The determination of whether an investigational device is significant risk or non-significant risk is required in clinical investigations subject to 21 CFR 812. Clinical investigations “involve one or more subjects to determine the safety or effectiveness of the device.” 21 CFR 812.3(h) If the clinical investigation is determined to be exempt from 21 CFR 812, a determination of whether the device is significant risk or non-significant risk is not required. See the Human Research Protection Program Manual 7-1 “Investigational Drugs and Devices” for further information on IDEs.

The initial device risk determination is made by the sponsor and provided to the Institutional Review Board (IRB) as part of the initial review process. If the sponsor believes the study is non-significant risk, the sponsor must provide the IRB with an explanation of why the device is not a significant risk device. 21 CFR 812.2(b)(1)(ii) The sponsor should also provide any additional information that will assist the IRB in the determination. This includes whether the FDA has made a determination of the risk level of the device.

As part of the initial review, the IRB reviews the research at a convened IRB meeting to make the device risk determination. The IRB should make the device risk determination prior to review under 21 CFR 56.

The information reviewed by the IRB should include:
- Description of the device
- Reports of prior investigations conducted with the device
- The proposed investigational plan
- Subject selection criteria
- Sponsor’s device risk assessment, explanation, and any supporting documents
- FDA determination, if any
- Copy of FDA approval of IDE application for significant risk devices, if appropriate

The determination of whether the device is significant risk is based on whether the device and its proposed use meet the criteria in 21 CFR 812.3(m).

A significant risk device is 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; or
• 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; or
• 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. 21 CFR 812.3(m)

A non-significant risk device is an investigational device that does not meet the definition of a significant risk device.

The IRB should consider the following in making the determination:
• Proposed use of the device, not the device alone
• Any additional procedures required as part of the clinical investigation and potential harm from the procedure and the device

The determination shall be documented in the convened IRB meeting minutes. The meeting minutes should include the IRB’s reason for the determination and any supporting documentation considered (e.g. sponsor assessment, FDA determination). If the FDA has provided the device risk determination, the IRB still needs to make and document the determination. The IRB may consult with the FDA as needed regarding the device risk determination. If the device risk determination has been made by the FDA, the determination of the FDA is final.

The IRB may agree or disagree with the sponsor’s assessment. If the device is determined by the IRB to be significant risk, the IRB must notify the investigator and where appropriate, the sponsor. 21 CFR 812.66. An IDE application is required and the sponsor may not begin the investigation until 21 CFR 812.30(a) is met. 21 CFR 812.66

If the device is determined to be a non-significant risk device and meets all other requirements under 21 CFR 812.2(b)(1), the investigation is considered to have approved applications for IDE’s, unless the FDA has notified a sponsor under 21 CFR 8120(1) that approval of an application is required. 21 CFR 812.2(b) Even if the device is considered to have an approved application for an IDE, the criteria requires IRB approval of the investigation. 21 CFR 812.2(b)(1)(ii).

Examples of significant risk and non-significant risk devices can be found in the Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors: Significant Risk and Non-significant Risk Medical Device Studies.