FLORIDA ATLANTIC UNIVERSITY

Division of Research

SUBJECT:	Effective Date: October 19, 2018	Policy Number: 10.3.12
Use of Drugs and Biologics in Human Subject Research	Supersedes: October 19, 2015 October 21, 2011 August 2, 2010	Page 1 of 5
	Responsible Authorities: Vice President, Research Institutional Review Board Associate/Assistant Vice President, Research Integrity	

I. Background

Florida Atlantic University faculty and students conduct a diverse array of human subject research projects, including clinical studies that involve marketed and investigational new drugs and biologics. Human subject research involving new drugs or biologics must be in compliance with relevant Food and Drug Administration (FDA) and Department of Health and Human Services (DHHS) laws and regulations. 45 CFR 46 requires all human subject research to undergo Institutional Review Board (IRB) review and to have informed consent provisions. FDA regulations under 21 CFR 312 Subpart D require the same, but also impose other regulatory responsibilities on investigators and sponsors. Investigators planning, designing and implementing clinical trials involving drugs or biologics need to be aware of these FDA, DHHS and FAU requirements.

II. Purpose

The purpose of this policy is to ensure that studies conducted by FAU faculty are in compliance with FDA and DHHS regulations and good clinical practices (GCP), and to ensure the protection and welfare of human research participants involved in clinical investigations of new drugs and/or biologics. In addition, this policy is intended to assist FAU faculty who plan to submit a protocol and conduct human subject research that uses an investigational new drug or biologic as part of treatment or therapy, or use an approved marketed drug for an unapproved use or utilization of a different route of administration or dose, about relevant FDA and DHHS laws and regulations.

III. General Statement

Prior to the administration of a) an investigational new drug or biologic, or b) an approved marketed drug (or biologic) for unapproved use, or c) an approved drug (or biologic) used with a different route of administration or in an unapproved dose, a Principal Investigator or sponsor must request and obtain an Investigational New Drug (IND) Application or Biologics License Application (BLA) from the FDA. An IND may be submitted for one or more phases of an investigation. Otherwise, a justification and documentation that use of the drug/biologic meets the requirements for an exemption from the IND requirements must be provided.

IV. Policy

All ongoing and proposed clinical trials conducted by FAU faculty that use investigational drugs or biologics must be fully compliant with all FDA and DHHS regulations. The Institutional Review Board of record will review all clinical research protocols involving drugs or biologics for evidence of compliance with the applicable laws and regulations.

V. Definitions

Biologic: A biologic (e.g. biological product) includes any virus, therapeutic serum, toxin, antitoxin or similar product applicable to the prevention, treatment or cure of human diseases or injuries. The term includes a biological product that is used *in vitro* for diagnostic purposes. (21 CFR 600.3)

Clinical Investigation: Any experiment in which a drug is administered to, dispensed to, or used involving one or more human subjects. An experiment is any use of a drug except for the use of a marketed drug in the course of medical practice (21 CFR 312.3).

Phases of an investigation
The clinical investigation of a previously untested drug is generally divided into three phases (21 CFR 312.21):

- **Phase 1** studies include the initial introduction of an investigational new drug into humans. Phase 1 studies are typically closely monitored and may be conducted in patients or normal volunteer subjects. These studies are designed to determine the metabolism and pharmacologic actions of the drug in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness. During Phase 1, sufficient information about the drug's pharmacokinetics and pharmacological effects should be obtained to permit the design of well- controlled, scientifically valid, Phase 2 studies. The total number of subjects and patients included in Phase 1 studies varies with the drug, but is generally in the range of 20 to 80.

  Phase 1 studies also include studies of drug metabolism, structure-activity relationships, and mechanism of action in humans, as well as studies in which investigational drugs are used as research tools to explore biological phenomena or disease processes.

- **Phase 2** includes the controlled clinical studies conducted to evaluate the effectiveness of the drug for a particular indication or indications in patients with the disease or condition under study and to determine the common short-term side effects and risks associated with the drug. Phase 2 studies are typically well controlled, closely monitored, and conducted in

a relatively small number of patients, usually involving no more than several hundred subjects.

- **Phase 3** studies are expanded controlled and uncontrolled trials. They are performed after preliminary evidence suggesting effectiveness of the drug has been obtained, and are intended to gather the additional information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug and to provide an adequate basis for physician labeling. Phase 3 studies usually include from several hundreds to several thousands of subjects.

Drug: As defined by the Food, Drug and Cosmetic Act, drugs are articles (other than food) intended for the use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals, or to affect the structure or any function of the body in man or other animals.

Investigational New Drug (IND): A drug or biologic that does not have an approved marketing application and is used in a clinical investigation. This includes marketed drugs being studied at new doses, routes of administration or indications that do not appear in the product label. "IND" is synonymous with "Notice of Claimed Investigational Exemption for a New Drug and also means an investigational new drug application (21 CFR 312.2).

Investigator: Under FDA definitions, an individual who actually conducts a clinical investigation (*i.e.*, under whose immediate direction the drug is administered or dispensed to a subject). In the event an investigation is conducted by a team of individuals, the investigator is the responsible leader of the team. "Sub-investigator" includes any other individual member of that team.

Marketing Application: An application to market a new drug or a biologics license application for a biological product after it has been clinically tested. This includes a New Drug Application (NDA) or Biologics License Application (BL A). A BLA is a request to FDA for permission to introduce, or deliver for introduction, a biologic product into interstate commerce (21 CFR 601.2).

Sponsor: 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. 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.

Sponsor-Investigator: An individual who both initiates and conducts an investigation, and under whose immediate direction the investigational drug is administered or dispensed. In some instances, clinical investigations subject to FDA regulation are initiated by an individual rather than a company or corporate entity.

Subject (Participant): A human who participates in an investigation, either as a recipient of the investigational new drug or as a control. A subject may be a healthy human or a patient with a disease.

VI. Accountability *(responsibilities for PI and sponsor are outlined under 21 CFR 312 subpart D unless otherwise indicated)*

The Principal Investigator will be responsible for:

- Not initiating the clinical investigation before obtaining all necessary approvals, specifically the IRB approval and if needed, an approved IND.
- Conducting the study in accordance with the protocol, and making changes only after he/she obtains approval from the IRB of record, except when necessary to protect the safety, rights or welfare of participants.
- Complying with all regulatory requirements regarding the protocol.
- Personally conducting and supervising the investigation.
- Informing any potential participant when a test article (drug or biologic) is being used for investigational purposes.
- Ensuring that the requirements of informed consent are met, including conveying in an understandable manner the information in the investigator's brochure or drug or biologic label, including the potential risks and side effects of the drug or biologic.
- Ensuring that the protocol has been reviewed and approved by the IRB of record before any participants are enrolled in the study.
- Reporting to the sponsor and IRB adverse events that occur in the course of the investigation.
- Ensuring that the investigation is conducted according to the signed statement, protocol and related investigational plan, and applicable laws and regulations.
- Protecting the rights, safety and welfare of the participants in the clinical study, including the confidentiality requirements.
- Maintaining control of the investigational drugs or biologics.
- Preparing and maintaining adequate documentation.

The Study Sponsor will be responsible for:

- Ensuring that the proposed clinical investigation, if it includes a new drug or biologic, has an approved IND, or an IND or BLA exemption, before the study can begin recruiting participants.
- Assuming all other functions of sponsor as outlined in 21 CFR 312 Subpart D.

The IRB of record will be responsible for:

- Reviewing any human subject clinical investigation involving a new drug or device for compliance with the FDA laws and regulations.
- Conducting its standard ethical oversight obligations for the study as outlined in 21 CFR Part 56, FDA Regulations for Institutional Review Boards.

VII. Procedures

Consult with Sponsored Programs or Research Integrity about procedures for initiating a clinical trial of an investigational drug or biologic at FAU.

- The PI must initiate the required IND or BLA documentation prior to submitting an IRB application package to the IRB of record. Researchers are strongly encouraged to contact FDA to obtain further guidance prior to the submission of an IND (or BLA) application, especially if they are uncertain about the proposed study's regulatory status.

- The PI and study team must obtain good clinical practices (GCP) training via CITI or another FAU approved GCP training mechanism.

- The PI must submit, as part of his IRB application package, a copy of the FDA IND/BLA paperwork (or exemption) letter. In addition, **if the sponsor doesn't supply a standard protocol and consent template**, the PI should complete his protocol and consent form(s) using the FAU templates, including Appendix A for Clinical Investigations and the informed consent template for clinical studies.

- The PI must await FDA, IRB, **and** Sponsored Programs approval before initiating any data collection for a clinical trial of an investigational new drug/biologic at FAU.

- Once the clinical investigation is approved to proceed, the PI is expected to adhere to both the IRB requirements and regulatory obligations outlined under Section V, Accountability.

VIII. Policy Renewal Date
N/A

IX. References
45 CFR 46
21 CFR 312
21 CFR 56

POLICY APPROVAL

Initiating Authority

Signature:  Date: 10/29/2018

Name: Daniel C. Flynn, Ph.D., Vice President for Research

Executed signature pages are available in the Initiating Authority Office(s)