SIGNIFICANT RISK OR NON-SIGNIFICANT RISK DEVICE DETERMINATIONS BY THE DUHS IRB
3/4/2016

For all research to determine the safety or effectiveness of a device the IRB must evaluate the applicability of the FDA’s Investigational Device Exemptions (IDE) regulation (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.

The definition of 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 which is:

- recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them,
- 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, and which 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 any of its primary intended purposes."

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

For information on device studies that are exempt from the IDE regulation, see the DUHS IRB Checklist titled “Checklist to Determine if an Investigational Device Exemption (IDE) is Required Where an IDE is not Provided” and the FDA Information Sheet Guidance entitled, “Frequently Asked Questions About Medical Devices” at http://www.fda.gov/oc/ohrt/irbs/irbreview.pdf. If an exempt study is being conducted to collect data to support either a clinical investigation or a marketing application, then the study must comply with 21 CFR Part 50 and 21 CFR Part 56. For device studies that are exempt from the IDE regulations, 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.
It is the policy of the DUHS IRB to make SR/NSR device determinations for every investigational medical device study reviewed, except when the study is exempt from IDE regulations. FDA considers this determination to be part of the IRB’s responsibilities for conducting its initial review of a study (21 CFR 56.108).

The SR/NSR determination is based on the proposed use of a device in the research study, and not on the device alone. The IRB must also consider the potential harm of any additional procedure(s) needed as part of the research to study the device, as well as the potential harm caused by the device itself.

The determination of the IRB will be documented in the meeting minutes and the study sponsor and/or study team will be notified of its obligations under the applicable part of 21 CFR 812.

**DEFINITIONS**

**Significant Risk Device**

Under 21 CFR 812.3(m), an SR device means an investigational device, that:
- Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject; or
- Is purported or represented to be for use supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject; or
- 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
- Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

**Nonsignificant Risk Device**

An NSR device study is one that does not meet the definition for an SR device study.

*See the January 2006 list of commonly studied medical devices for examples that may be helpful in making SR and NSR determinations, at the following website: [http://www.fda.gov/oc/ohrt/irbs/devrisk.pdf](http://www.fda.gov/oc/ohrt/irbs/devrisk.pdf).*

**MAJOR DIFFERENCES BETWEEN SR AND NSR DEVICE STUDIES**

The major differences between SR and NSR studies are in the IDE approval process and in the sponsor’s record keeping and reporting requirements, as outlined below.
1. Significant Risk (SR) Device Studies
   • SR device studies must have an IDE application approved by FDA before they may proceed or have written documentation from the FDA device section that a separate IDE application is not needed because the study data will be submitted under an IND application.
   • SR device studies must follow all applicable IDE regulations at 21 CFR 812 (even if conducted under an IND application).

2. Nonsignificant Risk (NSR) Device Studies
   • NSR device studies must follow the abbreviated requirements at 21 CFR 812.2(b).
   • These abbreviated requirements address labeling, IRB approval, informed consent, monitoring, records, reports, and prohibition against promotion. However, there is no need to make progress reports or final reports to FDA.
   • NSR device studies do not have to have an IDE application approved by FDA.
   • Sponsors and IRBs do not have to report the IRB approval of an NSR device study to FDA. Thus the IRB’s NSR determination is important because the IRB serves as the FDA’s surrogate for review, approval, and continuing review of the NSR device studies. An NSR device study may start at DUHS as soon as the DUHS HRPP reviews and approves the study and without prior approval by FDA.

SPONSOR/INVESTIGATOR RESPONSIBILITIES

Sponsors are responsible for making the initial risk determination and Investigators will present it to the IRB as part of the IRB submission. If the sponsor identifies a device as NSR, the sponsor must provide the DUHS IRB an explanation of its determination and any other information that may help the IRB in evaluating the risk of the device as proposed for use in the research study. For example, the IRB would need a description/specifications of the device, why the device qualifies as a NSR device, and if available, reports of prior investigations with the device. If FDA has already determined that the device, as used in the research study, is NSR, the sponsor should so inform the IRB.

IRB RESPONSIBILITIES

Unless FDA has already made a risk determination for the device study, the convened IRB must review the sponsor's SR or NSR determination for every investigational medical device study it reviews and modify the determination if the IRB disagrees with the sponsor.

If FDA has already made the SR or NSR determination for the device study, the agency's determination is final. If the device already has an approved IDE
application, the IRB will require documentation from the sponsor that the IDE number applies to the device to be used for the study under consideration. This may be reflected in the sponsor’s protocol, or correspondence from the sponsor or FDA. FDA will provide a written determination of SR/NSR status at the request of the IRB.

The DUHS IRB will make the SR or NSR determination about a device study by reviewing relevant information at a convened meeting (for IRB considerations when making the SR/NSR determination, see next section below). If the IRB determines the device, as used in the research study, is NSR, the IRB may approve the study using the criteria at 21 CFR 56.111. In that case no submission of an IDE application to FDA is needed.

If the IRB disagrees with the sponsor’s NSR assessment and determines the device study is a SR study, the IRB will tell the clinical investigator and the sponsor. The sponsor must submit a report of the IRB’s determination within 5 working days of receipt (21 CFR 812.150(b)(9)).

The IRB may conditionally approve the study as an SR device study, but final IRB approval will not occur until 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.

IRB CONSIDERATIONS WHEN MAKING THE SR/NSR DETERMINATION

The DUHS IRB will consider the following in determining whether a device study poses a SR or NSR:

• the sponsor’s description of why the study is not SR.
• whether the proposed NSR device study meets the definition of “significant risk” (see Definitions above).
• the proposed use of the device in the research study, as well as any protocol related procedures and tests, not just the device (test article) alone. (This process is different from the IRB review process found at 21 CFR 56.111(a)(2)).
• the nature of the harm that could potentially result from use of the device in the intended population.
• additional information from the sponsor, if needed.

DISTINCTIONS BETWEEN SR/NSR DETERMINATIONS AND MINIMAL RISK DETERMINATIONS

IRB members and staff should not confuse their responsibility to make an SR/NSR determination for a device study with the concept of “minimal risk.” The
term "Minimal Risk" is a Common Rule definition (45 CFR 46) 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 Greater than Minimal Risk/Not Greater than Minimal Risk determinations under the Common Rule.

For a device study to be eligible for expedited review, it must involve the use of an NSR device AND the research must present no greater than minimal risk to the subject (21 CFR 56.110). 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 (21 CFR 812.2b).

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.

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