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.

**Q: What are the responsibilities of investigators to control test articles to be used in research studies?**

Investigators have the responsibility to control the test articles under investigation in their research studies in compliance with applicable institutional and FDA regulations.

- PIs must assure that the test article is used only by those participating in the research study; stored, secured, and labeled so that they are identified as for research and/or investigational use only; and adequate records of test article disposition maintained.
- If a study involving a test article is terminated, the PI (or designee) must return or destroy unused supplies of the test article pursuant to sponsor requirements or applicable waste disposal regulations.
- If test article is subject to the Controlled Substances Act, other precautions must be taken to prevent theft or diversion of the drug.

**For Test Articles - Drugs/Biologics**

All human subjects research involving drugs or biologics conducted by UF-Investigators within the UF Health/Shands Hospital System must be coordinated through Investigational Drug Services (IDS) and must comply with IDS procedures for the control of study drugs used in research.

For research involving drugs and biologics conducted outside of the UF Health/Shands Hospital System, researchers are required to have adequate infrastructure in place to assure the proper control of investigational drugs and biologics.

It is the PI’s responsibility to assure that systems and procedures for control of the investigational drug or biologic comply with FDA and other applicable regulations.

All VA related research studies involving investigational drugs and biologics, must also comply with VA polices and requirements, as outlined in the VHA Handbook 1108.04, for control and procurement of investigational drugs and biologics.

**For Test Article - Investigational Devices**

It is the PI’s responsibility to assure that systems and procedures for control of the investigational device comply with FDA and other applicable regulations, including ensuring personnel who may use the device
are appropriately trained and qualified to use the device safely, and documenting who is designated to use the device, where the device will be shipped to and stored, the procedures for the release of the device, and how inventory will be maintained.

Researchers are required to have adequate infrastructure in place to assure the proper control of investigational devices.

For research involving investigational medical devices, procedures for controlling access to and use and disposal of devices and assuring maintenance of required records are established by the Investigator. When applicable, PIs may contact the Shands Hospital Supply Chain Services for any device that are intended to be purchased, received, and/or stored by Shands Hospital. A separate Study Device Custodial/Procurement Agreement between the sponsor and Shands may be required

All VA related research studies involving investigational devices, must also comply with VA polices and requirements, as outlined in the VHA Handbook 1108.04, for control and procurement of investigational devices.