

**UNIVERSITY OF TENNESSEE HEALTH SCIENCE CENTER
INSTITUTIONAL REVIEW BOARD
SIGNIFICANT RISK / NONSIGNIFICANT RISK DETERMINATIONS
FOR MEDICAL DEVICE STUDIES**

I. PURPOSE

To document the procedures for determination of significant risk/non-significant risk status for medical device studies.

II. SCOPE

This SOP applies to the IRB administrative staff, IRB members.

Personnel Responsible:

University of Tennessee Health Science Center Institutional Review Board
Sections administrative staff and members.

III. BACKGROUND

Clinical investigations undertaken to develop safety and effectiveness data for medical devices must be conducted according to the requirements of the IDE regulations found in 21 CFR 812. The Investigational Device Exemption (IDE) regulations describe three types of device studies: significant risk (SR), non-significant risk (NSR), and exempt studies. The major differences between SR and NSR status relate to the IDE approval process and the sponsor's record keeping and reporting requirements. If SR status is assigned to the use of a device in a particular study, then the sponsor must have an approved IDE application before the study can proceed. In addition, the sponsor must observe extensive requirements for reporting to the FDA on the progress of the research and report IRB approval to the FDA. If NSR status is assigned to a device study, then the sponsor may proceed without an approved IDE, must observe only abbreviated recordkeeping requirements, and is not required to inform the FDA about the conduct of the study or IRB approval. If a study is exempt from IDE regulations, then determination of risk status is not required.

Sponsors are responsible for making the initial risk determination and presenting it to the IRB. Unless the FDA has already made a risk determination for the study, the IRB must review the sponsor's SR or NSR determination for the proposed study and modify the determination if the IRB disagrees with the sponsor. If the FDA has already made the SR/NSR determination for the study, the determination

of the FDA is final and must be communicated by the sponsor to the IRB.

If the sponsor identifies a study as NSR, the sponsor must provide the reviewing IRB an explanation of its determination (21 CFR 812.2(b)(1)(ii)). The IRB may also use information from the application, protocol, the investigator's brochure, package insert, FDA Information Sheets, reports of prior investigations conducted with the device, description of subject selection criteria, monitoring procedures and other evaluations presented by the sponsor to categorize the device as "SR" or "NSR". If the IRB agrees with the NSR designation and a separate risk determination has not been made by the FDA, the study may proceed with IRB approval. If the IRB disagrees with a sponsor's classification of a device as NSR, then the investigation cannot proceed until the FDA has approved an IDE application and the IRB has approved the study under the regulations for the protection of human subjects.

In Accordance With:

21CFR56; 21CFR812

FDA Guidance on Significant Risk and Non-significant Risk Medical Device Studies located at <http://www.fda.gov/oc/ohrt/irbs/devrisk.pdf>

FDA Guidance on Frequently Asked Questions About Medical Devices located at <http://www.fda.gov/oc/ohrt/irbs/irbreview.pdf>

Compliance with this policy also requires compliance with state or local laws or regulations that provide additional protections for human subjects.

IV. DEFINITIONS

SR device means an investigational device that: (a) is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject; or (b) 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 (c) 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 (d) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

NSR device means an investigational device that does not satisfy the definition of a SR device, i.e., a device that does not satisfy any of the conditions listed above that would qualify it as a SR device.

Unanticipated adverse device effect means any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

V. PROCEDURES

1. The IRB (or FDA) will determine whether the medical device is significant risk (SR) or non-significant risk (NSR) per 21 CFR 812 by use of any of the following:
 - a. A risk assessment report from the sponsor explaining the device classification;
 - b. The FDA letter approving the IDE (in which case the IRB will consider the investigation an SR device study);
 - c. A Pre-Market Approval letter, supplement letter or amendment letter from the FDA;
 - d. Information from the study application, master protocol, investigator's brochure (or package insert) and other risk evaluations presented by the sponsor or investigator;
 - e. Review of the FDA Information Sheet containing examples of SR and NSR devices located at <http://www.fda.gov/oc/ohrt/irbs/devrisk.pdf>;
 - f. Reports of prior investigations conducted with the device;
 - g. Description of subject selection criteria;
 - h. Description of monitoring procedures;
 - i. Potential harm that may be caused by any surgical procedure used to place or implant the device; and
 - j. The proposed use of the device and the nature of harm that may result from its use in the study.
2. All SR device studies are considered more than minimal risk and require full IRB review.
3. If the IRB decides the study is significant risk, 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.

4. 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.
5. For NSR device studies, the IRB shall proceed to review the study per 21 CFR 56.111. If approved by the IRB, the investigator must comply with all abbreviated IDE requirements in 21 CFR 812.2(b), as well as informed consent and IRB regulations.
6. 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 or NSR determination and may also include the documents used to establish the IDE status for the study. For an SR determination, such documentation may include a copy of the IDE approval or conditional approval letter from the FDA. For an NSR determination, the documentation may include FDA's NSR classification if the agency has made such a determination.
7. The IRB will review reports of unanticipated device effects occurring during an investigation. Investigators are required to report these effects to the sponsor and to the IRB as soon as possible, but in no event later than within 10 working days after the investigator first learns of the effect. Should the IRB determine that the information gained in these reports changes the risk assessment, the IRB can reconsider any NSR decision and/or require the modification of the informed consent to contain the new information.
8. A copy of all correspondence will be kept in the IRB files for the study.