

<b>Title:</b>	Requirements for Investigational New Drug (IND) for Human-Subjects Research
<b>Department:</b>	Human Research Affairs
<b>Policy Type:</b>	<input checked="" type="checkbox"/> Partners System-wide <input type="checkbox"/> Partners System-wide Template <input type="checkbox"/> Partners HealthCare <input type="checkbox"/> Partners HealthCare Departmental <input type="checkbox"/> Institution
<b>Applies to:</b>	Employees, Professional Staff or Other Agents of Brigham and Women's Hospital (BWH), Faulkner Hospital (FH), Massachusetts General Hospital (MGH), McLean Hospital (McLean), and North Shore Medical Center (NSMC)
<b>Approved by:</b>	Chief Academic Officer
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<b>Next Review Date:</b>	August 18, 2018
<b>Contact Person:</b>	Director, Human Research Review and Compliance

**KEYWORDS:**

IRB, Institutional Review Board

**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.

**DEFINITIONS:**

See Definition of Human-Subjects Research

*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 contain trace quantities of naturally occurring radionuclides.

*Investigator* means an individual who actually conducts a clinical investigation (i.e., under whose immediate direction the test article 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. "Subinvestigator" includes any other individual member of that team. [21 CFR 312.3(b)]

*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)]

#### **POLICY STATEMENT:**

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

#### **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, 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 also requires review by the institution's 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).

#### **Clinical Investigations and Requirements for INDs**

##### **1. Drug Products that are not Marketed**

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

##### **2. Marketed Drug Products**

The clinical investigation of a drug product lawfully marketed in the United States requires submission of an Investigational New Drug (IND) Application to the FDA unless exemptions 21 CFR 312.2(b)(1), 21CFR 312(b)(2) or 21CFR312(b)(5) quoted below apply and the clinical investigation does not involve an exception from informed consent requirements for emergency research 21 CFR 50.24.

#### Exemption 312.2(b)(1)

The clinical investigation of a drug product that is lawfully marketed in the United States is exempt from the requirements of 21 CFR 312 if all of the following apply:

- The investigation is not intended to be reported to FDA in support of a new indication for use or to support any other significant change in the labeling for the drug;
- 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, use in a subject 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 IRB review and informed consent [21 CFR parts 56 and 50, respectively];
- The investigation is conducted in compliance with the requirements concerning the promotion and sale of drugs [21 CFR 312.7]; and
- The investigation does not intend to invoke 21 CFR 50.24.

Exemption 312.2(b)(1) applies to marketed drug products being evaluated for safety and efficacy or effectiveness, marketed drug products used as comparators, and 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*).

#### Exemption 312.2(b)(2)

A clinical investigation involving an *in vitro* diagnostic biological product is exempt from the requirements of 21 CFR. 312 if all of the following apply:

- It is intended to be used in a diagnostic procedure that confirms the diagnosis made by another medically established, diagnostic product or procedure
- It is shipped in compliance with 312.160
- The *in vitro* diagnostic biological product involves one or more of the following: Blood grouping serum, Reagent red blood cells, Anti-human globulin

#### Exemption 312.2(b)(5)

A Clinical investigation involving use of a placebo is exempt from the requirements of 21CFR. 312 if both the following apply:

- The clinical investigation involves use of a placebo
- The investigation does not otherwise require submission of an IND.

### 3. Dietary Supplements

When a lawfully marketed 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 21 CFR 312 IND requirements. However, investigators may request an exemption from 21 CFR 312 directly from the FDA.

When a lawfully marketed 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 21 CFR 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.

#### 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 21 CFR 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 21 CFR 312 IND requirements. Additionally, the research must be approved by the Radiation Safety Committee (RSC).

#### Clinical Investigations Conducted Under an Investigational New Drug (IND)

The PHRC requires the IND number be included in the application. As confirmation that the IND number is valid, the PHRC requires documentation from the sponsor or the FDA of the IND number. The IND goes into effect 30 days after the FDA receives the IND, unless the sponsor receives earlier notice from the FDA and must be in effect before the PHRC fully approves the research.

When a Partners investigator is the sponsor of the IND, the PHRC is responsible for ensuring that the investigator is knowledgeable about the following additional regulatory requirements of sponsors and will follow them:

- 21 CFR 11 (Electronic Records and Electronic Signatures)
- 21 CFR 54 (Financial Disclosure by Clinical Investigators)
- 21 CFR 210 (Current Good Manufacturing Practice in Manufacturing, Processing, Packing or Holding of Drugs: General)
- 21 CFR 211 (Current Good Manufacturing Practice for Finished Pharmaceuticals)
- 21 CFR 312 (Investigational New Drug Application)
- 21 CFR 314 (Applications for FDA Approval to Market a New Drug)
- 21 CFR 320 (Bioavailability and Bioequivalence Requirements)
- 21 CFR 330 (Over-The-Counter (OTC) Human Drugs which are Generally Recognized as Safe and Effective and Not Misbranded)
- 21 CFR 601 (Biologics Licensing)

Before allowing the sponsor-investigator to conduct the research as a first time Partners sponsor-investigator, the PHRC will require the investigator to undergo a review of FDA sponsor-investigator responsibilities with the Human Research Quality Improvement Program (QI Program). Should the PHRC or QI Program identify the need for additional expertise to fulfill FDA regulatory requirements, the PHRC will require the investigator to: (1) undergo an audit by a Contract Research Organization to ensure that procedures are in place so that all FDA regulatory requirements of sponsors will be met; (2) assign responsibility of compliance with all FDA regulatory requirements to a Contract Research Organization; or (3) assign responsibility of compliance with some FDA regulatory requirements to a Contract Research Organization and have the investigator obtain an audit from a Contract Research Organization to ensure that procedures are in place so that all other FDA regulatory requirements of sponsors will be met.

#### Drug Products not Manufactured by a Licensed Pharmaceutical Company

##### 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.

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.

**REFERENCE:**

21 CFR 312

**DEVELOPMENT AND CONSULTATION**

Human Research Office  
Human Research Quality Improvement Program

Reviewed by:	Original Review Date:	Revision Approval Dates:
Chief Academic Officer	December 16, 2010	May 5, 2015