	University of Puerto Rico Medical Sciences Campus Human Research Subjects Protection Office	Effective: 9/1/2008
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INVESTIGATIONAL NEW DRUG (IND) OR INVESTIGATIONAL DEVICE EXEMPTION (IDE)

Purpose:

To define the policy and procedures for the submission of protocols that includes the use of investigational new drugs or an investigational device exemption at UPR MSC. To describes the criteria for evaluating the requirement for an IND or IDE.

Sources:

21 CFR 812.2; 3
21 CFR 312.2
21 CFR 50; 56

Applicability:

Investigators, IRB Members, IRB Staff

Background:

FDA regulations apply to the use of therapeutics, vaccines, and other medical interventions as well as licensed products and devices used for a new purpose. The purpose of the regulation is to assure subject safety & rights and assure that the study is of sufficient quality to permit an evaluation of drug safety and effectiveness. The use of an investigational drug or devices is encouraged by FDA "consistent with the protection of public health and safety and with ethical standards".

Policy:

The use of an experimental drug or device in a protocol is allowable in the Medical Sciences Campus provided it complies with FDA regulations, CFR 21 and GCP.

All research protocols must receive full IRB review and approval prior to implementation.

Definitions:

For the purpose of this policy the following FDA defined terms apply:

IND means an investigational new drug application.

Investigational new drug means a new drug or biological product 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.

IDE means an investigational device exemption. For most studies involving devices, an investigator or sponsor must obtain an Investigational Device Exemption (IDE) from the FDA.

Investigator means 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.

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.

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 include both those applicable to an investigator and a sponsor.

Procedure:

Criteria for determination of the requirement of an IND or an IDE

IRB will determine if an IND or IDE are necessary according to the definitions and regulations in 21CFR 312 and 21 CFR 812. A sponsor shall submit an IND to FDA if the sponsor intends to conduct a clinical investigation with an investigational new drug that is subject to 21CFR312.2 (a). A sponsor shall submit an IDE to FDA if the sponsor intends to conduct clinical investigation with a device as defined in 21CFR 812.

For protocols submitting an IDE, IRB review and considerations will include a risk assessment according to the definitions in 21 CFR 812.3. For protocols including an IND the IRB review will be done according to 21 CFR 312 Subparts B, C, and D.

When is an IND needed?

An IND is needed **for all clinical investigations of products that are subject to section 505 of the Federal Food, Drug, and Cosmetic Act** or to the licensing provisions of the Public Health Service Act (58 Stat. 632, as amended (42 U.S.C. 201 *et seq):*

(a) Studies involving a drug or biologic that is not approved by the FDA.

(b) Studies involving an approved (i.e. commercially available) drug or biologic that is being tested to support a new indication or significant change in the labeling of the drug or biologic.

(c) Studies involving an approved drug or biologic that is being tested to support a significant change in advertising for the drug

or biologic.

(d) Studies involving an approved drug or biologic that is being tested in a new route of administration, new dosage level, or new patient population that may increase the risk of the drug or biologic.

(1) The clinical investigation of a drug product that is lawfully marketed in the United States **is exempt** from the requirements of an IND **if all 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.

(2) A clinical investigation involving an in vitro diagnostic biological product is exempt from the requirements of this part 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 312.160.

(i) In accordance regulations, the following products are exempt from the requirements of this part: (*a*) blood grouping serum; (*b*) reagent red blood cells; and (*c*) anti-human globulin.

(3) A drug intended solely for tests in vitro or in laboratory research animals is exempt from the requirements of this part if shipped in accordance with 312.160.

(4) 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) A clinical investigation involving an exception from informed consent under 50.24 of this chapter is not exempt from the requirements of this part.

When is an Investigational Device Exemption (IDE) Required?

A device is considered investigational if either the device is not approved for marketing in the United States or the device is approved for marketing but is being clinically evaluated for a new indication.

FDA regulations (21 CFR 812.2) state that for studies involving use of an investigational device, the investigator (or sponsor) must obtain either a "significant risk" Investigational Device Exemption (IDE) from the FDA, or a determination of "non-significant risk" from the institutional review board.

Definition of a Significant Risk Device

As per 21 CFR 812.3 a **Significant Risk Device** (SR) is an investigational device that:

(1) Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;

(2) Is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;

(3) Is for a use of substantial importance in diagnosing, curing,

mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or

(4) Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

A non-significant risk (NSR) device is one that does not meet the definition of a significant risk device.

To request approval of a protocol that involves an IND or IDE the researcher must include with the IRB application the following:

(1) The name and institution of the IND or IDE sponsor,

(2) The date it was filed with FDA,

(3) IND or IDE number,

(4) Written comments from FDA, and written responses to those comments.

(5) Risk information from the investigator's brochure, a review of the published literature, or other credible source.

(6) Justification for use of the experimental drug or device (e.g., documentation that no available alternative therapy exists).

(7) Therapeutic plan (e.g., dose, mode of administration, duration of planned therapy).

(8) Provide a high level summary of preclinical data to date including mechanism of action, efficacy and safety.

(9) Provide a high level summary of prior human experience with the investigational drug. Include a statement about whether the drug has been withdrawn from investigation or marketing in any country for reason related to safety or efficacy. Cite the reason for the withdrawal.

(10) A proposed consent document that meets the criteria described in

the informed consent section.

(11) Include copies of the applicable forms, exs. FDA 1571,1572,3454,3455

(12) In the case of intervention studies done in foreign countries the researcher must include the regulatory oversight of the foreign regulatory body and send written documentation from the regulatory body showing full compliance with local laws.

(13) Any other documentation and information requested in CFR 21.

IRB determinations

For projects involving drugs and biologics the IRB must assess the requirement of IND based of the criteria defined above.

For projects involving devices the IRB must make two separate decisions, based on different criteria. First: Is the investigation approvable or not? Second: Does the device present significant SR or non-significant risk? If NSR, an IDE can be given by the board. If not, the investigator must be advised to seek a SR IDE from the FDA.

The criteria for deciding if a study involving drugs, biologics or either a significant or non-significant risk device should be approved are the same as those used to evaluate any proposed research project, i.e., the IRB's determination that risks to subjects are minimized, risks to subjects are reasonable in relation to anticipated benefits and knowledge to be gained, subject selection is equitable, informed consent materials and procedures are adequate, and there are acceptable provisions for monitoring the study and protecting patient information.