

FDA Guidance - Significant Risk and Non-Significant Medical Device Studies

The information below is from the FDA Information Sheets – October 1, 1995 and provides guidance on use of medical devices in research and the appropriate FDA and IRB review that is needed.

An approved investigational device exemption (IDE) permits a device that is not approved (via premarket authorization, PMA) or cleared to market (via 510(k)) by the FDA to be shipped to conduct clinical investigations of that device. Significant risk investigational devices must have an IDE issued by FDA before they can be shipped. Nonsignificant risk devices are considered to have an approved IDE when the IRB agrees with the sponsor that the device meets the criteria for a nonsignificant risk device.

The Investigational Device Exemption (IDE) regulations [21 CFR part 812] describe two types of device studies; "significant risk" (SR) and "nonsignificant risk" (NSR).

Significant risk device [21 CFR 812.3(m)] means an investigational device that: (1) is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject; (2) 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; (3) 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 (4) Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

NSR device investigation: is one that does not meet the definition for a significant risk study. NSR device studies, however, should not be confused with the concept of "minimal risk," a term utilized in the Institutional Review Board (IRB) regulations [21 CFR part 56] to identify certain studies that may be approved through an "expedited review" procedure.

For both SR and NSR device studies, IRB approval prior to conducting clinical trials and continuing review by the IRB are required. In addition, informed consent must be obtained for either type of study [21 CFR part 50].

Distinguishing Between SRC and NSR Device Studies

The effect of the SR/NSR decision is very important to research sponsors and investigators. SR device studies are governed by the IDE regulations [21 CFR part 812]. NSR device studies have fewer regulatory controls than SR studies and are governed by the abbreviated requirements [21 CFR 812.2(b)].

The major differences are in the approval process and in the record keeping and reporting requirements. The SR/NSR decision is also important to FDA because **the IRB serves, in a sense, as the Agency's surrogate with respect to review and approval of NSR studies.** FDA is usually not apprised of the existence of approved NSR studies because sponsors and IRBs are not required to report NSR device study approvals to FDA. If an investigator or a sponsor proposes the initiation of a claimed NSR investigation to an IRB, and **if the IRB agrees that the device study is NSR and approves the study, the investigation may begin at that institution immediately, without submission of an IDE application to FDA.**

SR/NSR Studies and the IRB: The NSR/SR Decision

The assessment of whether or not a device study presents a NSR is initially made by the sponsor. If the sponsor considers that a study is NSR, the sponsor provides the reviewing IRB an explanation of its determination and any other information that may assist the IRB in evaluating the risk of the study. **The sponsor should provide the IRB with 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 sponsor should inform the IRB whether other IRBs have reviewed the proposed study and what determination was made. The sponsor must inform the IRB of the Agency's assessment of the device's risk if such an assessment has been made. The IRB may also consult with FDA for its opinion.**

The IRB may agree or disagree with the sponsor's initial NSR assessment. If the IRB agrees with the sponsor's initial NSR assessment and approves the study, the study may begin without submission of an IDE application to FDA. If the IRB disagrees, the sponsor should notify FDA that an SR determination has been made. The study can be conducted as an SR investigation following FDA approval of an IDE application.

<p>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, an IRB must consider 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 subject must undergo a procedure as part of the investigational study, e.g., a surgical procedure, the IRB must consider the potential harm that could be caused by the procedure in addition to the potential harm caused by the device.</p> <p>If the IRB decides that the study is Significant Risk:</p> <p>1. IRB Responsibilities:</p> <p>Notify sponsor and investigator of SR decision After IDE obtained by sponsor, proceed to review study applying requisite criteria [21 CFR 56.111]</p> <p>2. Sponsor Responsibilities:</p> <p>Submit IDE to FDA or, if electing not to proceed with study, notify FDA (CDRH Program Operations Staff 301-594-1190) of the SR determination; Study may not begin until FDA approves IDE and IRB approves the study. Sponsor and investigator(s) must comply with IDE regulations [21 CFR part 812], as well as informed consent and IRB regulations [21 CFR parts 50 and 56].</p> <p>If the IRB decides the study is Non-significant Risk:</p> <p>1. IRB proceeds to review study applying requisite criteria [21 CFR 56.111]</p> <p>2. If the study is approved by the IRB, the sponsor and investigator must comply with "abbreviated IDE requirements" [21 CFR 812.2(b)], and informed consent and IRB regulations [21 CFR parts 50 and 56].</p>	<p>EXAMPLES OF NSR DEVICES</p> <ul style="list-style-type: none"> ✓ Low Power Lasers for treatment of pain ✓ Caries Removal Solution ✓ Daily Wear Contact Lenses and Associated Lens Care Products not intended for use directly in the eye (e.g., cleaners; disinfecting, rinsing and storage solutions) ✓ Contact Lens Solutions intended for use directly in the eye (e.g., lubricating/rewetting solutions) using active ingredients or preservation systems with a history of prior ophthalmic/contact lens use or generally recognized as safe for ophthalmic use ✓ Conventional Gastroenterology and ✓ Urology Endoscopes and/or Accessories ✓ Conventional General Hospital Catheters (long-term percutaneous, implanted, subcutaneous and intravascular) ✓ Conventional Implantable Vascular Access Devices (Ports) ✓ Conventional Laparoscopes, ✓ Culdoscopes, and Hysteroscopes ✓ Dental Filling Materials, Cushions or Pads made from traditional materials and designs ✓ Denture Repair Kits and Realigners ✓ Digital Mammography [Note: an IDE is required when safety and effectiveness data are collected which will be submitted in support of a marketing application.] ✓ Electroencephalography (e.g., new recording and analysis methods, enhanced diagnostic capabilities) ✓ Externally Worn Monitors for Insulin Reactions ✓ Functional Electrical Neuromuscular Stimulators ✓ General Biliary Catheters ✓ General Urological Catheters (e.g., Foley and diagnostic catheters) ✓ Jaundice Monitors for Infants ✓ Magnetic Resonance Imaging (MRI) ✓ Devices within FDA specified parameters ✓ Manual Image Guided Surgery ✓ Menstrual Pads (Cotton or Rayon, only) Menstrual Tampons (Cotton or Rayon, only) ✓ Nonimplantable Electrical Incontinence Devices ✓ Nonimplantable Male Reproductive Aids with no components that enter the vagina ✓ Ob/Gyn Diagnostic Ultrasound within FDA approved parameters ✓ Transcutaneous Electric Nerve Stimulation (TENS) Devices for treatment of pain ✓ Wound Dressings, excluding absorbable hemostatic devices and dressings (also excluding Interactive Wound and Burn Dressings)