Department: UAMS Human Research Advisory Committee
Policy Number: 18.2
Section: Drugs and Devices
Effective Date: July 31, 2002
Revision Date:

SUBJECT: Investigational Devices

The Investigational Device Exemption (IDE) regulations (21 CFR Part 812) describe two types of device studies, "significant risk" (SR) and "nonsignificant risk" (NSR). An SR device study is defined [21 CFR812.3(m) ; 45 CFR).] 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 an implant; or (2) is used in supporting or sustaining human life; or (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," a term utilized in the Institutional Review Board (HRAC) regulations (21CF56) to identify certain studies that may be approved through an "expedited review" procedure. For both SR and NSR device studies, HRAC approval prior to conducting clinical trials and continuing review by the HRAC are required. In addition, informed consent must be obtained for either type of study (21 CFR 50; 45 CFR).).

Distinguishing Between SR and NSR Device Studies

The effect of the SR/NSR decision is very important to research sponsors and investigators. SR device studies are governed by the IDE regulations (21CFR812; 45 CFR).). NSR device studies have fewer regulatory controls than SR studies and are governed by the abbreviated requirements [21 CFR812.2(b); 45 CFR).]. The major differences are in the approval process and in the record keeping and reporting requirements. The SR/NSR decision is also important to FDA because the HRAC serves, in a sense, as the FDA's surrogate with respect to review and approval of NSR studies. FDA is usually not apprised of the existence of approved NSR studies because sponsors and HRACs are not required to report NSR device study approvals to FDA.

If an investigator or a sponsor proposes the initiation of a claimed NSR investigation to an HRAC, and if the HRAC agrees that the device study is NSR and approves the study, the investigation may begin at that institution immediately, without submission of an IDE application to FDA. If an HRAC believes that a device study is SR, the investigation may not begin until both the HRAC and FDA approve the investigation. To help in the determination of the risk status of the device, HRACs should review information such as reports of prior investigations conducted with the device, the proposed investigational plan, a description of subject selection criteria, and monitoring procedures. The sponsor should provide the HRAC with a risk assessment and the rationale used in making its risk determination [21 CFR812.150(b)(10); 45 CFR).].

SR/NSR Studies and the HRAC

The assessment of whether or not a device study presents a NSR is initially made by the sponsor. If the sponsor considers that a study is NSR, the sponsor provides the reviewing HRAC an explanation of its determination and any other information that may assist the HRAC in evaluating the risk of the study. The HRAC may ask the sponsor for information such as a description of the device, reports of prior investigations with the device, the proposed investigational plan, a description of patient selection criteria and monitoring procedures, as well as any other information that the HRAC deems necessary to make its decision. The HRAC should ask the sponsor whether other HRACs have reviewed the proposed study and what determination was made. The sponsor should inform the HRAC of the FDA's assessment of the device's risk if such an assessment has been made. The HRAC may also consult with FDA for its opinion.

The HRAC may agree or disagree with the sponsor's initial NSR assessment. If the HRAC agrees with the sponsor's initial NSR assessment and approves the study, the study may begin without submission of an IDE application to FDA. If the HRAC disagrees, the sponsor must notify FDA that a SR determination has been made. The study can be conducted at that institution as a SR investigation following FDA approval of an IDE application.

The risk determination should be based on the proposed use of a device in an investigation, and not on the device alone. In deciding if a study poses a SR, an

HRAC must 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 should be considered SR. Also, if the subject must undergo a procedure as part of the investigational study, e.g., a surgical procedure, the HRAC must consider the potential harm that could be caused by the procedure in addition to the potential harm caused by the device.

FDA has the ultimate decision in determining if a device study is SR or NSR. If the FDA does not agree with an HRAC'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 FDA will return the IDE application to the sponsor and the study would be presented to HRACs as an NSR investigation.

If HRAC decides the study is *Significant* Risk:

1. HRAC 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 (CDRH Program Operations Staff 3015941190) of the SR determination;
    b. Study may not begin until FDA approves IDE and HRAC approves the study.
    c. Sponsor and investigator(s) must comply with IDE regulations (21 CFR Part 812), as well as informed consent and HRAC regulations (21 CFR Parts 50 and 56).

If the HRAC decides the study is *Non-significant* Risk:

1. HRAC proceeds to review study applying requisite criteria (21 CFR56.111; 45 CFR).
2. If the study is approved by the HRAC, the sponsor and investigator must comply with "abbreviated IDE requirements" [21 CFR812.2(b); 45 CFR).], and the Informed Consent and HRAC regulations (21 CFR50,56; 45 CFR).

The Decision to Approve or Disapprove

Once the SR/NSR decision has been reached, the HRAC should consider whether the study should be approved or not. The criteria for deciding if SR and NSR studies should be approved are the same as for any other FDA regulated study (21 CFR56.111; 45 CFR).). The HRAC should assure that risks to subjects are minimized and are reasonable in relation to anticipated benefits and knowledge to be gained, subject selection is equitable, informed consent materials and procedures are adequate, and provisions for monitoring the study and protecting the privacy of subjects are acceptable. To assure that the risks to the subject are reasonable in relation to the anticipated benefits, the risks and benefits of the investigation should be compared to the risks and benefits of alternative devices or procedures. This differs from the judgment about whether a study poses a SR or NSR which is based solely upon the seriousness of the harm that may result from the use of the device. Minutes of HRAC meetings must document the rationale for SR/NSR and subsequent approval or disapproval decisions for the clinical investigation.

FDA considers studies of all significant risk devices to present more than minimal risk; thus, full HRAC review for all studies involving significant risk devices is necessary. Generally, HRAC review at a convened meeting is also required when reviewing NSR studies. Some NSR studies, however, may qualify as minimal risk [21 CFR56.102(i); 45 CFR).] and the HRAC may choose to review those studies under its expedited review procedures (21 CFR56.110; 45 CFR).

Examples of NSR/SR Devices: The following examples are provided to assist sponsors and HRACs 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. Refer to this website for a current list: http://www.fda.gov/oc/ohrt/HRACs/devices.html#nonsig

NONSIGNIFICANT RISK DEVICES

☐ Low Power Lasers for treatment of pain (Note: an IDE is required when safety and effectiveness data are collected which will be submitted in support of a marketing application.)

- Caries Removal Solution
- 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)
- 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
- Conventional Gastroenterology and Urology Endoscopes and/or Accessories
- Conventional Laparoscopes, Culdoscopes, and Hysteroscopesental Filling Materials, Cushions or Pads made from traditional materials and designs
- Denture Repair Kits and Realigners
- Digital Mammography (Note: an IDE is required when safety and effectiveness data are collected which will be submitted in support of a marketing application.)
- Electroencephalography (e.g., new recording and analysis methods, enhanced diagnostic capabilities)
- Externally Worn Monitors for Insulin Reactions
- Functional Electrical Neuromuscular Stimulators
- General Biliary Catheters
- General Urological Catheters (e.g., Foley and diagnostic catheters)
- Jaundice Monitors for Infants
- Magnetic Resonance Imaging (MRI) Devices within FDA specified parameters
- 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
- Transcutaneous Electric Nerve Stimulation (TENS) Devices for treatment of pain
- Wound Dressings, excluding absorbable hemostatic devices and dressings (also excluding Interactive Wound and Burn Dressings)

SIGNIFICANT RISK DEVICES

GENERAL MEDICAL USE

☐ Catheters:

☐ Urology urologic with antiinfective coatings

- General Hospital - longterm percutaneous, implanted, subcutaneous
- Neurological - cerebrovascular, occlusion balloon
- Cardiology - transluminal coronary angioplasty, intraaortic balloon with

and control
intravascular system

- Collagen Implant Material for use in ear, nose and throat, orthopedics, plastic surgery, urological and dental applications
- Surgical Lasers for use in various medical specialties
- Tissue Adhesives for use in neurosurgery, gastroenterology, ophthalmology, general and plastic surgery, and cardiology

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

CARDIOVASCULAR

- Aortic and Mitral Valvuplasty Catheters
- Arterial Embolization Devices
- Cardiac Assist Devices: artificial heart (permanent implant and short term use), cardiomyoplasty devices, intraaortic balloon pumps, ventricular assist devices
- Cardiac Bypass Devices: oxygenators, cardiopulmonary nonroller 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 and 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 and Peripheral Stints
- Replacement Heart Valves
- RF Catheter Ablation and Mapping Systems
- Ultrasonic Angioplasty Catheters
- Vascular and Arterial Graft Prostheses
- Vascular Hemostasis Devices

GASTROENTEROLOGY AND UROLOGY

☐ Anastomosis Devices

- Balloon Dilation Catheters for benign prostatic hyperplasia (BPH)
- Biliary Stints
- 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 and Subclavian Catheters
- Hemodialyzers
- Hemofilters
- Implantable Electrical Urinary Incontinence Systems
- Implantable Penile Prostheses
- Injectable Bulking Agents for incontinence
- Lithotripters (e.g., electrohydraulic extracorporeal shockwave, 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 Stints (e.g., ureteral, prostate)

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

GENERAL HOSPITAL

- Implantable Vascular Access Devices
- Infusion Pumps (implantable and closedloop depending on the infused drug

NEUROLOGICAL

- Electroconvulsive Therapy (ECT) Devices
- Hydrocephalus Shunts
- Implanted Intracerebral/Subcortical Stimulators
- Implanted Intracranial Pressure Monitors
- Implanted Spinal Cord and Nerve Stimulators and Electrodes

OBSTETRICS AND GYNECOLOGY

- Antepartum Home Monitors for NonStress Tests
- Antepartum Home Uterine Activity Monitors
- Catheters for Chorionic Villus Sampling (CVS)
- Catheters Introduced into the Fallopian Tubes
- Cervical Dilation Devices
- Devices to Prevent Postop 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
- 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)

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 Lenticulas
- 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

ORTHOPEDICS AND RESTORATIVE

- ☐ Bone Growth Stimulators
- Calcium TriPhosphate Hydroxyapatite Ceramics
- Collagen and Bone Morphogenic Protein Meniscus Replacements
- Implantable Prostheses (ligament, tendon, hip, knee, finger)

RADIOLOGY

- ☐ Boron Neutron Capture Therapy
- Hyperthermia Systems and Applicators
- Image Guided Surgery