

Department: UAMS Institutional Review Board
Policy Number: 18.2
Section: Drugs and Devices
Effective Date: July 31, 2002
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SUBJECT: Investigational Devices

DEFINITIONS:

1. **Consumer Preference Testing:** Studies in which preferences are measured for approved devices or modifications of approved devices. Such testing does NOT involve the collecting of safety or efficacy data.
2. **Food and Drug Administration (FDA):** The FDA is the federal oversight agency responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation.
3. **Investigational Device:** Any healthcare product that does not achieve its primary intended purposes by chemical action or by being metabolized. A medical device that is the subject of a clinical study designed to evaluate the effectiveness and/or safety of the device. Investigational use also includes clinical evaluation of certain modifications or new intended uses of legally marketed devices.
4. **Investigational Device Exemption:** An FDA approved investigational device exemption (IDE) permits a device that otherwise would be required to comply with a performance standard or to have pre-market approval to be shipped lawfully for the purpose of conducting investigations of that device.
5. **Non-significant Risk (NSR) Device Study:** A study of a device that does not meet the definition for a significant risk device and does not present a potential for serious risk to the health, safety, or welfare of participants. NSR device studies should not be confused with the concept of "minimal risk".
6. **Significant Risk (SR) Device Study:** A study of a device that presents a potential for serious risk to the health, safety, or welfare of a participant and 1) is intended as an implant; 2) is used in supporting or sustaining human life; or otherwise prevents impairment of human health; 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 participant.
7. **Sponsor/Investigator:** An individual who both initiates and actually conducts, alone or with others, an investigation, that is, under whose immediate direction the investigational device is administered, dispensed, or used. The term does not include any person other than an individual. The regulatory obligations of a sponsor/investigator include both those of an investigator and those of a sponsor in 21 CFR 812 and 21 CFR 814.
8. **Treatment IDE:** A mechanism through the FDA for providing eligible participants with investigational devices for the treatment of a serious or life-threatening illness for which there are no satisfactory alternatives.
9. **Unanticipated Adverse Device Effect:** 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 to participants or others associated with a device that relates to the rights, safety, or welfare of participants.

Policy: It is the policy of the UAMS Institutional Review Board (IRB) that all investigational device use be reviewed and approved by the IRB in accordance with applicable laws and regulations.

Exemptions from IDE requirements.

1. A device can be exempt from the IDE requirements. A claim that the device is exempt must reference the exemption category being claimed. There are seven exemption categories that may be claimed. Categories 3 and 4 are the most common. Full information regarding the seven exemption categories that may be claimed can be found in the FDA regulations 21 CFR Sec. 812.2(c).
2. Under category 3, (21 CFR Sec. 812.2(c)(3)), in addition to the sponsor's compliance with applicable requirements in 21 CFR Sec. 809.10(c), the diagnostic device testing must comply with the following:
 - 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.
3. Under category 4, (21 CFR Sec. 812(c)(4)), to qualify for this exemption, the device testing must not be for the purposes of determining safety and effectiveness and must not put subjects at risk. The device testing must be limited to the following:
 - a. Consumer preference testing;
 - b. Testing of a modification; or
 - c. Testing of a combination of two or more devices in commercial distribution.
4. The sponsor or sponsor/investigator should provide sufficient justification to the IRB that supports the exemption category being claimed.
5. An exemption from the IDE requirement is not an exemption from the requirement for prospective IRB review or informed consent.

Significant Risk (SR) vs. Non-Significant (NSR) Risk Devices.

1. 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). NSR device studies have fewer regulatory controls than SR studies and are governed by the abbreviated requirements (21CFR812.2(b)).
2. Unless exempt by the IDE regulations, an investigational device must be categorized as either a Significant Risk (SR) device or a Non-Significant Risk (NSR) device. The initial risk assessment is determined by the sponsor, but the IRB must make a formal determination during a convened meeting regarding the appropriate SR/NSR category. The SR/NSR decision by the IRB is important to

- the FDA because the IRB serves, as the FDA's surrogate with respect to review and approval of NSR studies
3. Research involving the use of a Significant Risk (SR) device must be conducted in accordance with the full requirements of the FDA and must have an approved IDE from the FDA.
 4. Research involving the use of a Non-significant Risk (NSR) device must be conducted in accordance with the "abbreviated" requirements of the FDA as described in the FDA regulations 21 CFR Sec. 812.2(b). In some cases, the FDA may notify the sponsor that it does not agree with the NSR determination and will require the submission of an IDE.
 5. If an investigator or a sponsor proposes the initiation of a claimed NSR investigation to an IRB, and if the IRB 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 IRB believes that a device study is SR, the investigation may not begin until both the IRB and FDA approve the investigation. To help in the determination of the risk status of the device, IRBs should review information such as the device manual, 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 IRB with a risk assessment and the rationale used in making its risk determination.

If IRB decides the device is *Significant Risk*:

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 (CDRH Program Operations Staff 3015941190) 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 device is *Non-significant Risk*:

1. IRB proceeds to review study applying requisite criteria for IRB approval (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 the Informed Consent and IRB regulations (21 CFR 50, 56).

IRB Determination of the risk of the device study

Once the SR/NSR decision has been reached regarding the device, the IRB should deliberate on the approval of the study. The approval criteria for deciding if SR and NSR device studies are the same as for any other FDA regulated study (21 CFR56.111).

1. **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 IRB must consider
 - a. 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.
 - b. Also, if the subject must undergo a procedure as part of the investigational study, e.g., a surgical procedure, the IRB must consider the potential harm that could be caused by the procedure in addition to the potential harm caused by the device.
2. The IRB should assure that:
 - a. risks to subjects are minimized and are reasonable in relation to anticipated benefits and knowledge to be gained,
 - b. subject selection is equitable,
 - c. informed consent materials and procedures are adequate, and
 - d. provisions for FDA required IDE monitoring of the study are in place and
 - e. Protecting the privacy of subjects is acceptable.
3. 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.
4. Minutes of IRB meetings must document the rationale for SR/NSR and subsequent approval or disapproval decisions for the clinical investigation.
5. FDA considers studies of all significant risk devices to present more than minimal risk; thus, full IRB review for all studies involving significant risk devices is necessary. Generally, IRB 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).and the IRB may choose to review those studies under its expedited review procedures (21 CFR56.110).

Informed Consent Documentation and Process for IDE Research

1. Informed consent must meet the requirements outlined in the IRB Informed Consent policies and procedures (See IRB Policy 15.1);

2. No claims are to be made which state or imply, directly or indirectly, that the IDE is safe or effective for the purposes under investigation or that the device is in any way superior to any other device;
3. The informed consent document must contain a statement that the IDE is “investigational, meaning non-FDA approved”;
4. The informed consent document must contain a statement that the FDA may have access to the participant’s medical records as they pertain to the study; and
5. The Investigator must ensure that throughout the consenting process and study participation the participant understands that the IDE is experimental, and that its benefits for the condition under study are unproven

Investigator Responsibilities for Investigational Device Studies

The Investigator is responsible for the tracking and oversight of FDA-regulated devices in research and must meet the following requirements in order to use an investigational device in research conducted under the jurisdiction of the IRB:

1. The investigational device must be used only by the Investigator or under his/her direct supervision;
2. The investigational device must be used only as approved by the FDA and as described in the currently approved IRB documents;
3. The Investigator must not supply the investigational device to any persons not authorized under the IDE; and
4. Informed consent from the participant or the participant’s legally authorized representative must be prospectively obtained, unless waived by the IRB.
5. Research with the use of an investigational device must be conducted under all UAMS IRB applicable policies and procedures.
6. Proper disposing or return of investigational devices
7. Storage of the investigational device under lock and key
8. The investigator shall maintain the following accurate, complete and current records related to the device:
 - a. Correspondence with the IRB, sponsor, monitor, other investigators and FDA
 - b. Records of receipt, use or disposition of a device that relate to:
 - i. The type and quantity of the device, dates of receipt, and batch numbers or code marks
 - ii. Names of all persons who received, used , or disposed of each device
 - iii. The number of units of the device return to the sponsor, repaired, or otherwise disposed of, and the reason(s)
 - c. Records of each subject exposure to the device, including;
 - i. Informed consent
 - ii. All relevant observations
 - iii. Adverse device effects

- iv. A record of the exposure of each participant to the investigational device, including the date and time of each use and any other therapy
- d. Dates and reasons for any deviations from the protocol
- 9. The investigator will send an accounting report to the UAMS IRB with each continuing review that includes following information
 - a. Total devices received
 - b. Total devices used or participants exposed to the device
 - c. Devices on hand
 - d. Devices disposed of or returned
 - e. Summary of any adverse events
 - f. Record of any deviations from the protocol and the reason for deviation
- 10. In the case of a sponsor/investigator IDE, a written IDE monitoring plan must be presented to the IRB, reviewed by ORC for regulatory compliance and approved by the IRB before the study begins. Sponsor/Investigators will be referred to ORC for assistance with the plan.
- 11. Sponsor/investigators holding IDEs are required to submit a quarterly report of monitoring activities on the study to the ORC. The ORC will review the monitoring and report to the IRB of any deficiencies.

Additional Reporting Requirements.

- 1. Devices may have an unanticipated adverse device effect to participants or others. An investigator must submit to the sponsor and to the UAMS IRB a report of any unanticipated adverse device effect to participants or others occurring during an investigation as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect. Should the IRB determine that the new information gained in the adverse effect report changes its risk assessment, the IRB has the ability to reconsider its prior NSR decision and ask for FDA review..
- 2. A sponsor must immediately conduct an evaluation of any unanticipated adverse device effect to participants or others.
- 3. A sponsor who determines that an unanticipated adverse device effect presents an unreasonable risk to subjects must terminate or suspend all investigations or parts of investigations presenting that risk as soon as possible. Termination or suspension must occur no later than 5 working days after the sponsor makes this determination and no later than 15 working days after the sponsor first received notice of the effect.
- 4. If the device is a significant risk device, a sponsor may not resume a terminated or suspended investigation without IRB and FDA approval. If the device is not a significant risk device, a sponsor may not resume a terminated or suspended investigation without IRB approval and, if the investigation was terminated or suspended for an unanticipated adverse device effect that presented an unreasonable risk to participants or others, FDA approval.
- 5. Within 3 months after termination or completion of the investigation or the Investigator's part of the investigation, the Investigator must submit a final report to the sponsor and the UAMS IRB.