The Investigational Device Exemptions (IDE) regulation (21 CFR 812) describes three types of device studies, the first two of which are subject to the IDE regulation: 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.

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;
• 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;
• 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 follow all the IDE regulations at 21 CFR 812.
   - SR device studies must have an IDE application approved by FDA before they may proceed.

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 IRB 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. 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 is NSR, the sponsor should so inform the IRB.
For Significant Risk device studies, the sponsor must submit an IDE application to FDA and obtain the agency’s approval of the study. Sponsors/Investigators must provide the IDE number and/or a copy of the IDE approval letter to the IRB as a part of the IRB submission.

**IRB RESPONSIBILITIES**

Unless FDA has already made a risk determination for the device study, the 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, 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 is NSR, the IRB may approve the study using the criteria at 21 CFR 56.111. In that case the study may then begin without submission of an IDE application to FDA.

If the IRB disagrees with the sponsor’s NSR assessment and decides the device study is a SR study, the IRB will tell the clinical investigator, and where appropriate, the sponsor. The IRB may conditionally approve the study as an SR device study, but the study may not begin until FDA approves the sponsor’s IDE application, or provides a determination that the device as proposed for use in the investigation is Nonsignificant Risk. Notification of FDA’s approval of the IDE application will be required via the “Approval with Modifications” mechanism used by the IRB.

The IRB will document its SR or NSR determination in the meeting minutes. The IRB study file will also include, as applicable, the documentation used to establish the IDE status for the study. For an SR determination, such documentation may include, for example, a copy of the IDE approval or conditional approval letter from FDA.

**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 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 used in the regulations in part to identify certain studies that the IRB may approve through an expedited review procedure. SR/NSR determinations are separate and distinct from Greater than Minimal Risk/Not Greater than Minimal Risk determinations. For a device study to be eligible for expedited review, it must be 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 Category 9 at the time of continuing review the following year, assuming no change in risk level in the interim.