FRIENDS RESEARCH INSTITUTE, INC.
1040 Park Avenue, Suite 103
Baltimore, MD 21201

Subject: Reviews Requiring Special Consideration
Division: IRB
Date: March 1, 2012

IRB Policy 110.4: INVESTIGATIONAL USE OF DRUGS AND BIOLOGICS

Policy

All investigational drug studies involving human subjects must be submitted to the IRB for review at a convened meeting.

An "investigational new drug" is 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 [21 CFR 312].

Investigational New Drug Application (IND)

An IND must be filed when:

1. The research involves a drug or biologic that is NOT approved by the FDA.

2. The research is being conducted with a commercially available drug to support a new indication or support a change in advertising or labeling of the product.

3. The research uses a commercially available drug that is being administered via a new route or for use in a different part of the body

4. The research uses a commercially available drug that is being given at a dosage level that might significantly increase the risk to the subject population.

5. The research uses a commercially available drug that is going to be used in a new patient population that may result in a significant increase in risk to the patient population.

If a drug is already licensed and approved by the FDA for marketing in the United States, it may be studied without an IND, as long as the study is not designed to change the approved indications, advertising claims, or labeling of the product. The study must not be one that changes dose, route of administration, or target population in a way that is likely to increase risk. The study is still subject to all of the usual requirements for IRB oversight, and the study must not violate any of the FDA's rules about advertising and promotion of drugs.

A sponsor may withdraw an IND at any time, with or without cause. The FDA may also terminate an IND under a number of circumstances. A "clinical hold" is a suspension of an IND, during which no new subjects may be enrolled, and subjects who have already been enrolled may only continue the study drug if it is clinically necessary for them to do so. This action may be taken when it appears that subjects are being exposed to greater risk than had originally been recognized; the IND, and the study are then

often reactivated when appropriate adjustments in study design have been made. A “clinical hold” may also result if the researchers’ qualifications are called into serious question, or if the study design proves flawed in a way that precludes meaningful results.

More serious deficiencies may lead to termination of an IND. In that case, reactivation is not foreseen and the project is shut down. If the cause is clear and compelling danger to research subjects, this may be a rather precipitous action. If it is for problems in study conduct that do not place subjects at increased risk, the FDA will ordinarily notify the sponsor of the intent to terminate the IND and give the sponsor an opportunity to respond.

IND Exemptions

"Investigational use" suggests the use of an approved product in the context of a clinical study protocol. When the principal intent of the investigational use of a test article is to develop information about the product's safety or efficacy, submission of an IND or IDE is required.

However, according to 21 CFR 312.2(b)(1), the clinical investigation of a marketed drug or biologic does not require submission of an IND if all six of the following conditions are met:

1. It 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;

2. It is not intended to support a significant change in the advertising for the product;

3. It 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;

4. It is conducted in compliance with the requirements for IRB review and informed consent;

5. It is conducted in compliance with the requirements concerning the promotion and sale of drugs [21 CFR 312.7]; and

6. It does not intend to invoke 21 CFR 50.24, Exception from Informed Consent Requirements for Emergency Research.

FRI’s IRB will review studies submitted with IND exemption requests to determine whether they meet the above exemption criteria. If the IRB determines that the exemption criteria are not met or the IRB is not certain whether the exemption criteria are met and an IND has not been obtained, it will ask the investigator to submit an IND or have the FDA make a determination on the requirement for an IND.

If the FDA determines that an IND is not necessary, it will provide an exemption letter. A copy of this letter should be provided to the IRB. Should the FDA determine that an IND is required, a complete IND application must be submitted to the FDA for review. Upon completion of review, the FDA will send the investigator a letter. The IRB will withhold approval of the study until the investigator provides a copy of either the FDA determination letter or the IND number provided by the FDA.

IND application and approval/exemption is specific to the protocol rather than to the drug. Any proposed modifications to the protocol that significantly affect the safety of the subject or the scope of the investigation (e.g., a new protocol with the same drug) must be submitted to the FDA for review.

Applicable Regulations and Guidelines

21 CFR 312