigator and/or sponsor who holds the IND and establishes procedures for the proper control, storage, use, and handling of investigational drugs and biologics.

When human subjects research involves the use of drugs or biological products, the Food and Drug Administration (FDA) regulations apply. Investigators must provide sufficient information about the drug or biologic for the IRB to evaluate its associated risks and benefits, including the FDA approval status of the product (i.e., approved for marketing or investigational).

An Investigational New Drug Application (IND) must be filed with the FDA to test the safety and efficacy of a new/investigational drug for marketing approval. Studies involving the "investigational/research use" of an approved drug also require an IND if the intent of the study is to generate data that will lead to a new clinical indication, formulation or advertising claim, or the study includes a new dose, population, or other factor that significantly increases risk (or decreases acceptability of the risk).

5.0 Procedure

5.1 Exemptions

The clinical investigation of a marketed drug product requires submission of an IND application to the FDA unless one of the exemption categories (21 CFR 312.2(b)(1)) below applies and the investigation does not involve an exception from the informed consent requirements for emergency research (21 CFR 50.24):

5.1.1 The clinical investigation of a drug product that is lawfully marketed in the United States is exempt from the requirements if all of the following apply (21 CFR 312.2(b)(1):

- The investigation is not intended to be reported to the 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 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 the requirements for institutional review set forth in 21 CFR 56 and with the requirements for informed consent set forth in 21 CFR 50; and

- The investigation is conducted in compliance with the requirements of 21 CFR 312.7 regarding promotion of investigational drugs.

5.1.2 A clinical investigation involving blood grouping serum, reagent red blood cells, or anti-human globulin if:

- It is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure and

- It is shipped in compliance with 312.160.

5.1.3 Investigational drug use intended solely for tests in vitro or in laboratory research animals also is exempt from IND requirements.

It is important to understand that exemption from IND requirement is not the same as exemption from IRB review and approval. Investigators conducting research that is exempt under 5.1.1 or 5.1.2 must still meet all other human subject research requirements.

5.2 Investigator Submission Requirements for Research Involving an IND

Investigators relying on the IRB for review of human subject research are required to complete the Initial Review Form via electronic submission system and provide all required information and documents for review so that the IRB can assess the risks and potential benefits to subjects. As part of this submission, documentation regarding the IND number granted by the FDA must be provided – either via a copy of sponsor/FDA correspondence or the sponsor's protocol cover sheet. The investigator and members of the research team also must complete a Form FDA 1571 and maintain it in the regulatory binder/study file.

Investigators who also want to act as the study sponsor (i.e. prepare, submit, and maintain IND) must contact the Wright State Vice Provost for Research (and relevant hospital officials, when applicable) to obtain permission prior to submission to the IRB or FDA.

It is important to also understand that "off-label" use of an FDA-approved, marketed drug (i.e., a use other than the indication(s) approved by the FDA) by a physician for treatment/clinical care purposes does not require an IND or IRB approval. However, when such uses meet the regulatory definitions of human subject research or clinical investigation, IRB approval is required. An IND may also be required unless research qualifies for exemption described in Section 5.1.

Additional requirements apply to the emergency or "compassionate" use of an investigational drug or biologic. For more information about those requirements see the *Emergency Use* and/or *Expanded Access Program for Drugs and Biologics* policies.

5.3 IRB Review

Research involving a drug or biologic for which an IND is required is not eligible for expedited review. The convened IRB will review proposed research involving investigational drugs or biologics in accordance with the *Convened Institutional Review Board Review* policy and confirm the following prior to granting final approval:

5.3.1 There is available clinical and non-clinical information on the investigational product that is adequate to support the proposed research.

5.3.2 There is documentation of a valid IND unless the proposed use of the drug or biologic meets one of the FDA exemptions from the IND requirements.

5.3.3 There is an adequate plan for monitoring data to ensure the safety of subjects and for reporting adverse events and unanticipated problems involving risks to subjects or others.

5.3.4 There is a plan for control, accountability, and storage of the investigational drug or biologic that ensures that the product will be used only in the approved research under the direction of the approved investigator(s).

6.0 Responsibilities and Authorities

In accordance with FDA regulations 21 CFR 312 and Wright State/relying hospital policies, the sponsors and/or investigators are responsible for the proper ordering, handling, storage, and disposition of investigational drugs in clinical trials. Additionally, the following items must be ensured:

6.1 Prescribing

Prescribing an investigational drug or biologic must be done by an authorized prescriber listed on the IRB-approved protocol.

6.2 Procurement

Procurement of and investigational drug or biologic must be done by the Principal Investigator (PI) or designated study personnel in partnership with the designated pharmacy in accordance with the terms of the executed research agreement and only after the study has been approved by the IRB.

6.3 Receipt

6.3.1 Investigational drugs or biologics may only be received by the designated pharmacy, PI or designated personnel at the business address listed on FDA Form 1572.

6.3.2 Upon receipt of the investigational drug or biologic, the designated pharmacy, PI or designee will inventory the shipment to ensure that the information on the packing slip matches exactly with what has been shipped, including lot numbers and quantity.

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

6.4 Storage/Labeling

6.4.1 Investigational drugs used in conjunction with a research protocol must be kept in a locked and secured area and must be labeled in a way to inform non-research staff of the investigational product status (e.g. “Caution: New Drug-Limited by Federal (or United States) law to Investigational Use”).

6.4.2 Any other information pertinent to administration of the investigational drug may also be included on the label (e.g., expiration date).

6.4.3 Labeling for outpatient investigational drugs must include:

- Subject study identification (ID) number
- Date dispensed
- Prescription number
- Study drug name
- Directions for use
- Name of the PI, and
- Name and address of the prescriber and quantity dispensed.

6.5.4 Access to investigational drugs/biologics must be limited to personnel designated by the PI.

6.5.5 Drugs/biologics must be stored according to IRB-approved study protocol.

6.5 Dispensing

6.5.1 The investigational drug/biologic may not be given to anyone not enrolled in the study.

6.3.2 Dispensing of the study drug must be done by an authorized prescriber listed on the IRB approved protocol.

6.6.3 For accountability purposes, an investigational drug/biologic accountability log(s) must be kept for all investigational drug studies. Documentation of the following elements should be recorded for each drug/biologic used:

- Name of PI
- Name of study drug/biologic
- Protocol title
- Drug dose, form, and strength
- Expiration date of the drug (if available)
- Research subject study ID number

- Date dispensed
- Time dispensed, when applicable
- Quantity dispensed
- Dose
- Date returned
- Quantity returned
- Lot #, and
- Signature and/or initials of staff member

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

6.7 Maintaining a drug accountability log

6.7.1 Investigational drug/biologic log(s) must be maintained with the study's regulatory binder/file.

6.7.2 The full names, titles/positions, signatures and/or initials of all study personnel responsible for maintaining or documenting in the log(s) must be indicated on either a cover sheet or in the log(s) itself.

6.7.3 The PI or designated study personnel must regularly review the drug log(s) to ensure that there is an adequate amount of drug available to conduct the study procedures.

6.7.4 Records must show the receipt, shipment, or other disposition of the investigational drug/biologic.

6.7.5 The disposition of the drug/biologic, including dates, quantity, and use by research subjects must be recorded.

6.8 Disposition/Return

6.8.1 Upon conclusion or termination of the clinical investigation, or by the sponsor's request, the PI shall return to the sponsor any remaining supply of the investigational drug/biologic or otherwise dispose of the drug as the sponsor directs. The investigational drug should not be disposed of

by the PI or study personnel without obtaining written permission from the sponsor.

6.8.2 Documentation of why, when, and the personnel involved in disposition or return is required.

7.0 Records:

All records related to this policy will be stored and maintained in accordance with any Wright State policy, federal regulations and sponsor requirements associated with the human subject research under review by the IRB.

8.0 References:

8.1 21 CFR 312
8.2 21 CFR 50
8.3 21 CFR 56
8.4 21 CFR 600
8.5 VA Handbook 1108.04 and 1200.05
8.6 38 CFR 16