Information Sheet Guidance For IRBs, Clinical Investigators, and Sponsors

Significant Risk and Nonsignificant Risk Medical Device Studies

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or

Contains Nonbinding Recommendations

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I. INTRODUCTION

This guidance is intended to provide advice to sponsors, clinical investigators, and institutional review boards (IRBs) on how to determine the differences between significant risk and nonsignificant risk medical device studies. This document supersedes *Significant Risk and Nonsignificant Risk Medical Device Studies* (September 1998) Office of Health Affairs, Food and Drug Administration. This document was revised to update the list of examples of significant and nonsignificant risk devices, to clarify the IRB's responsibilities when making the risk determination for investigational medical devices, and to make the guidance consistent with the Agency's good guidance practices regulations (21 CFR 10.115).

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

[1] This guidance document was developed by the Good Clinical Practice Program in coordination with the Agency Centers.

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.

- the sensor pad does not present a potential for serious risk to the health, safety, or welfare of a subject (for example, placing the pad would not prolong or interfere with the operation);
- the sensor pad is not implanted;
- the pad is not of substantial importance in diagnosing, curing, mitigating or treating disease.

VII. HOW DOES AN IRB DOCUMENT THE SR OR NSR DETERMINATION?

The IRB should write its decision in the meeting minutes. The minutes should describe the IRB's reason for its SR or NSR determination and may also include the documentation used to establish the IDE status for the study. For an SR determination, such documentation may include, for example, a copy of the IDE approval or conditional approval letter from FDA. For an NSR determination, the documentation may include FDA's NSR determination where the agency has made the determination. FDA will issue an NSR letter upon written request.

VIII. WHAT SHOULD AN IRB DO FOR DEVICE STUDIES THAT ARE EXEMPT FROM THE REQUIREMENTS OF THE IDE REGULATIONS (21 CFR 812.2(C))?

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 IRB regulations before the investigation may begin.

IRBs should understand distinctions between certain important concepts that are frequently confused:

A. Difference between NSR and Minimal Risk Determinations

IRBs should not confuse their responsibility to make an SR/NSR determination for a device study with the concept of "minimal risk." "Minimal Risk" is a term used in the IRB regulations in part to identify certain studies that IRBs may approve through an expedited review procedure. For a device study to be eligible for expedited review, it must be an NSR study AND present no more than minimal risk to the subject. (See 21 CFR 56.110)

B. Difference Between SR/NSR Determinations and Approval Decisions

IRBs should not confuse their responsibility to review and approve research for conduct at a clinical site with the SR/NSR determination. IRBs make the SR/NSR determination before the IRB conducts its review of the study under Part 56. The judgment about whether a study poses a significant risk or nonsignificant risk is based on the significance of the potential harm that may result from participation in the study, including the use of the device; whereas

the IRB's decision to approve a study for implementation is based on the study's risk-benefit assessment.

IX. WHAT ARE FDA'S RESPONSIBILITIES?

- As discussed, FDA is the final arbiter in deciding whether a device study poses a significant or nonsignificant risk. It should be noted, however, that FDA generally only sees those studies that sponsors submit to the agency or those studies for which an IRB or clinical investigator asks for FDA's opinion.

- If FDA disagrees with an IRB's NSR decision and determines that the study poses a significant risk, the sponsor may not begin their study until FDA approves an IDE. (See 21 CFR 812.42)

- If a sponsor submits an IDE to FDA because the sponsor presumed it to be an SR study, and FDA determines that the device study poses a nonsignificant risk, FDA will tell the sponsor in writing. The study may then be reviewed by the IRB as an NSR study.

X. EXAMPLES OF NSR AND SR DEVICES

The following examples may help sponsors and IRBs in making SR and NSR determinations. The list includes many commonly studied medical devices. Inclusion of a device in the NSR list is not a final determination because the evaluation of risk must reflect the proposed use of a device in a study.

A. Nonsignificant Risk Devices

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- Electroencephalography (e.g., new recording and analysis methods, enhanced diagnostic capabilities, measuring depth of anesthesia if anesthetic administration is not based on device output)
- Externally Worn Monitors for Insulin Reactions
- Functional Non-Invasive Electrical Neuromuscular Stimulators
- General Biliary Catheters
- General Urological Catheters (e.g., Foley and diagnostic catheters) for short term use (< 28 days)
- Jaundice Monitors for Infants
- Low Power Lasers for treatment of pain
- Magnetic Resonance Imaging (MRI) Devices within FDA specified parameters
- Manual Image Guided Surgery
- Menstrual Pads (Cotton or Rayon, only)
- Menstrual Tampons (Cotton or Rayon, only)
- Nonimplantable Electrical Incontinence Devices
- Nonimplantable Male Reproductive Aids with no components that enter the vagina
- Ob/Gyn Diagnostic Ultrasound within FDA approved parameters
- Partial Ossicular Replacement Prosthesis (PORP)
- Total Ossicular Replacement Prosthesis (TORP)
- Transcutaneous Electric Nerve Stimulation (TENS) Devices for treatment of pain (except for chest pain/angina)
- Ureteral Stents
- Urethral Occlusion Device for less than 14 days

- Transmyocardial Revascularization, Percutaneous Myocardial Revascularization Devices
- Ultrasonic Angioplasty Catheters
- Vascular and Arterial Graft Prostheses
- Vascular Hemostasis Devices

4. Dental

- Absorbable Materials to aid in the healing of periodontal defects and other maxillofacial applications
- Bone Morphogenic Proteins with and without bone, e.g., Hydroxyapatite (HA)
- Dental Lasers for hard tissue applications
- Endosseous Implants and associated bone filling and augmentation materials used in conjunction with the implants

- Femoral, Jugular and Subclavian Catheters
- Hemodialyzers
- Hemofilters

- Implanted Spinal Cord and Nerve Stimulators and Electrodes
- Neurological Catheters (e.g., cerebrovascular, occlusion balloon, etc.)
- Transcutaneous Electric Nerve Stimulation (TENS) Devices for treatment of chest pain/angina

10. Obstetrics And Gynecology

- Abdominal Decompression Chamber
- Antepartum Home Monitors for Non-Stress Tests
- Antepartum Home Uterine Activity Monitors
- Catheters for Chorionic Villus Sampling (CVS)
- Catheters Introduced into the Fallopian Tubes
- Cervical Dilation Devices
- Contraceptive Devices:
    - Cervical Caps
    - Condoms (for men) made from new materials (e.g., polyurethane)
    - Contraceptive *In Vitro* Diagnostics (IVDs)
    - Diaphragms
    - Female Condoms
    - Intrauterine Devices (IUDs)
    - New Electrosurgical Instruments for Tubal Coagulation
    - New Devices for Occlusion of the Vas Deferens
    - Sponges
    - Tubal Occlusion Devices (Bands or Clips)
- Cryomyolysis
- Devices to Prevent Post-op Pelvic Adhesions
- Embryoscopes and Devices intended for fetal surgery
- Endometrial Ablation Systems
- Falloposcopes and Falloposcopic Delivery Systems
- Fundal Pressure Belt (for vaginal assisted delivery)
- Gamete and Embryo Surgical Systems
- Intrapartum Fetal Monitors using new physiological markers
- New Devices to Facilitate Assisted Vaginal Delivery
- Operative Hysteroscopy and Laparoscopy
- Uterine Artery Embolization

11. Ophthalmics

- Aniridia Intraocular Lenses (IOLs) or Rings (for iris reconstruction)
- Capsular Tension Rings
- Class III Ophthalmic Lasers

- Contact Lens Solutions intended for direct instillation (e.g., lubrication/rewetting solutions) in the eye using new active agents or preservatives with no history of prior ophthalmic/contact lens use or not generally