UNIVERSITY OF SOUTH ALABAMA

IRB SOP 1001
Medical Device Studies:
Significant Risk/Non-Significant Risk Determinations

Purpose

The purpose of this Standard Operating Procedure (SOP) is to document procedures for determination of significant risk/non-significant risk status for medical device studies.

Scope

This SOP applies to IRB administrative staff and IRB members reviewing or processing FDA regulated medical device trials.

Definitions

Significant Risk (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.

Non-significant Risk (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.

Policy

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: SR, 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.

Procedures

1.0 Determination of Significant Risk (SR) vs. Non-significant Risk (NSR) for Non-Exempt Medical Devices

For determination of the need for an IDE, the convened IRB will address the applicability of FDA regulations under 21 CFR 812.2 and, if necessary, make a significant risk determination. The Investigational Device Exemption (IDE) regulations [21 CFR part 812] describe two types of device studies, "significant risk" (SR) and "nonsignificant risk" (NSR). 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].

1.1 A Significant Risk (SR) device study is one that presents a potential for serious risk to the health, safety, or welfare of a subject and

- is intended as an implant; or

- is used in supporting or sustaining human life; or
- is for use of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or
- otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

1.2 **A Non-significant Risk (NSR) device** investigation is one that does not meet the definition for a SR study.

The risk determination is 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, the IRB considers 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

2.0 The following items must be addressed:

2.1 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:

2.1.1 A risk assessment report from the sponsor explaining the device classification;
2.1.2 The FDA letter approving the IDE (in which case the IRB will consider the investigation an SR device study);
2.1.3 A Pre-Market Approval letter, supplement letter or amendment letter from the FDA;
2.1.4 Information from the study application, master protocol, investigator's brochure (or package insert) and other risk evaluations presented by the sponsor or investigator;
2.1.5 Review of the FDA Information Sheet containing examples of SR and NSR devices located at http://www.fda.gov/oc/ohrt/irbs/devrisk.pdf;
2.1.6 Reports of prior investigations conducted with the device;
2.1.7 Description of subject selection criteria;
2.1.8 Description of monitoring procedures;
2.1.9 Potential harm that may be caused by any surgical procedure used to place or implant the device; and
2.1.10 The proposed use of the device and the nature of harm that may result from its use in the study.

2.2 All SR device studies are considered more than minimal risk and require full IRB review.

2.3 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.

2.4 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.

2.5 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.

2.6 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.

2.7 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.

Regulated Documents

21CFR56; 21CFR812

Guidance Documents

FDA Guidance on Significant Risk and Non-significant Risk Medical Device Studies
FDA Guidance on Frequently Asked Questions About Medical Devices

HISTORY

Effective Date:
Revisions: October, 2018