Purpose

The purpose of this guidance is to provide the reader with information on investigational medical devices used as part of a research study, and IRB review required by the Advocate Aurora IRB when overseeing the research study. There are instances where investigational devices may be used in treatment situations – these are cases of Expanded Access/’compassionate use’ or Emergency Use situations. In expanded access of investigational devices, prospective convened IRB review must be completed before the device may be used at AAH. Emergency use situations may allow for a waiver of prospective IRB review, but then require a report made to the IRB within 5 working days. Information on these instances can be found in RSPP SOP 1 and 2, as well as RSPP guidance documents: Expanded Access, and Emergency Use.

Investigational Device Exemptions (IDE) regulations (21 CFR 812) describe three types of device studies in human subject research: significant risk (SR), nonsignificant risk (NSR), and those that are exempt from the IDE regulations. This document will provide an overview of what is required for IRB submission of these studies, and information on the IRB’s review of studies that use such devices.

NOTE that when a physician uses a legally marketed device outside its labeling to treat a patient and no research is being done, IRB review is not required.

Definitions of italicized words can be found in the AAH RSPP Glossary.

Guidance

What is an investigational device in human subject research?

Investigational devices are medical devices which are the object of clinical research to determine their safety or effectiveness. Medical devices that are "cleared" by the FDA, which means the manufacturer can demonstrate that their product is "substantially equivalent" to another (similar) legally marketed device that already has FDA clearance or approval. Once the FDA declares that a new medical device is substantially equivalent to an earlier device (a predicate), it is "cleared," and can be marketed and sold in the US.

Studies undertaken to develop safety and effectiveness data for medical devices involving human subjects must be conducted according to the requirements of the Investigational Device Exemption (IDE) regulations. Investigational devices are classified as either significant risk or non-significant risk devices.

Certain device studies are exempt from the requirements of the IDE regulations (21 CFR 812.2(C)).
What is a significant risk device?

A significant risk (SR) device is one that presents a potential for serious risk to the health, safety, or welfare of the subject.

Such a device is

- intended as an implant;
- is to be used in supporting or sustaining human life;
- or is of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health.

Examples of significant risk devices are catheters (other than urological), ventilators, CPR devices, TMJ prostheses, stents, lithotripters, sutures and absorbable bandages/materials, ECT devices, extended wear contact lenses, pacemakers, contraceptive devices, most laser systems, and most hemodialysis systems.

- Issuance of an IDE to a study by the FDA automatically confers significant risk categorization to the study.
- SR device studies must follow all the IDE regulations at 21 CFR 812.

What is a non-significant risk device?

A non-significant risk device is one that does not present a potential for serious risk to the health, safety, or welfare of the subject. Examples of non-significant risk devices are: most daily wear contact lenses, lens solutions, heel cups, antibacterial surgical garments, incontinence devices, oral training splints, and ultrasonic tooth cleaners.

- NSR device studies do not have to have an IDE application approved by FDA.
- NSR device studies must follow the abbreviated requirements at 21 CFR 812.2(b).
- Sponsors and IRBs do not have to report the IRB approval of an NSR device study to FDA. This means that an IRB may approve an NSR device study and an investigator may conduct the study without FDA knowing about it. An IRB’s NSR determination is important because the IRB serves as the FDA’s surrogate for review, approval, and continuing review of the NSR device studies.
- An NSR device study may start at the institution as soon as the IRB reviews and approves the study and without prior approval by FDA.

What about device studies that are exempt from the FDA IDE regulations?

Certain devices/studies are exempt from the requirements of the IDE regulations. Examples of such studies are consumer preference testing; testing of a device modification; testing of two or more devices in commercial distribution if the testing does not collect safety or effectiveness data, or put subjects at risk; some diagnostic device studies (e.g. in vitro diagnostic studies); studies of an already cleared medical device in which the device is used or investigated in accordance with the indications in the cleared labeling.
For studies that are exempt from the IDE regulations, the IRB does not need to decide whether the study poses a significant risk or nonsignificant risk. However, the IRB must still review the study in accordance with the regulatory criteria for approval and informed consent regulations. Risk level of the study will determine whether expedited or convened IRB review may occur.

See FDA guidance: Frequently Asked Questions About Medical Devices for more information.

**What is the Advocate Aurora IRB’s review process for investigational device protocols used in human subject research?**

**Submission requirements**

If the sponsor identifies a research study as NSR, the sponsor must provide the IRB an explanation of its determination (21 CFR 812.2(b)(1)(ii)) and any other information that may help the IRB in evaluating the risk of the study. For example, a description of the device, reports of prior investigations with the device, the proposed investigational plan, subject selection criteria, and other information the IRB may need.

If FDA has determined that the study is NSR, the sponsor should provide that information to the IRB.

If the device has been issued an IDE by the FDA, the printed protocol should reference the FDA issued IDE number. If the protocol does not include a reference to the IDE number a copy of the FDA’s letter noting the IDE number must be provided.

If the sponsor has submitted an IDE application to the FDA, but has not yet received an IDE number, the study team may submit an IRB application to the Advocate Aurora IRB with the IDE number as pending. However the IRB will not consider the study until the FDA has issued their decision.

The AAH IRB submission application asks questions about the use of the device in the research study, as well as storage, maintenance, and control of the investigational devices, and the responsible individual at each research location.

**Review Checklist**

The RCA/Primary Reviewer will complete a Reviewer Device Checklist. This checklist documents one of the following:

- the existence of an IDE for the study (confirmed in the sponsor’s protocol or via documentation from the sponsor or the FDA);
- an FDA-issued IDE exemption for the study; or
- the sponsor’s determination that the device qualifies for an IDE exemption.

If completed by the RCA, the document will be provided to the Primary Reviewer in his/her consideration of device risk level.
IRB Review

It is the responsibility of the IRB to determine which device studies pose significant risk or non-significant risk. IRBs will make the SR or NSR determination about a study by reviewing relevant information including a description of the device, reports of prior investigations conducted with the device, the proposed investigational plan, and subject selection criteria.

- The sponsor should provide the IRB with a risk assessment and the rationale used in making its SR or NSR determination.
- The IRB may ask the sponsor to obtain input from the FDA if uncertainty exists.
- An IRB may agree or disagree with the sponsor’s initial NSR assessment. If the IRB determines the study is NSR, and it is approved by the IRB, the study may begin without submission of an IDE application to FDA.
- If the IRB disagrees with the sponsor’s NSR assessment and decides the study is SR, the IRB must inform the clinical investigator, and where appropriate, the sponsor. The IRB will defer review of the study until such time that FDA input/IDE number is received.

In deciding if a device presents significant or non-significant risks, the IRB will consider the device’s total risks, and not compare these with the risks of alternative devices or procedures. If the device is used in conjunction with a procedure involving risk, the IRB will consider the risks of the procedure in conjunction with the risks of the device.

Once a decision on the degree of risk is reached, the IRB will consider whether the study should be approved using the regulatory criteria for approval (21 CFR 56.111) as the basis for their decision.

- In considering whether a study should be approved, the IRB will use the same criteria it would use in considering approval of any research involving an FDA-regulated product.
- The IRB will consider the risks and benefits of the investigational medical device compared to the risks and benefits of alternative devices or procedures in deciding the approvability of a study.

Some studies involving non-significant risk devices may be considered minimal risk studies and thus may be reviewed through the expedited review procedure established by the IRB.

- FDA considers studies of all significant risk devices to present more than minimal risk; thus, IRB review at a convened meeting is required for all studies involving significant risk devices.
- For studies reviewed via expedited review procedures, the Reviewer Device checklist will be retained in the study file to document the risk level of the device.
- For studies reviewed at a convened IRB meeting, the Primary Reviewer will use the Device checklist in his/her presentation to the IRB. The risk level of the device and any IRB discussion of the matter will be documented in the meeting minutes. The checklist does not need to be retained in the study file.
REQUIREMENTS

- FDA Regulations: 21 CFR 812; 21 CFR 46.111
- FDA guidance: Significant Risk and Nonsignificant Risk Medical Device Studies; Frequently Asked Questions About Medical Devices; Expanded Access for Medical Devices
- RSPP SOPs 1, 2
- RSPP guidance: Expanded Access; Emergency Use.
- AAHRPP Accreditation Standards/Elements: I.7.A; II.5.B