Research Using FDA Test Articles

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Background:

The term “test article” is found in the FDA regulations on Protection of Human Subjects (21 CFR 50.3 (j)). The term includes drugs (including botanicals, biologicals, and gene therapy, and genetically derived products that meet the definition of a “drug”), and medical devices for human use. The FDA has statutory authority to regulate the development and marketing of these products.

Q: What is the definition of a drug?

A substance recognized by an official pharmacopoeia or formulary. A substance intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease. A substance (other than food) intended to affect the structure or any function of the body.

Q: What kinds of review process will the IRB conduct for human research intended to develop information about safety and efficacy of drugs?

If a test article does not meet the criteria for an expedited review procedure, the study must be reviewed at a convened IRB meeting. Most test articles will require Full Board review.

Q: Does research conducted on a Drug, Botanical, Biological, or Other Substances require an Investigational New Drug Application (IND)?

Maybe. UF IRB review of research involving unlicensed or unapproved drugs, botanicals, biologicals, or other substances (e.g., food additives, food derivatives, vitamins, minerals, extracts, etc.) must be conducted at a convened meeting. The IRB review will address the need for submission of an FDA IND prior to the use of the test article in the research study. The IRB may determine that an IND is not required if all the conditions set forth in 21 CFR 312.2(b) have been met. The IRB will determine whether to require submission of an IND, or if appropriate, to require the Principal Investigator (PI) to seek clarification from the FDA about the need for obtaining an IND before the IRB completes its review, and before the research may begin. Consent forms for IND studies must clearly state that the “test article” is investigational or experimental. To save time, it is a good idea to submit a request to the FDA regarding the need for an IND before submission of the protocol to the IRB.

For all studies that involve a drug product, the PI must complete the myIRB section on Drugs. The PI must clarify for the IRB whether or not there is an FDA issued IND number for the use of the test article in the protocol, and if not, why not. Appropriate documentation (investigator drug brochure, package insert, FDA issued IND letter when the PI or other study team member holds the IND, etc.) should be included in the myIRB application.

Q: What kinds of review process will the IRB conduct for human research intended to develop information about safety and efficacy of medical devices?
When the test article is a medical device, the UF IRB reviewing the investigational medical device study will determine if the application will involve:

- an FDA-approved device to be used for an FDA-approved indication,
- an FDA-approved device to be used for an unapproved indication, or
- an FDA unapproved device.

If the device is a “significant risk” device, or if the study is “greater-than-minimal risk,” the review of the protocol must be completed by the Full Board.

Q: When a research study involves an unapproved device, or an FDA approved device being studied for an off-label use, what will the IRB consider?

A. Whether the test article requires an Investigational Device Exemption (IDE) from the FDA or is exempt from the IDE requirements.
   1. The UF IRB will ask the PI to consult the FDA for an opinion for difficult device assessments.

B. Whether the device poses a “Significant Risk” (SR) or “Non-Significant” to the participants in the study.
   1. Significant Risk (SR) to the participants in the study.
      a. The risk determination made by the IRB will be based upon both the nature of the device AND the proposed use of the device in the study as outlined in 21 CFR 812(3)(m)(1-4).
      b. If the device is SR, the investigator must provide documentation from the FDA that the device either:
         1. Has a 510(k) designation or an IDE before the IRB may take final action to approve a protocol; or
         2. If the UF IRB believes that a device is SR, and the sponsor believes it to be NSR, the UF IRB will require the PI to notify the sponsor of the UF IRB determination. The sponsor may then consult with the FDA for an agency opinion. The FDA opinion must be provided to the IRB in writing. If the sponsor chooses not to consult with the FDA and/or not to submit an IDE application to the FDA, the protocol will not be approved at UF.
   2. “Non-Significant Risk” (NSR) to the participants in the study.
      a. In the case of an NSR claim, the initial assessment of whether or not the device study is NSR is made by the sponsor/investigator and the justification for this assessment is submitted in the myIRB application. The IRB then determines whether that assessment is appropriate. If it agrees, the IRB will record the rationale for its NSR assessment on the review sheet for determinations and in the minutes for a convened meeting. All NSR devices under 21 CFR 812.2(b) are “considered to have approved applications for IDEs.”
      b. The IRB will consider whether some NSR devices meet the criteria for exempt classification as a diagnostic device under 21 CFR 812(c)(3). If an
investigational device meets those criteria, the IRB will document that it is exempt from the IDE requirements.

Consent forms for IDE studies must clearly state that the “test article” is investigational or experimental.

**Q: What are the responsibilities of investigators who are also the sponsor of IND or IDE clinical investigations?**

UF investigators who submit protocols involving FDA test articles and for which they hold the IND or IDE are sponsor-investigators and must adhere to the same regulatory responsibilities as any other sponsor. The application must include all supporting FDA documentation. Any conflict of interest must be addressed by the University, and any method to address the conflict must be included as part of the IRB review and approval.