IRB Policy 19: Research involving Devices
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I. Summary Policy

The policy of the East Tennessee State University/Veterans Affairs Institutional Review Board (ETSU/VA) IRB is that all applicable rules and regulations will be followed in the review and approval of any clinical investigations using investigational devices. The U.S. Food and Drug Administration (FDA) regulates clinical studies conducted on drugs, biologics, devices, diagnostics, and in some cases dietary supplements and food additives. All such research studies must be conducted in accordance with FDA requirements for the protection of human subjects and IRBs, regardless of source of funding (21 CFR Parts 50 and 56).

II. Definitions

A. Clinical investigation or research involving one or more subjects to determine the safety or effectiveness of a device.

B. Medical device is an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article that does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and is not dependent upon being metabolized for the achievement of its primary intended purposes (21 U.S.C. 321(h)), which is intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or intended to affect the structure or any function of the body of man or other animals.

C. Investigational device means a device, including a transitional device, that is the object of an investigation.

D. Significant Risk (SR) device is defined [21 CFR 812.3(m)] as a study of a device that presents a potential for serious risk to the health, safety, or welfare of a subject and (1) is intended as an implant; or (2) is used in supporting or sustaining human life; or (3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or (4) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

E. Non-Significant Risk (NSR) device is a clinical device investigation that does not meet the definition for a significant risk device study.

III. IRB Evaluation of Device Studies

The ETSU/VA IRB reviews projects that involve devices to protect the rights and welfare of human subjects involved and to assure compliance with applicable regulations. The IRB evaluates whether the submission constitutes research involving human subjects and whether a device used is an investigational medical device involving human subjects. A medical device is considered investigational if the device is not approved for marketing in the U.S. or the device is approved for marketing but is being clinically evaluated for a new indication. Clinical device investigations are evaluated by the IRB to determine whether submission to the FDA is required, and if required, has been completed (as indicated by documentation from the sponsor that a valid IDE has been received) or; the use of the device is exempt from prior submission to the FDA or; if the use of device may be approved under abbreviated requirements. It is the policy of the ETSU/VA IRB that when research is conducted to determine the safety or effectiveness of a device, the device must have an IDE issued by the FDA, unless the device (1) meets one of the four exemptions from the requirement to have an IDE or (2) meets the requirements for an abbreviated IDE.

There are two types of clinical studies involving medical devices that require than an Investigational Device Exemption (IDE) be obtained from the FDA in addition to IRB approval before a research study may commence.

1. A clinical study involving an unapproved device that poses significant risk to subjects
2. A clinical study involving an approved (legally marketed) device being tested for a new indication

If an IDE is required, validation of an IDE will be done by determining that the IDE number matches the Sponsor protocol, communication from the Sponsor, or communication from the FDA. In the case of an Investigator who holds the IDE, the number must match information provided by the FDA. An investigator's brochure will not be used for validation because one investigator brochure often covers multiple IDEs.

There are three types of clinical studies involving medical devices that do not require that an IDE from the FDA be obtained be obtained. However, IRB approval is required before the study may commence.

1. Studies involving approved devices used with their approved labeling or devices that are substantially equivalent (already granted an 510(k) by the FDA) to currently marketed devices
2. Studies involving approved devices that are determined by the IRB or the FDA to pose non-significant risks to the subjects
3. Other specific IDE-exempt studies, in accordance with FDA regulations, as described below.

IV. IDE Exempt

With the exception of 21 CFR 812.119, the rest of the IDE regulations do not apply to device studies that meet the criteria for an exempted investigation under 21 CFR 812.2(c). They also do not require the FDA, the sponsor, the investigator or the IRB to make an NSR or SR determination. The device is exempt from the IDE requirements only if one of the following categories is met. If none of the categories is met, the device is not exempt from an IDE.

1) Devices, other than transitional devices, in commercial distribution prior to May 28, 1976, when used or investigated in accordance with labeling in effect at that time or devices, other than transitional devices, introduced into commercial distribution on or after May 28, 1976, that the FDA determines to be substantially equivalent to a device in commercial distribution prior to May 28, 1976, and which is used or investigated in accordance with approved labeling;
2) A diagnostic device (including in vitro diagnostic products in compliance with 21 CFR 809.10(c)) if the testing:
    - Is non-invasive
    - Does not require an invasive sampling procedure that presents significant risk
    - Does not by design or intention introduce energy into a subject, and
    - Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.
3) Devices undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution, if the testing is not for the purpose of determining safety or effectiveness and does not put the subject at risk.
4) Custom devices, as defined by FDA in 21 CFR 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.

V. Non-significant risk determination

If the ETSU/VA IRB receives a submission involving a medical device investigation that does not already have an IDE and cannot be determined IDE exempt, the IRB will review the submission to make a non-significant risk (NSR) determination. NSR device studies, however, should not be confused with the concept of "minimal risk," a term utilized in the IRB regulations to identify certain studies that may be approved through an expedited review procedure.

The initial assessment of whether or not a device study presents NSR is made by the sponsor, and the sponsor’s determination and rationale should be made

available to the IRB. In addition, the IRB must be informed of the FDA's assessment of the device's risk if such an assessment has been made. The ETSU/VA IRB may disagree with the sponsor and may seek FDA consultation in making the NSR determination. FDA has the ultimate decision in determining if a device study is SR or NSR, and the determination cannot be overturned by the ETSU/VA IRB.

The risk determination should be based on the proposed use of a device in an investigation, and not on the device alone. In deciding if a study poses an SR, the IRB considers the nature of the harm that may result from use of the device. Studies where the potential harm to subjects could be life-threatening, could result in permanent impairment of a body function or permanent damage to body structure, or could necessitate medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to body structure should be considered SR. Also, if the participant must undergo a procedure as part of the investigational study, e.g., a surgical procedure, the IRB considers the potential harm that could be caused by the procedure in addition to the potential harm caused by the device.

VI. Submission and IRB Review

Investigators will be asked on New Protocol Submission xform to indicate whether the research involves devices. If so, the investigator must complete the appropriate sections of the New Protocol Submission xform to describe the device study and attach supporting documentation as necessary such as sponsor protocol, device brochure, 510K documentation, etc. In addition to receiving a completed xform, informed consent, protocol, and investigator's brochure (if available), the IRB must receive a description of the device, reports of prior investigations with the device, the proposed investigational plan, a description of patient selection criteria and monitoring procedures, as well as any other information that the IRB deems necessary to make its decision. The IRB must also be informed whether other IRBs have reviewed the proposed study and what determinations were made. If the study does not already have an IDE, the investigator will provide the rationale in the xform and address questions to help the IRB determine if the study is IDE exempt or to provide information in support of a NSR determination. If the FDA has made a determination of NSR, then a copy of the determination letter received from FDA should be submitted with the protocol.

When a study involving a device is received by the IRB, the IRB coordinator verifies the New Protocol Submission xform for appropriate device description and confirms receipt of required attachments. If the study has an IDE, the IRB Coordinator confirms the IDE number with the sponsor protocol or FDA communication. If the investigator requests IDE exemption, the IRB Coordinator ensures that the xform includes the appropriate rationale and attachments. The supplemental device

checklist is used by IRB Chair/Vice-Chair as a tool to evaluate device studies.

If the study does not have an IDE and is not eligible for IDE exemption, the IRB Coordinator verifies receipt of the sponsor NSR determination and forwards the submission for full board review. The Non-Significant Risk Device Checklist is used to assist with this determination. If the IRB decides the study is NSR, the IRB proceeds to review study applying requisite criteria. For NSR investigational devices, studies follow abbreviated IDE requirements and do not have to have an IDE application approved by the FDA.

For any device protocol considered by FDA to present SR, an IDE number will be required prior to submission to the ETSU/VA IRB for initial review. If the IRB decides the study is Significant Risk:

1. The IRB Coordinator forwards a letter to notify the sponsor and investigator of the decision that the study is significant risk.
2. The IRB tables the study until an IDE is obtained by the sponsor.
3. The sponsor should notify FDA that an SR determination has been made.
4. After IDE is obtained and submitted, the convened IRB reviews the study.

If the IRB determines that a device study is SR, the study may not begin until both the IRB and FDA approve the investigation. The study can be conducted as an SR investigation following FDA approval of an IDE application.

Minutes of convened IRB meetings must document the rationale for SR/NSR and subsequent approval or disapproval decisions for the clinical investigation.

VII. Investigator Responsibilities

The investigator is responsible for ensuring that the research is conducted according to all regulatory guidelines and must obtain approval from the ETSU/VA IRB. The investigator is responsible for the investigational drug/device accountability which includes storage, security, dispensing, administration, return, disposition and records of accountability. The investigator is responsible for reporting all unexpected fatal or life-threatening suspected adverse reactions associated with the use of an investigational device to the FDA within 7 calendar days after determination; suspected adverse reactions or similar events within 15 calendar days. The investigator is responsible for notifying the sponsor as specified in the protocol.

If the investigator or organization is acting as the sponsor, the investigator or sponsor must follow all the additional regulatory requirements of sponsors. Sponsor-Investigator refers to a situation in which the individual investigator is the holder of the IDE and, therefore, assumes the duties of the sponsor of the clinical

investigation under the applicable FDA regulations as well as being an investigator conducting the study under whose immediate direction the investigational device is administered, dispensed, or used. The IRB requires any investigator acting as the sponsor to be familiar with the FDA sponsor and investigator requirements. The sponsor-investigator must read “Responsibilities for Sponsors of Significant Risk Device Studies” or “Responsibilities for Sponsors of Non-Significant Risk Device Studies,” as applicable, published by the FDA. The IRB receives a signed attestation that the sponsor-investigator understands his/her responsibilities prior to issuing final study approval.

References:

IDE Regulations
Information Sheet Guidance For IRBs, Clinical Investigators, and Sponsors
Significant Risk and Nonsignificant Risk Medical Device Studies
IDE Institutional Review Boards (IRB)
IDE Responsibilities
IDE Approval Process