

## APPENDIX F

### INVESTIGATIONAL DEVICES

#### A. Background

A medical device is defined, in part, as any health care product that does not achieve its primary intended purpose by chemical action or by being metabolized. Examples of medical devices include, but are not limited to, surgical lasers, wheelchairs, sutures, pacemakers, vascular grafts or stents, intraocular lenses, orthopedic pins, and radiographic imaging equipment. Medical devices also include diagnostic aids such as reagents and test kits for in vitro diagnosis of disease or other medical conditions such as pregnancy.

Except for certain low risk devices, each manufacturer who wishes to introduce a new medical device to the market must submit a premarket notification to the Food and Drug Administration (FDA). The FDA reviews these notifications to determine if the new device is "substantially equivalent" to a device that was marketed prior to the passage of the Medical Device Amendments of 1976 (i.e., a "pre-amendments device"). If the new device is deemed to be substantially equivalent to a pre-amendments device, it may be marketed immediately and is regulated in the same regulatory class as the pre-amendments device to which it is equivalent. Devices determined by FDA to be "substantially equivalent" are often referred to as "510k devices" (i.e., the premarket notification requirement for new devices is set forth in section 510(k) of the Federal Food Drug and Cosmetic Act). If a new device is deemed not to be equivalent to a pre-amendments device, clinical studies of its safety and effectiveness must be performed and FDA approval granted before the device can be marketed.

#### B. Investigational Devices

An investigational device is a medical device which is the subject of a human research study to evaluate its safety and/or effectiveness. Clinical studies of investigational devices must comply with FDA's investigational device exemption (IDE) regulations.

- 1) IDE Regulations - Significant Risk and Nonsignificant Risk Medical Device Studies

The IDE regulations (21 CFR part 812) describe two types of investigational device studies, "significant risk" and "nonsignificant risk." A "significant risk" device study is defined as a study of a device that presents a potential for serious risk to the health, safety, or welfare of a subject and/or (1) is an implant; (2) is used in supporting or sustaining human life; or (3) is of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health. A "nonsignificant risk" device study is a study of a device that does not fit the definition of a "significant risk" device study. Note that this risk determination should be based not only on the nature of the device, but also on the proposed use of the device in the research study. Two examples follow:

The research evaluation of a pacemaker that is a modification of a commercially available pacemaker is a "significant risk" device study because the use of any pacemaker involves the potential for serious harm to involved patients. This is true even though the modified pacemaker may pose less risk, or only slightly greater risk, in comparison with the commercially available product.

The research evaluation of contact lens wherein the proposed study involves its extended wear constitutes "significant risk." Although the contact lens, itself, poses minimal risk, wearing it continuously for several days/nights presents a potential for injuries not normally seen with limited daily use.

"Significant risk" device studies must be conducted in accordance with the complete requirements of the IDE regulations and necessitate the prospective approval of an IDE application by the FDA and approval by the IRB. In contrast, "nonsignificant risk" device studies are conducted in accordance with "abbreviated requirements" of the IDE regulations and may be approved by the IRB and commence without the requirement for submission of an IDE application to, or other notification of, the FDA. (I.e., for "nonsignificant risk" device studies, the IRB serves as the FDA's surrogate with respect to study review and approval.) Informed consent must be obtained for either type of study.

## 2) IRB and Sponsor/Investigator Responsibilities Re. "Significant Risk" or "Nonsignificant Risk" Device Studies

The determination that a device study presents a "significant risk" or a "nonsignificant risk" is initially made by the sponsor/investigator. If the sponsor/investigator considers the device study to be of "nonsignificant risk", the sponsor/investigator must provide the IRB with an explanation of this determination and copies of the respective research protocol and informed consent document. The sponsor should inform the IRB of the FDA's assessment of the risk status of the proposed device study, if such an assessment has been made. The IRB may question whether other IRB's have reviewed the proposed device study and what determination they made, or the IRB may consult with the FDA for its opinion.

The IRB may agree or disagree with the sponsor's/ investigator's initial "nonsignificant risk" assessment.

- If the IRB agrees with the determination that the device study presents "nonsignificant risk" and approves the research study and informed consent document(s), the study may proceed without further notification of the FDA. Under this scenario, the sponsor and principal investigator are required to comply with the "abbreviated requirements" of the IDE regulations (21 CFR 812.2(b)).
- If the IRB disagrees with the determination that the device study presents "nonsignificant risk", the sponsor must notify the FDA that the device study has been determined to be of "significant risk" and, if electing to proceed with the study, must submit an IDE application. The device study may not commence until the FDA approves the IDE and the IRB approves the device study and informed consent document(s). Under this scenario, the

sponsor and principal investigator are required to comply with the complete IDE regulations (21 CFR 812).

The FDA has the ultimate decision in determining if a device study presents a "significant risk" or "nonsignificant risk." If the FDA, upon review of IRB activities, disagrees with the IRB's decision that a device study presents a "nonsignificant risk, an IDE application must be submitted to the FDA. On the other hand, if a sponsor/investigator submits an IDE to the FDA because it is presumed to be a "significant risk" study, but the FDA classifies it as a "nonsignificant risk", the FDA will return the IDE application with the recommendation that it be presented to the IRB as a "nonsignificant risk" device study.