UNIVERSITY OF TENNESSEE GRADUATE SCHOOL OF MEDICINE INSTITUTIONAL REVIEW BOARD SIGNIFICANT RISK / NONSIGNIFICANT RISK DETERMINATIONS FOR MEDICAL DEVICES

I. PURPOSE

To document the procedures for review of medical device studies

II. SCOPE

This SOP applies to the IRB administrative staff, IRB members.

Personnel Responsible:

University of Tennessee Graduate School of Medicine Institutional Review Board (UTGSM IRB) administrative staff and members

III. BACKGROUND

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. Certain research studies of devices may be exempt from IDE regulations (e.g., marketed devices). If the device is not exempt from IDE regulations, the device must be categorized as either "significant risk" (SR) or "non-significant risk" (NSR). 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 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.

If the sponsor identifies a study as NSR, the sponsor must provide the reviewing IRB an explanation of its determination (21 CFR 812.2(b)(1)(ii)). The IRB may also use information from the application, protocol, the investigator's brochure, package insert, FDA Information Sheets, reports of prior investigations conducted with the device, description of subject selection criteria, monitoring procedures and other evaluations presented by the sponsor to

categorize the device as “SR” or “NSR”. If the IRB agrees with the NSR designation and a separate risk determination has not been made by the FDA, the study may proceed with IRB approval. If the IRB disagrees with a sponsor’s classification of a device as NSR,”, then the investigation cannot proceed until the FDA has approved an IDE application and the IRB has approved the study under the regulations for the protection of human subjects.

In Accordance With:

21 CFR 56; 21 CFR 812

FDA Guidance on Significant Risk and Non-significant Risk Medical Device Studies located at
http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126418.pdf

FDA Guidance on Frequently Asked Questions About Medical Devices located at
http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM127067.pdf

Compliance with this policy also requires compliance with state or local laws or regulations that provide additional protections for human subjects.

IV. DEFINITIONS

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.

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.

IV. PROCEDURES

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 the following:

a. A "Risk Assessment Report" from the sponsor explaining the device classification
b. FDA letter approving the IDE or a 510K clearance
c. A Pre-Market Approval letter, supplement letter or amendment letter from FDA
d. Use of information from the project descriptors, protocol, investigator's brochure (or package insert) and other risk evaluations presented by the applicant (Sponsor, Investigator, etc.).
e. Review of the FDA Information Sheet located at: http://www.fda.gov/oc/ohrt/irbs/devrisk.pdf
f. Reports of prior investigations conducted with the device
g. Description of subject selection criteria
h. Description of monitoring procedures
i. Potential harm that may be caused by any surgical procedure used to place or implant the device; and
j. The proposed use of the device and the nature of harm that may result from its use in the study.

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

3. 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.
   i. If the IRB decides the device is a Significant Risk, the IRB shall notify the investigator (in writing) that they must submit an IDE application to the FDA. If the FDA determines that a device is a NSR device, the IRB will accept FDA's determination.
   ii. Any amendments or corrections of deficiencies required by FDA during the IDE process must be submitted for review and approval of the IRB.
   iii. If an IDE application is or has been submitted to 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.
   iv. Once the IDE is obtained, the investigator may submit the IDE# and FDA letter to the IRB for review. The study will be reviewed by the IRB at the next convened meeting.

4. 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 FDA. For an NSR determination, the documentation may include FDA's NSR classification if the agency has made such a determination.

5. The IRB will review reports of unanticipated device effects. Investigators are required to report these events to the IRB within 10 working days of their receipt of the information. 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. (See SOP #18 Review of External Reports)

6. A copy of this correspondence will be kept in iMEdRIS for the study.