Marshfield Clinic

Assuring Research Involving Test Articles (Drugs, Biologics, Nutritional Supplements, or Devices) Complies with FDA Requirements

1. SCOPE

1.1. System Wide

2. DEFINITIONS & EXPLANATIONS OF TERMS

2.1. Test Article

- Any drug for human use, biological product for human use, medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the act or under sections 351 or 354-360F of the Public Health Service Act (21 CFR 56.102(1)).

2.2. Investigational Test Article:

- i) An unapproved test article, or (ii) an approved test article being studied, in a formal research study, for a new indication, route of administration, dosage level, subject population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the product.

3. PROCEDURE BODY

This document describes how the Marshfield Clinic Research Foundation (MCRF) assures that research involving test articles complies with FDA requirements.

3.1. Policy:

a. Research involving investigational or unlicensed test articles will be conducted in compliance with FDA regulations Investigational New Drug regulations (21 CFR 312) and Investigational Device Exemption regulations (21 CFR 812).

b. An investigator who sponsors his or her own test article research must assume all the responsibilities imposed on both the sponsor and investigator by FDA regulations and all applicable MCRF policies. See the "Clinician/Investigator-Held IND" and "Clinician/Investigator-Held IDE" policies.

c. When research involves the use of a drug, other than a marketed drug in the course of medical practice, Marshfield Clinic investigators will demonstrate, and Office of Research Integrity & Protections (ORIP) staff will confirm, that the drug either has an IND or the protocol meets one of the following FDA exemptions from the requirement to have an IND:

- Exemption 1
  The drug product is lawfully marketed in the United States. 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. 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. 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. The investigation is conducted in compliance with 21 CFR 50 and 56. The investigation is conducted in compliance with the requirements of 21 CFR 312.7.

- Exemption 2
  A clinical investigation is for an *in vitro* diagnostic biological product that involves one or more of the following: blood grouping serum; reagent red blood cells; anti-human globulin. The diagnostic test is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure. The diagnostic test is shipped in compliance with 21 CFR 312.160.
- Exemption 3
  A clinical investigation involving use of a placebo if the investigation does not otherwise require submission of an IND.

See section 3.2.b for ORIP staff confirmation process.

d. When research is conducted to determine the safety or effectiveness of a device, Marshfield Clinic investigators will demonstrate and ORIP staff will confirm that the device has an IDE, the device fulfills the requirements for an abbreviated IDE, or the research meets one of the FDA exemptions from the requirement to have an IDE.

e. When research involves a drug or device with an IND or IDE, ORIP staff will evaluate whether the IND or IDE number is valid.

f. Research will not commence until a valid IND or IDE is in place, if required.

3.2. Procedure:

a. Investigator Demonstration Process

- As part of the initial application process, the IRB application will, at a minimum, ask the investigator to:
  - Indicate whether the research involves the use of an investigational test article (i.e., unapproved drug, biologic or medical device), or an approved test article being used for a new indication, route of administration, dosage level, subject population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the product;
  - Indicate whether an existing Investigational New Drug (IND) or Investigational Device Exemption (IDE) covers the test article proposed to be used and the number of any applicable IND or IDE;
  - Provide documentation that an IND or IDE exists or an application has been filed, where applicable, or if no IND or IDE will be sought, an explanation regarding why no IND or IDE is required;
  - If an unapproved medical device is involved and no IDE will be sought, provide clarification as to whether the sponsor of the device considers the device to be exempt or a significant or non-significant risk device

and the basis for that determination and supporting documentation (see Review of Investigational Device Research)

b. IRB Confirmation Process

- In pre-review of research involving a test article, ORIP staff will use the information provided by the investigator to determine the following:
  - Whether an IND or IDE is required;

    - Sponsors and investigator are responsible for making the initial determination of whether an IND or IDE is required. The Clinical Research Center, the Office of Scientific Writing and the Office of Research Integrity & Protections are available to assist with this determination.

    - FDA regulations at 21 CFR 312 (drugs & biologics) and 21 CFR 812 (devices) as well as related FDA guidance should be used to make the determination. Also see the policies Clinician/Investigator-Held IND and Clinician/Investigator-Held IDE for additional guidance.

    - The final determination as to the need for an IND or IDE will be made by staff within the Office of Research Integrity & Protections based on information provided in the IRB application and study protocol.

  - Whether a required IND or IDE is valid;

    - In test article studies initiated by the Marshfield Clinic investigators (i.e., the investigator also serves as the regulatory sponsor), the IRB will require the investigator to produce a copy of the FDA application for an IND or IDE to confirm the validity of the IND or IDE before approving the research study.

    - In sponsored research involving test articles, in addition to the IND or IDE number, the Marshfield Clinic investigator may be asked to provide documentation from the sponsor demonstrating the validity of the IND or IDE (e.g., FDA approval letter or IND/IDE application).

    - If a proposed study does not have an IND or IDE, and ORIP staff believes one is required, the investigator will be notified in writing that an IND or IDE is required for the research to be approved. If the investigator does not agree with ORIP's determination, the investigator may provide further justification that an IND or IDE is not required, for example, by demonstrating all the conditions stated in 21 CFR 312.2(b)(1) have been met. If necessary, the investigator may also be asked to provide written documentation from the FDA that an IND or IDE is not required.

  - If a device is involved, whether the device is exempt or a significant risk or non-significant risk device

- See the procedure document, "Review of Investigational Device Research."

4. ADDITIONAL RESOURCES

4.1. References:
- None

4.2. Supporting documents available:
- None

5. DOCUMENT HISTORY

Version No.	Revision Description
1.0	New Document in Document Control transferred from Policy & Handbook Library - #5267.1 (no changes made)
2.0	
3.0	

6. DOCUMENT PROPERTIES

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