

The Food and Drug Administration defines a *significant risk device* as any investigational medical device that presents a potential for serious risk to the health, safety, or welfare of a study subject.

A *nonsignificant risk device* is one that does not present a potential for serious risk to subjects' health, safety, or welfare.

Although devices used to diagnose, cure, mitigate, or treat disease often meet the criteria for significant risk devices, some nonsignificant risk devices may be used for these purposes, as well.

An ophthalmological study, for example, involving use of an investigational intraocular lens, which researchers will implant surgically in subjects' eyes, presents a potential for serious harm to subjects. Therefore, the intraocular lens is considered a significant risk device. On the other hand, a study involving use of an investigational daily-wear contact lens, worn on the surface of the eye, may be a nonsignificant risk device study if it does not present a potential for serious risk to the health, safety, or welfare of study subjects.

Unless the FDA has already made a risk determination, the IRB must review the sponsor's own determination of significant or nonsignificant risk and must modify that determination if it disagrees with the sponsor. This means that with each IRB application for a study involving use of an investigational medical device, the sponsor should provide its own determination of significant or nonsignificant risk, indicating its rationale for that determination. If the FDA has already made a risk determination, its determination is final.

Significant risk device studies must follow all of the FDA's investigational device exemption (or IDE) regulations. This includes submitting an IDE application to the FDA. A significant risk device study may not begin until the FDA has approved the IDE application and the IRB has approved the research.

Nonsignificant risk device studies are subject to the FDA's abbreviated requirements for research involving devices. These requirements address:

- a device's labeling
- IRB approval
- informed consent
- study monitoring

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Significant and Nonsignificant Risk Devices

- records
- reports

and

- prohibition against promoting or marketing an investigational device

Nonsignificant risk device studies do not require an FDA-approved IDE application, and sponsors and IRBs do not need to notify the FDA of IRB approval. The IRB serves as the FDA's surrogate for review and approval. Research involving a nonsignificant risk device may begin as soon as the IRB approves the study.

The IRB should base its risk determination on the nature of the device itself and on its proposed use. It should make its determination by reviewing relevant information at a convened meeting. This information includes:

- a description of the device
- reports of past research involving the device
- the proposed study plan

and

- the criteria for selecting study subjects

The IRB should document its significant or nonsignificant risk determination in the meeting minutes. Minutes should indicate the IRB's rationale for its determination and may also include documentation used to establish the study's IDE status. For a significant risk determination, IRB minutes may, for example, include a copy of the FDA's IDE approval or conditional approval letter. For an nonsignificant risk determination, documentation may include a letter from the FDA indicating its determination of nonsignificant risk.

IRBs should be careful not to conflate the notions of nonsignificant risk devices and minimal risk studies. The significant and nonsignificant risk designations apply only to device studies. Federal regulations use the term *minimal risk* in part to identify studies that IRBs may approve by expedited review. For a device study to be eligible for expedited review, the device and its proposed use must present nonsignificant risk *and* the study at large must present no more than minimal risk to subjects.

IRBs should also not confuse their responsibility to review and approve research for conduct at a clinical site with the significant or nonsignificant risk determination. An IRB makes the risk

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determination before reviewing the study as a whole, under Part 56 of the FDA's human subjects research regulations. The risk determination relates to the potential harm that the study—including use of the device—presents to subjects. The IRB's decision whether to approve a study for implementation, on the other hand, is based on the study's risk-benefit ratio.

Contact the IRB for more information about significant and nonsignificant risk device studies.

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