

Guidance: Significant and Non-Significant Risk Devices (last updated August 30, 2011)

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Brief Overview

IMPORTANT NOTE: If your investigation involves a medical device, please also read [OHRPP Guidance on the Use of Devices in Clinical Research and Treatment](#).

FDA regulations ([21 CFR 812.2](#)) state that for studies involving use of an investigational device, the investigator (or sponsor) must obtain either a "significant risk" (SR) Investigational Device Exemption (IDE) from the FDA, or a determination of "non-significant risk" (NSR) from the institutional review board (IRB). FDA "[Guidance for Institutional Review Boards and Clinical Investigators, 2006 Update, Medical Devices](#)" provides criteria for the investigator and institutional review board to use in making these decisions.

If your study involves a NSR device, you must complete the "Device/Diagnostics and/or Humanitarian Devices" section in [webIRB](#).

Definition of a Significant Risk Device

[21 CFR 812.3\(m\)](#) defines a Significant Risk (SR) Device as 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.
- A non-significant risk (NSR) device is one that does not meet the definition of a significant risk device.

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The IRB Decision-Making Process

Two Separate IRB Decisions, based on different criteria.

1. Is the investigation approvable or not?
2. Does the device present significant risk (SR) or non-significant risk (NSR)?
 - If NSR, an IDE can be given by the board.
 - If not, the investigator must be advised to seek a SR IDE from the FDA.

IRB Application Requirements

- If the investigator or sponsor believes a device poses non-significant risk (NSR), complete the "Device/Diagnostics and/or Humanitarian Devices" section in [webIRB](#).
- Additional supporting information (e.g., any reports of prior investigations) should be submitted, as appropriate. The IRB should also be informed if the FDA or any other IRB has determined the device to present significant or non-significant risk, and provide any further information requested by the IRB.

Criteria for Approval

The criteria for deciding if a study involving either a significant or non-significant risk device should be approved are the same as those used to evaluate any proposed research project, i.e., the IRB's determination that risks to subjects are minimized, risks to subjects are reasonable in relation to anticipated benefits and knowledge to be gained, subject selection is equitable, informed consent materials and procedures are adequate, and there are acceptable provisions for monitoring the study and protecting patient information.

Significant and Non-Significant Risk Determinations

- ***The IRB may agree or disagree with the investigator's or sponsor's initial non-significant risk (NSR) assessment.***
 - If the IRB agrees, and approves the study, the investigation may proceed without FDA approval.
 - If the IRB disagrees, the study can only be conducted at this institution as a study involving a significant risk (SR) device, and the investigator or sponsor must notify the FDA that a SR determination has been made for the device (whether or not the study is ultimately conducted at that institution).
- While the IRB is serving as FDA's surrogate with respect to review and approval of NSR devices, ***the ultimate decision in determining if a device is SR or NSR is the FDA's.*** On some occasions, FDA may overrule an IRB's decision that a device presents non-significant or significant risk.
 - When FDA overrules an IRB's NSR determination, an IDE application must be submitted to FDA.
 - On the other hand, when FDA considers the device to NSR, FDA may return an IDE application to the investigator or sponsor, and the IRB must then determine if it wants the study to take place at its institution as a NSR device investigation.
- ***Criteria for Determining Significant Risk (SR) vs. Non-Significant Risk (NSR):*** To determine if a device involves a SR, the IRB must consider the ***nature of the harm*** that may result from use of the device.

- If a device being investigated might cause significant harm to any of the subjects, the device should be considered "significant risk".
- If the subject must undergo a procedure as part of the study, e.g., a surgical procedure to implant the device, the IRB must consider the potential harm caused by the procedure as well as the potential harm caused by the device.
- Devices for which 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, are included among those devices that present significant risk.
- ***The determination of significant risk depends on the use of the device*** in the particular study as well as the inherent risks of the device itself. Some examples follow:
 - A pacemaker that is a modification of a commercially available pacemaker poses a significant risk because the use of any pacemaker presents a potential for serious harm to the subjects. This is true even though the modified pacemaker may pose less risk, or only slightly greater risk, in comparison to the commercially available model. The degree of possibly reduced or increased risk associated with the investigational pacemaker should only be considered (in relation to possible decreased or increased benefits) when assessing the approvability of the study.
 - An extended-wear contact lens is considered SR because wearing the lens continuously for 30 days presents a potential for injuries not normally seen with daily wear lenses, which are considered NSR.

Examples of Non-Significant Risk and Significant Risk Devices

- Please refer to FDA "[Guidance for Institutional Review Boards and Clinical Investigators, 2006 Update, Medical Devices](#)" for examples of non-significant and significant risk devices.
- To find information on a specific device or type of device, search [the database maintained by CDRH](#).