

<b>Human Research Involving Drugs and Biologics</b>	Effective Date	
	Revisions Date	11.2.2020

- 1.0 Purpose:** The purpose of this standard operating practice (SOP) is to provide guidance on requirements for IRB approval of human research using drugs.
- 2.0 Reviews Affected:**
- 2.1** Proposed or ongoing research involving investigational drugs, approved drugs for unapproved use, approved drugs with different route of administration or in an unapproved dose.
- 3.0 SOP:** This SOP is to ensure that the use of investigational drugs, biologics, approved drugs for an unapproved use, approved drugs used in a manner inconsistent with approved labeling (e.g. dose or route of administration) meet the requirements of the Food and Drug Administration (FDA) and, when applicable, the regulations set forth by the Department of Health and Human Services (DHHS), as well as state law and the SOPs of the UMCIRB.
- 4.0 Definitions:**
- 4.1 IND:** an investigational new drug application.
- 4.2 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 synonymous.
- 4.3 Biologics License Application (BLA)** is a request for permission to introduce, or deliver for introduction, a biologic product into interstate commerce.
- 4.4 Approved Drugs administered for Unapproved Use:** Any approved drug (including biological products for human use) [Off-Label Use] : Any approved drug (including biological products for human use) used in a manner of administration or dose that is not consistent with the package insert and data being collected impacts safety and efficacy;
- 4.2.1** Off-label use of a marketed product when the intent is solely for the practice of medicine does not require IRB review or the submission of an IND or BLA;
- 4.2.2** Off-label use of a marketed product in research (i.e., as part of a clinical investigation, including pilot studies) does require IRB review and approval;
- 4.2.3** Off-label use of a marketed product in research (i.e., as part of a clinical investigation, including pilot studies) will require that the investigator seek consultation with FDA regarding the need for an IND or BLA. Documentation of the FDA’s response (e.g., an IND or BLA number or a letter exempting the research from such requirement) must be presented to the IRB at the time of initial review;
- 4.2.4** Off-label use of a marketed product intended to support a change in labeling requires both IRB review and submission of an IND or BLA.
- 4.5 Investigator:** an individual who actually conducts a clinical investigation (*i.e.*, under whose immediate direction the drug is administered or dispensed to a participant). In the event an investigation is conducted by a team of individuals, the investigator is the responsible leader of the team.
- 4.5.1** Subinvestigator includes any other individual member of that team who holds the same responsibilities for the conduct of the study as the Principal Investigator.

- 4.6 Sponsor:** an entity that takes responsibility for and initiates a clinical investigation.
- 4.6.1** The sponsor may be an individual or pharmaceutical company, governmental agency, academic institution, private organization, or other organization.
- 4.6.2** The sponsor does not actually conduct the investigation unless the sponsor is a sponsor-investigator.
- 4.6.3** 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.
- 4.7 Sponsor-Investigator:** an individual who both initiates and conducts an investigation, and under whose immediate direction the investigational drug is administered or dispensed.
- 4.7.1** The term does not include any person other than an individual.
- 4.7.2** The requirements applicable to a sponsor-investigator include both those applicable to an investigator and a sponsor.
- 4.7.3** This individual must meet all of the applicable responsibilities set forth in 21 CFR 312 Subpart D.
- 4.8 Gene Transfer Research:** Gene transfer involves the administration of genetic material to alter the biological properties of living cells for therapeutic use.
- 4.8.1** Gene transfer activities in humans are investigational and are regulated by both the FDA and the NIH Office of Biotechnology Activities (OBA).
- 4.8.2** FDA regulations require the submission of an IND for human gene transfer research
- 4.8.3** Institutional Biosafety Committee as well as UMCIRB approval is required before any gene transfer research can begin.
- 4.9 Parallel Track Studies:** FDA studies permitting wider access to promising new drugs for HIV/AIDs related diseases under a “separate access” protocol that “parallel” the controlled clinical trials that are essential to establish the safety and effectiveness of new drugs. Parallel Track studies require prospective IRB review and approval as well as the implementation of informed consent.

**5.0 Responsibilities:**

- 5.1 The Principal Investigator (PI)/study team members will**
- 5.1.1** Determine the need for an IND if the investigator is the sponsor of the drug research.
- 5.1.2** Assure IRB approval is in place prior to beginning the study and is appropriately maintained until the study is closed.
- 5.1.3** Ensure that the investigation is conducted according to the investigational plan and applicable regulations.
- 5.1.4** Protect the rights, safety, and welfare of participants under the investigator's care.
- 5.1.5** Ensure there is appropriate control of drugs or biologics under investigation including appropriate storage and dispensing.
- 5.1.6** Obtain the informed consent of each human participant to whom the drug or biologic is administered.
- 5.1.7** Promptly submit an amendment to the IRB for all proposed changes in the research activity and report all unanticipated problems involving risk to human participants or others.
- 5.1.8** Make no changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to human participants.

**5.2** UMCIRB office staff will

**5.2.1** Confirm the drug has an IND number that is valid by assuring consistency across documents (e.g., FDA letters, sponsor protocol, etc.); or

**5.2.2** Verify the protocol meets one of the FDA exemptions from the requirement to have an IND:

**5.2.2.1** The clinical investigation of a drug product that is lawfully marketed in the United States is exempt from the requirements to obtain an IND if all the following apply:

**5.2.2.1.1** 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;

**5.2.2.1.2** 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;

**5.2.2.1.3** 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;

**5.2.2.1.4** The investigation is conducted in compliance with the requirements for institutional review and with the requirements for informed consent in the federal regulations; and

**5.2.2.1.5** The investigation is conducted in compliance with the requirements concerning the promotion and sale of drugs.

**5.2.2.2** A clinical investigation involving an in vitro diagnostic biological product listed below is exempt from the requirements to obtain an IND if (a) it is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure and (b) it is shipped in compliance with FDA regulations.

**5.2.2.2.1** The following products are exempt from the IND requirements: (a) blood grouping serum; (b) reagent red blood cells; and (c) anti-human globulin.

**5.2.2.3** A clinical investigation involving use of a placebo is exempt from the requirements of this part if the investigation does not otherwise require submission of an IND.

**5.2.3** Assist sponsor-investigators in determining whether an IND is required.

**5.3** Institutional Review Board/IRB Chairperson or designee will

**5.3.1** Review the study drug information provided by the PI/study team within the IRB application.

**5.3.2** Request any clarification needed about the status of the drug(s) used for research.

**5.3.3** Ensure consistency among study material (protocol, investigator brochure, informed consent document, advertisements, etc.) with regard to study drug(s).

**6.0** **Procedures:**

**6.1** Investigators will provide the IND number as a part of the IRB application when applicable.

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- 6.1.1 Investigators that are also the sponsor of the human research drug study are responsible for all required FDA reporting.
- 6.2 Off-Label Use of commercially available drugs
  - 6.2.1 Good medical practice and patient interests require that physicians be free to use commercially available drugs according to their best knowledge and judgment. If a physician uses a drug for an indication not in the approved labeling, he/she has the responsibility to be well informed about the drug and to base its use on a firm scientific rationale and on sound medical evidence, and to maintain records of the drug's use and effects. Use of a drug as part of the "practice of medicine" does not require review by the UMCIRB or FDA notification.

**Revision History:**

Date	Change	Reference Section(s)
2.26.2016	Pulled information to a stand-alone document.	All
11.2.2020	Updated office name from ORIC to UMCIRB	Section 5.2

**References**

US FDA. Code of Federal Regulations, Title 21, Part 312 Investigational New Drug Application: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=312&showFR=1>

US FDA. "Off-Label" and Investigational Use of Marketed Drugs, Biologics, and Medical Devices - Information Sheet: <http://www.fda.gov/RegulatoryInformation/Guidances/ucm126486.htm>