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Subject: Reviews Requiring Special Consideration
Division: IRB
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IRB Policy 110.3: MEDICAL DEVICES

Policy

An investigational device is a medical device, which is the subject of a clinical study designed to evaluate the effectiveness and/or safety of the device. A medical device is defined, in part, as any health care product that does not achieve its primary intended purposes by chemical action or by being metabolized.

All investigational device studies involving human subjects must be submitted to the IRB for review. Clinical investigations undertaken to develop safety and effectiveness data for medical devices must be conducted according to the requirements of the IDE regulations (21 CFR 812).

Investigational Device Exemption (IDE)

The following clinical investigations of devices may be exempt from the IDE regulations [21 CFR 812.2(c)].

1. A device, other than a transitional device, in commercial distribution immediately before May 28, 1976, when used or investigated in accordance with the indications in labeling in effect at that time.

2. A device, other than a transitional device, introduced into commercial distribution on or after May 28, 1976, that FDA has determined to be substantially equivalent to a device in commercial distribution immediately before May 28, 1976, and that is used or investigated in accordance with the indications in the labeling FDA reviewed under subpart E of part 807 in determining substantial equivalence.

3. A diagnostic device, if the sponsor complies with applicable requirements in Sec. 809.10(c) and if the testing:
   a) Is noninvasive,
   b) Does not require an invasive sampling procedure that presents significant risk,
   c) Does not by design or intention introduce energy into a subject, and
   d) Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.
4. A device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution, if the testing is not for the purpose of determining safety or effectiveness and does not put subjects at risk.

5. A device intended solely for veterinary use.

6. A device shipped solely for research on or with laboratory animals and labeled in accordance with Sec. 812.5(c).

7. A custom device as defined in Sec. 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.

Significant Risk or Non-Significant Risk

Unless exempt from the IDE regulations, an investigational device must be categorized as either "significant risk" (SR) or "non-significant risk" (NSR).

An SR 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 (1) is intended as an implant; (2) is used in supporting or sustaining human life; (3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; OR (4) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

An NSR device investigation is one that does not meet the definition for a significant risk study. NSR device studies, however, should not be confused with the concept of "minimal risk."

The determination that a device presents a NSR or SR is initially made by the sponsor. The proposed study is then submitted to FDA, for SR studies, or to the IRB, for NSR studies.

The sponsor/investigator should provide the IRB with the following information:
1. A risk assessment,
2. The rationale used in making the risk determination,
3. A description of the device,
4. Reports of prior investigations with the device,
5. The proposed investigational plan,
6. A description of patient selection criteria and monitoring procedures,
7. Information regarding whether other IRBs have reviewed the proposed study and what determination was made, and
8. FDA's assessment of the device's risk if such an assessment has been made.

The IRB will review the above-mentioned material, and make a final risk determination based on its own review. The IRB may also consult with FDA for its opinion.

The IRB's SR/NSR determination has significant consequences for the study sponsor, investigator, FDA, and prospective research subjects. SR device studies must be conducted in accordance with the full IDE requirements (21 CFR part 812), and may not commence until 30 days following the sponsor's submission of an IDE application to FDA. Submission of the IDE application enables FDA to review information about the technical characteristics of the device, the results of any prior studies (laboratory, animal and human) involving the device, and the proposed study protocol and consent documents. Based upon the review of this information, FDA may impose restrictions on the study to ensure that risks to subjects are minimized and do not outweigh the anticipated benefits to the subjects and the importance of the knowledge to be gained. The study may not commence until FDA has approved the IDE application and the IRB has approved the study.

NSR device studies do not require submission of an IDE application to FDA. Instead, the sponsor is required to conduct the study in accordance with the "abbreviated requirements" of the IDE regulations [21 CFR 812.2(b)]. Unless otherwise notified by FDA, an NSR study is considered to have an approved IDE if the sponsor fulfills the abbreviated requirements. The abbreviated requirements address, among other things, the requirements for IRB approval and informed consent, recordkeeping, labeling, promotion, and study monitoring. NSR studies may commence immediately following IRB approval.

If an investigator or a sponsor proposes the initiation of a claimed NSR investigation to the IRB, and if the

IRB agrees that the device study is NSR and approves the study, the investigation may begin immediately, without submission of an IDE application to FDA. If the IRB believes that a device study is SR, the investigation may not begin until both the IRB and FDA approve the investigation.

FDA has the ultimate decision in determining if a device study is SR or NSR. If the FDA does not agree with the IRB's decision that a device study presents an NSR, an IDE application must be submitted to FDA. On the other hand, if a sponsor files an IDE with FDA because it is presumed to be an SR study, but FDA classifies the device study as NSR, the Agency will return the IDE application to the sponsor and the study would be presented to the IRB as an NSR investigation.

Risk Determination

Risk determination will be 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 will consider 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 result in permanent impairment of a body function or permanent damage to body structure, or could necessitate medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to body structure will be considered SR. Also, if the subject must undergo a procedure as part of the investigational study, e.g., a surgical procedure, the IRB will consider the potential harm that could be caused by the procedure in addition to the potential harm caused by the device. For example:

1. The study of a pacemaker that is a modification of a commercially-available pacemaker poses a SR because the use of any pacemaker presents a potential for serious harm to the subjects. This is true even though the modified pacemaker may pose less risk, or only slightly greater risk, in comparison to the commercially-available model. The amount of potential reduced or increased risk associated with the investigational pacemaker will only be considered (in relation to possible decreased or increased benefits) when assessing whether the study can be approved.

2. The study of an extended wear contact lens is considered SR because wearing the lens continuously overnight while sleeping presents a potential for injuries not normally seen with daily wear lenses, which are considered NSR.

The following examples are provided to assist the IRB in making SR/NSR determinations. The list includes many commonly used medical devices. Inclusion of a device in the NSR category should not be viewed as a conclusive determination, because the proposed use of a device in a study is the ultimate determinant of the potential risk to subjects. It is unlikely that a device included in the SR category could be deemed NSR due to the inherent risks associated with most such devices.

Examples of NONSIGNIFICANT RISK DEVICES: (1) Low Power Lasers for treatment of pain, (2) Caries Removal Solution, (3) Daily Wear Contact Lenses and Associated Lens Care Products not intended for use directly in the eye (e.g., cleaners; disinfecting, rinsing and storage solutions), (4) Contact Lens Solutions intended for use directly in the eye (e.g., lubricating/rewetting solutions) using active ingredients or preservation systems with a history of prior ophthalmic/contact lens use or generally recognized as safe for ophthalmic use, (5) Conventional Gastroenterology and Urology Endoscopes and/or Accessories, (6) Conventional General Hospital Catheters (long-term percutaneous, implanted, subcutaneous and intravascular), (7) Conventional Implantable Vascular Access Devices (Ports), (8) Conventional Laparoscopes, Culdoscopes, and Hysteroscope, (9) Dental Filling Materials, Cushions or Pads made from traditional materials and designs, (10) Denture Repair Kits and Realigners, (11) Digital Mammography [Note: an IDE is required when safety and effectiveness data are collected which will be submitted in support of a marketing application.], (12) Electroencephalography (e.g., new recording and analysis methods, enhanced diagnostic capabilities), (13) Externally Worn Monitors for Insulin Reactions, (14) Functional Electrical Neuromuscular Stimulators, (15) General Biliary Catheters General Urological

Catheters (e.g., Foley and diagnostic catheters), (16) Jaundice Monitors for Infants, (17) Magnetic Resonance Imaging (MRI) Devices within FDA specified parameters, (18) Manual Image Guided Surgery, (19) Menstrual Pads (Cotton or Rayon, only), (20) Menstrual Tampons (Cotton or Rayon, only), (21) Nonimplantable Electrical Incontinence Devices, (22) Nonimplantable Male Reproductive Aids with no components that enter the vagina, (23) Ob/Gyn Diagnostic Ultrasound within FDA approved parameters, (24) Transcutaneous Electric Nerve Stimulation (TENS) Devices for treatment of pain, (25) Wound Dressings, excluding absorbable hemostatic devices and dressings (also excluding Interactive Wound and Burn Dressings).

Examples of SIGNIFICANT RISK DEVICES:

1. *General Medical Use:*
   a) Catheters:
      - Urology - urologic with anti-infective coatings
      - General Hospital - except for conventional long-term percutaneous, implanted, subcutaneous, intravascular
      - Neurological - cerebrovascular, occlusion balloon
      - Cardiology - transluminal coronary angioplasty, intra-aortic balloon with control system
   b) Collagen Implant Material for use in ear, nose and throat, orthopedics, plastic surgery, urological and dental applications
   c) Surgical Lasers for use in various medical specialties
   d) Tissue Adhesives for use in neurosurgery, gastroenterology, ophthalmology, general and plastic surgery, and cardiology.

2. *Anesthesiology***:** Breathing Gas Mixers, Bronchial Tubes, Electroanesthesia Apparatus, Epidural and Spinal Catheters, Epidural and Spinal Needles, Esophageal Obturators, Gas Machines for anesthesia or analgesia, High Frequency Jet Ventilators greater than 150 BPM, Rebreathing Devices, Respiratory Ventilators, Tracheal Tubes.

3. *Cardiovascular:* Aortic and Mitral Valvuplasty Catheters, Arterial Embolization Devices Cardiac Assist Devices [artificial heart (permanent implant and short term use), cardiomyoplasty devices, intra-aortic balloon pumps, ventricular assist devices], Cardiac Bypass Devices [oxygenators, cardiopulmonary non-roller blood pumps, closed chest devices], Cardiac Pacemaker/Pulse Generators [antitachycardia, esophageal, external transcutaneous, implantable], Cardiopulmonary Resuscitation (CPR) Devices, Cardiovascular/Intravascular Filters, Coronary Artery Retroperfusion Systems, Coronary Occluders for ductus arteriosus/atrial/septal defects, Coronary and Peripheral Arthrectomy Devices, Extracorporeal Membrane Oxygenators (ECMO), Implantable Cardioverters/Defibrillators, Laser Coronary and Peripheral Angioplasty Devices, Myoplasty Laser Catheters, Organ Storage/Transport Units, Pacing Leads, Percutaneous Conduction Tissue Ablation Electrodes, Peripheral/Coronary/Pulmonary/Renal/Vena Caval/Peripheral Stents, Replacement Heart Valves, RF Catheter, Ablation and Mapping Systems, 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, Subperiosteal Implants, Temporomandibular Joint (TMJ) Prostheses.

5. *Ear, Nose, and Throat*: Auditory Brainstem Implants, Cochlear Implants, Laryngeal Implants, Total Ossicular Prosthesis Replacements.

6. *Gastroenterology and Urology:* Anastomosis Devices, Balloon Dilation Catheters for benign prostatic hyperplasia (BPH), Biliary Stents, Components of Water Treatment Systems for Hemodialysis,

Dialysis Delivery Systems, Electrical Stimulation Devices for sperm collection, Embolization Devices for general urological use, Extracorporeal Circulation Systems, Extracorporeal Hyperthermia Systems, Extracorporeal Photopheresis Systems, Femoral/Jugular/Subclavian Catheters, Hemodialyzers, Hemofilters, Implantable Electrical Urinary Incontinence Systems, Implantable Penile Prostheses, Injectable Bulking Agents for incontinence, Lithotripters (e.g., electrohydraulic extracorporeal shock-wave, laser, powered mechanical, ultrasonic), Mechanical/Hydraulic Urinary Incontinence Devices, Penetrating External Penile Rigidity Devices with components that enter the vagina, Peritoneal Dialysis Devices, Peritoneal Shunt, Plasmapheresis Systems, Prostatic Hyperthermia Devices, Urethral Occlusion Devices, Urethral Sphincter Prostheses, Urological Stents (e.g., ureteral, prostatG).

7. *General and Plastic Surgery:* Absorbable Adhesion Barrier Devices, Absorbable Hemostatic Agents, Artificial Skin and Interactive Wound and Burn Dressings, Injectable Collagen, Implantable Craniofacial Prostheses, Repeat Access Devices for surgical procedures, Sutures.

8. *General Hospital*: Implantable Vascular Access Devices (Ports) - if new routes of administration or new design, Infusion Pumps (implantable and closed-loop - depending on the infused drug).

9. *Neurological***:** Electroconvulsive Therapy (ECT) Devices, Hydrocephalus Shunts, Implanted Intracerebral/Subcortical Stimulators, Implanted Intracranial Pressure Monitors, Implanted Spinal Cord and Nerve Stimulators and Electrodes.

10. *Obstetrics and Gynecology*: 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)], Devices to Prevent Post-op Pelvic Adhesions, Embryoscopes and Devices intended for fetal surgery, Falloposcopes and Falloposcopic Delivery Systems, Intrapartum Fetal Monitors using new physiological markers, New Devices to Facilitate Assisted Vaginal Delivery, Thermal Systems for Endometrial Ablation.

11. *Ophthalmics:* 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 recognized as safe for ophthalmic use, Corneal Implants, Corneal Storage Media, Epikeratophakia Lenticules, Extended Wear Contact Lens, Eye Valve Implants (glaucoma implant), Intraocular Lenses (IOLs) [21 CFR part 813], Keratoprostheses Retinal Reattachment Systems [fluids, gases, perfluorocarbons, perfluorpropane, silicone oil, sulfur hexafluoride, tacks], Viscosurgical Fluids.

12. *Orthopedics and Restorative***:** Bone Growth Stimulators, Calcium Tri-Phosphate Hydroxyapatite, Ceramics Collagen and Bone Morphogenic Protein Meniscus Replacements, Implantable Prostheses (ligament, tendon, hip, knee, finger), Computer Guided Robotic Surgery.

13. *Radiology*: Boron Neutron Capture Therapy, Hyperthermia Systems and Applicators.

IRB and Sponsor Responsibilities Following SR/NSR Determination

If the IRB decides the study is SR:

1. IRB Responsibilities:
   a) Notify sponsor and investigator of SR decision

b) After IDE obtained by sponsor, proceed to review study applying requisite criteria [21 CFR 56.111]

2. Sponsor Responsibilities:
   a) Submit IDE to FDA or, if electing not to proceed with study, notify FDA of the SR determination;
   b) Study may not begin until FDA approves IDE and IRB approves the study.
   c) Sponsor and investigator(s) must comply with IDE regulations [21 CFR part 812], as well as informed consent and IRB regulations [21 CFR parts 50 and 56].

If the IRB decides the study is NSR:

1. IRB proceeds to review study applying requisite criteria [21 CFR 56.111]

2. If the study is approved by the IRB, the sponsor and investigator must comply with "abbreviated IDE requirements" [21 CFR 812.2(b)], and informed consent and IRB regulations [21 CFR parts 50 & 56].

IRB Review of the Protocol and Informed Consent

Once the final SR/NSR decision has been rendered by the IRB (or FDA), the IRB will consider whether or not the study should be approved. 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 [21 CFR 56.111]. Some NSR studies may also qualify as "minimal risk" studies, and thus may be reviewed through an expedited review procedure. FDA considers all SR studies to present more than minimal risk, and thus, full IRB review is necessary. In making its determination on approval, the IRB will consider the risks and benefits of the medical device compared to the risks and benefits of alternative devices or procedures.

Applicable Regulations and Guidelines

21 CFR 812
FDA Guidance: Significant Risk and Non-significant Risk Medical Device Studies