

**PARTNERS HUMAN RESEARCH COMMITTEE
POLICIES AND PROCEDURES**

**Review of Research Involving Drugs or Biological Drug Products
Requirement for an Investigational New Drug (IND)**

1.0 PURPOSE

The purpose of this policy is to define the applicability of the United States Code of Federal Regulations Title 21 - Food & Drugs Part 312 - Investigational New Drug Application (IND) and the procedures the Partners Human Research Committees (PHRC) follow to determine whether an IND is needed for a clinical investigation.

2.0 SCOPE

Non-exempt human-subjects research and clinical investigations reviewed by the PHRC are subject to this policy.

3.0 DEFINITIONS

As used in this document, human-subjects research encompasses activities that meet the DHHS definitions of *research* and *human subject* and/or the FDA definitions of *clinical investigation* and *human subject*. The DHHS definition for *research* and *human subject* and the FDA definition for *clinical investigation* and *human subject* are provided below.

Research means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. [45 CFR 46.102(d)]

Human subject means a living individual about whom an investigator (whether professional or student) conducting research obtains (1) Data through intervention or interaction with the individual, or (2) Identifiable private information. *Intervention* includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. *Interaction* includes communication or interpersonal contact between investigator and subject. *Private information* includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the

individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects. [45 CFR 46.102(f)(1)(2)]

Clinical investigation means any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or is not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that are subject to the provisions of part 58 of this chapter, regarding nonclinical studies. The terms *research*, *clinical research*, *clinical study*, *study*, and *clinical investigation* are deemed to be synonymous... [21 CFR 50.3(c) and 21 CFR 56.102(c)]

Human subject means an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient. [21 CFR 50.3(g) and 21 CFR 56.102(g)]

Botanical drug products consist of vegetable materials, which may include plant materials, algae, macroscopic fungi, or combinations thereof, that are intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease in humans.

Clinical investigation means any experiment in which a drug is administered or 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(b)]

Investigational new drug means a new drug or biologic 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 deemed to be synonymous. [21 CFR 312.3(b)]

Radioactive drug means any substance defined as a drug in section 201(g)(1) of the Federal Food, Drug, and Cosmetic Act which exhibits spontaneous disintegration of unstable nuclei with the emission of nuclear particles or photons and includes any non-radioactive reagent kit or nuclide generator which is intended to be used in the preparation of any such substance but does

not include drugs such as carbon-containing compounds or potassium-containing salts which contact trace quantities of naturally occurring radionuclides.

Sponsor means 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. [21 CFR 312.3(b)]

Sponsor-investigator means an individual who both initiates and conducts an investigation, and under whose immediate direction the investigational drug is administered or dispensed. The term does not include any person other than an individual. The requirements applicable to a sponsor-investigator under this part [21 CFR 312 Subpart D] include both those applicable to an investigator and a sponsor. [21 CFR 312.3(b)]

4.0 POLICY

Non-exempt clinical investigations reviewed and approved by the PHRC must comply with Food and Drug Administration (FDA) regulations 21 CFR 312 - Investigational New Drug Applications (INDs).

5.0 PROCEDURES

Investigators relying on the PHRC for review of human-subjects research are required to complete application forms and provide all required information and documents for review as described in the Protocol Submission Instructions and forms for continuing review, amendments, and unanticipated problems involving risks to subjects or others and adverse events.

When the research involves drug products or botanical dietary supplements, the investigator is required to provide the PHRC with sufficient information about the drug product, including FDA status, and its intended use to assess the risks and potential benefits to subjects.

Research involving drug products or botanical dietary supplements also require review by the BWH Investigational Drug Service (IDS) and/or MGH Research Pharmacy Committee. The pharmacy committees are responsible for providing the Partners Human Research Office with written documentation of approval.

Approval to initiate the research is contingent upon receipt of written documentation of approval from the relevant pharmacy committee(s).

5.1 Clinical Investigations

5.1.1 Drug Products that are not Marketed

The clinical investigation of a drug product that is not marketed requires submission of an Investigational New Drug (IND) Application to the FDA, unless exempt according to 21 CFR 312.2.

5.1.2 Marketed Drug Products

The clinical investigation of a marketed drug product requires submission of an Investigational New Drug (IND) Application to the FDA unless exemption 21 CFR 312.2(b)(1) quoted below applies and the clinical investigation does not involve an exception from informed consent requirements for emergency research 21 CFR 50.24.

The clinical investigation of a drug product that is lawfully marketed in the United States is exempt from the requirements of this part if all of the following apply:

- (i) 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;
- (ii) 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;
- (iii) 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;
- (iv) The investigation is conducted in compliance with the requirements for institutional review set forth in part 56 and with the requirements for informed consent set forth in part 50; and
- (v) The investigation is conducted in compliance with the requirements of 312.7.

Exemption 312.2(b)(1) applies to marketed drug products being evaluated for safety and efficacy or effectiveness and marketed

drug products used as comparators as well as marketed drug products that will be administered to study human physiology or as part of a procedure or test required by the protocol (*ancillary drugs*).

5.1.3 Botanical Drug Products and Botanical Dietary Supplements

When a lawfully marketed botanical dietary supplement is being studied for its effects on diseases (i.e., to cure, treat, mitigate, prevent, or diagnose disease including its associated symptoms) it is an investigational new drug and is subject to the Part 312 IND requirements. However, investigators may request an exemption from Part 312 from the FDA.

When a lawfully marketed botanical dietary supplement is being studied for its dietary supplement use (i.e., structure and/or function claims), it is not an investigational new drug and is not subject to the Part 312 IND requirements. Structure and function claims are statements that describe the effect a dietary supplement may have on the structure or function of the human body.

5.1.4 Radioactive Drugs

When a radioactive drug is used in humans for research intended to obtain basic information regarding the metabolism (including kinetics, distribution, and localization) of a radioactively labeled drug or regarding human physiology, pathophysiology, or biochemistry, but not intended for immediate therapeutic, diagnostic, or similar purposes or to determine the safety and effectiveness of the drug in humans for such purposes (i.e., to carry out a clinical trial), the radioactive drug is not an investigational new drug subject to the Part 312 IND requirements; however the research is subject to review and approval of the Radioactive Drug Research Committee (RDRC).

When the research is designed to conduct a clinical trial of a radioactive drug, the radioactive drug is an investigational new drug and is subject to the Part 312 IND requirements. Additionally, the research must be approved by the Radiation Safety Committee (RSC).

5.1.5 Investigational New Drugs (INDs)

When the PHRC determines an IND is needed, the investigator must provide the PHRC with a copy of the letter from the FDA with the IND assignment for the clinical investigation under

review or a letter from the FDA stating that an IND is not needed. The PHRC will not approve the clinical investigation of an investigational drug product unless the IND is in effect as defined in 21 CFR 312.40(b)(1)(2).

When a BWH or MGH investigator is the sponsor of the IND (sponsor-investigator), the PHRC requires the investigator to meet with a representative of the Human Research Quality Improvement Program (QI Program) to review his/her FDA responsibilities as a sponsor-investigator. The QI program is responsible for providing the Partners Human Research Office with documentation in writing that the review has taken place, and that the investigator understands his/her FDA IND responsibilities. Approval to initiate the research is contingent upon receipt of written documentation from the QI Program.

5.2 Drug Products not Manufactured by a Licensed Pharmaceutical Company

5.2.1 Drug Products with INDs

When an individual or entity other than a licensed pharmaceutical company manufactures the drug product being investigated, the PHRC will rely upon FDA review of the chemistry, manufacturing, and control information contained in the IND Application.

5.2.2 Drug Products without INDs

When an individual or entity other than a licensed pharmaceutical company manufactures the drug being administered to human subjects and an IND is not required, the PHRC will request a Certificate of Analysis.