

Grand Valley State University Institutional Review Board (IRB)	
Title: <i>Significant Risk, Nonsignificant Risk, and Exempt Medical Device Studies</i>	
Section: 920	
Approved by IRBPPC: 03/31/2020	Approved by AIO/RIO: 04/06/2020
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Related documents: 900: <i>IRB Protocol Review</i> 1020: <i>Reportable Events: Protocol Deviations, Unanticipated Problems and Adverse Events</i>	

Policy

1. For all human subjects research being conducted to determine the safety or effectiveness of a United States Food and Drug Administration (FDA)-regulated device, the IRB must evaluate the applicability of the FDA’s Investigational Device Exemptions (IDE) regulation at 21 CFR 812. This includes any device that is investigational (not FDA-approved), is FDA-approved but used off-label in the research, or is used according to its FDA-approved label in the research but for which data about its safety or effectiveness will be submitted to or held for inspection by the FDA. It is the policy of the IRB to make device risk determinations for every investigational device study reviewed, except when the study is exempt from IDE regulations. The FDA considers this determination to be part of the IRB’s responsibilities for conducting its initial review of a study (21 CFR 56.108).
2. Sponsors or sponsor-investigators are responsible for making the initial device risk determination and presenting it to the IRB. Unless the FDA has already made a risk determination for the research, the IRB must review the sponsor’s device risk determination for the proposed study and modify the determination if the IRB disagrees with the sponsor. If the FDA has already made the device risk determination for the study, the determination of the FDA is final and must be communicated by the sponsor to the IRB.
3. If the sponsor, sponsor-investigator or IRB determines the device is significant risk, then the sponsor or sponsor-investigator must have an approved IDE application before the study can proceed and before IRB approval can be granted.

Procedures

1. Types of Devices

The IDE regulations describe three types of device studies: exempt, significant risk (SR) and nonsignificant risk (NSR) studies.

A. IDE Exempt Device

- i. Under 21 CFR 812.2(c), a device study is exempt from the IDE regulations if at least one of the following criteria are met:

1. A device, other than a transitional device, in commercial distribution immediately before May 28, 1976, when used or investigated in accordance with the indications in labeling in effect at that time;
 2. A device other than a transitional device, introduced into commercial distribution on or after May 28, 1976, that the FDA has determined to be substantially equivalent to a device in commercial distribution immediately before May 28, 1976, and that is used or investigated in accordance with the indications in the labeling the FDA reviewed under subpart E of part 807 in determining substantial equivalence;
 3. A diagnostic device, if the sponsor complies with applicable requirements in 809.10(c) and if the testing
 - a. Is noninvasive,
 - b. Does not require an invasive sampling procedure that presents significant risk,
 - c. Does not by design or intention introduce energy into a subject, and
 - d. Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure
 4. A device 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 subjects at risk;
 5. A device intended solely for veterinary use;
 6. A device shipped solely for research on or with laboratory animals and labeled in accordance with 21 CFR 812.5(c); or
 7. A custom device as defined in 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.
- ii. Verification of IDE exemption can be completed by expedited review or at a convened IRB meeting. If the research is IDE exempt and is being conducted to collect data to support either a clinical investigation or an FDA marketing application, then the study must comply with 21 CFR 50 and 56. The IRB does not need to decide whether the device poses a significant risk or nonsignificant risk. However, IRB approval is still required before the investigation may begin.

B. Determination of Significant Risk vs. Nonsignificant Risk for Non-Exempt Devices

For determination of the need for an IDE, the convened IRB will address the applicability of FDA regulations under 21 CFR 812.2 and, if necessary, make a device risk determination. All device risk determinations for non-IDE exempt studies must be completed at a convened IRB meeting, and the IRB meeting minutes must document the IRB's reason for the SR or NSR determination.

C. Significant Risk Device

Under 21 CFR 812.3(m), an SR device means an investigational device that meets at least one of the following criteria:

- i. Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;
- ii. Is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;
- iii. Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or
- iv. Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject

D. Nonsignificant Risk Device

An NSR device is one that does not meet the above definition of an SR device.

2. IRB Review of Medical Device Studies

A. The IRB will determine whether the medical device is SR or NSR by use of any of the following:

- i. A risk assessment report from the sponsor or sponsor-investigator explaining the device classification;
- ii. The FDA letter approving the IDE (in which case the IRB will consider the investigation an SR device study);
- iii. A Pre-Market Approval letter, supplement letter or amendment letter from the FDA;
- iv. Information from the study application, master protocol, investigator's brochure (or package insert) and other risk evaluations presented by the sponsor or investigator;
- v. Review of the FDA Information Sheet for IRBs, Clinical Investigators, and Sponsors entitled, "Significant Risk and Nonsignificant Risk Medical Device Studies," containing examples of SR and NSR devices;
- vi. Reports of prior investigations conducted with the device;
- vii. Description of subject selection criteria;
- viii. Description of monitoring procedures;
- ix. Potential harm that may be caused by any surgical procedure used to place or implant the device; and
- x. The proposed use of the device and the nature of harm that may result from its use in the study; and
- xi. Any other information that the IRB requires in order to conduct its review and make a determination

- B. If an IDE application is or has been submitted to the FDA, but final approval has not been granted, the IRB can proceed with the review of the study, but final approval will not be granted until documentation of the FDA approval is submitted.
- C. If the IRB decides the study is SR, the IRB shall notify the investigator in writing that an IDE must be obtained from the FDA prior to IRB review of the study. Any amendments or corrections of deficiencies required by the FDA during the IDE process must be submitted for review and approval of the IRB. Once the IDE is obtained, the investigator may resubmit the study for IRB review.
- D. The IRB may conditionally approve a study as an SR device study, but final IRB approval will not occur until the FDA approves the sponsor's IDE application, or provides a determination that the device as proposed for use in the investigation is NSR and this information has been submitted to the IRB.
- E. If the IRB determines the study is NSR, the IRB will verify that the investigator will comply with all Abbreviated IDE requirements in 21 CFR 812.2(b). Verification of the Abbreviated IDE will be documented in the minutes of the meeting.
- F. The IRB shall proceed to review the study under 21 CFR 56 only after the SR/NSR determination has been made.
- G. The IRB will record its determination of SR/NSR status in the minutes of the meeting. The minutes will describe the IRB's reasons for its SR/NSR determination and will reference any applicable documents used to establish the IDE status for the study.
- H. For a device study to be eligible for expedited review at the time of continuing review, it must involve the use of an NSR device AND the research must present no greater than minimal risk to the subject. Upon making its initial determination that a proposed device study is NSR, and that the study is "minimal risk," the convened board may vote to expedite the study under expedited Category 1 at the time of continuing review the following year, assuming no change in risk level in the interim. Expedited Category 9 may not be used for an NSR device study because the study is considered to have an approved IDE (though not an approved IDE application) under the abbreviated IDE regulations.

Background

1. Definition of Device

Per Section 201(h) of the Food, Drug, and Cosmetic Act, a device is:

An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory for which both conditions A and B are satisfied:

- A. Any of the following are true about the device:

- i. It is recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them;
- ii. It 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
- iii. It is intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals.

B. The device does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes. The term "device" does not include software functions excluded pursuant to section 520(o).

2. Definition of Transitional Device

Per 21 CFR 812.3(r), transitional device means a device subject to section 520(l) of the Federal Food, Drug, and Cosmetic Act, that is, a device that the FDA considered to be a new drug or an antibiotic drug before May 28, 1976.

3. Distinctions Between SR/NSR Determinations and Minimal Risk Determinations

The IRB should not confuse the responsibility to make an SR/NSR determination for a device study with the concept of “minimal risk.” “Minimal risk” is a regulatory definition used in part to identify certain studies that the IRB may approve through an expedited review procedure. SR/NSR determinations are based on the FDA definitions under 21 CFR 812 and are separate and distinct from minimal risk determinations under the Common Rule.

The judgment about whether a study poses a significant risk or nonsignificant risk is based on the significance of the potential harm that may result from participation in the study, including the use of the device; whereas the IRB’s decision to approve a study for implementation is based on the study’s overall risk-benefit assessment.

For a significant risk device study, the research will always involve more than minimal risk. However, a non-significant risk device study may, for reasons other than those related to the device portion of the study, also involve more than minimal risk. All research requiring an SR/NSR determination to be made will be initially reviewed by the convened IRB, regardless of risk level. Subsequent IRB reviews can be completed by expedited review, consistent with the process described in Procedures section 2.H.