CONFORMITY OF INVESTIGATIONAL OR UNLICENSED TEST ARTICLES (DEVICES) TO FEDERAL REGULATIONS

1.0 POLICY

1.1 Background.

1.1.1 **Device** means an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent of other similar or related article, including any component, part, or accessory, which is (1) recognized in the official National Formulary or the United States Pharmacopeia, or any supplement to them; (2) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man . . . ; or (3) intended to affect the structure or any function of the body . . . , and which does not achieve its primary intended purposes through chemical action within or on the body . . . and which is not dependent on being metabolized for the achievement of its primary intended purposes. (FD&C Act, 291 (g).

1.1.2 Devices may have potential for significant risk. The determination of whether a device has significant or non-significant risk is a key decision for IRB when reviewing applications for use of devices.

1.1.2.1 **Significant Risk device (SR)** means 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 presents impairment of human health; or (4) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject. (21 CFR 812.3 (m). SR device studies are governed by the Investigational Device Exemption (IDE) regulations (21 CFR Part 812).

1.1.2.2 **Non-Significant Risk device (NSR)** means a device that does not meet the definition for a significant risk study. NSR studies have fewer regulatory controls than SR studies are governed by the abbreviated requirements (21 CFR 812.2 (b)). FDA is usually not apprised of the existence of NSR device studies because sponsors and IRB are not required to report NSR device study approvals to FDA.

1.1.3 This policy deals only with devices. See POLICY: Conformity of Investigational or Unlicensed Test Articles (Drugs, Biologics) to Federal Regulations for information about those investigational articles.

1.2 Policy Statement.
1.2.1 It is the policy of the University of Alabama that investigational or unlicensed test articles will be used in conformity with federal regulations.

1.2.2 All initial requests for IRB approval of a study that include the use of an investigational device will be reviewed by the full Medical IRB.

1.3 Objective

1.3.1 Implementation of this policy will ensure conformity of UA research with federal regulations, thus advancing the protection of human research participants.

1.4 Responsibility

1.4.1 The Vice President for Research is ultimately responsible for this policy. Enabling parties include the Director of Research Compliance, Research Compliance Specialists, IRB chairs and members, and principal investigators.

2.0 PROCEDURE

2.1 The investigator will follow relevant federal regulations (see GUIDANCE: Regulatory Requirements for Investigators Who Hold INDs or IDEs) and provide the following information regarding the use of devices in the IRB application or the appendixes:

2.1.1 Providing all information regarding the use of the device, including the IDE number, if applicable.

2.1.2 When an IDE is required, completing the FDA’s Investigator’s Agreement Form for submission to the FDA and includes a copy with the initial IRB application.

2.1.3 Including all correspondence from the sponsor and/or FDA regarding the determination of whether the device is a NSR (non-significant) or SR (significant risk) device. Provide the IRB with an explanation of the determination, reports of prior investigations with the device, information about whether other IRBs have reviewed the proposed study and what determination was made, whether or not the FDA has assessed the device’s risk and, if so, their conclusion, and other information that may assist the IRB in evaluating the study risk.

2.1.4 Providing a description of the component, ingredient, property, principles of operation and each anticipated change in the device during the course of the research;

2.1.5 Describing and completing the informed consent process and documentation, unless a waiver is requested;

2.1.6 Notifying the sponsor of the SR decision made by the IRB;

2.1.7 Maintaining all case report forms and records as required by the sponsor, the IRB, and/or FDA;
2.1.8 Storing, dispensing, tracking, and oversight of the FDA-regulated devices in accordance with applicable institutional and State and Federal laws and regulations;

2.1.9 Completing and submitting applications for continuing renewal at the review intervals required by the IRB, according to POLICY: Continuing Review and Closure of IRB Protocols. In addition to reports of unanticipated or adverse events (requested on the form), submit a summary of the clinical indications for the use of the device with each participant; the clinical outcomes of each participant (if known), and a copy of the accountability records;

2.1.10 Notifying the IRB of any modifications, unanticipated device effects, serious adverse events, or unanticipated problems to participants or others while conducting the research or follow-up. See POLICY: Reportable Events: Protocol Deviations; Unanticipated Problems, and Adverse Events Involving Participants or Others; FORM: Reporting of Study Problem;

2.1.11 Ensuring that the device is used only under PI’s direct supervision and that unused devices will be discarded or returned to the sponsor as specified by the sponsor;

2.1.12 Notifying the IRB of study closure and submitting the final report.

2.2 The Research Compliance Specialist will pre-review applications and request any necessary revisions or additional materials. Once the application is complete it will be assigned to a primary reviewer and placed on the agenda for the next IRB meeting.

2.3 The IRB will review the application in accordance with usual procedures for full board review but will pay special attention to the process to control investigational devices so that they were used only in approved research protocols and under the direction of approved investigators:

2.3.1 The device has an IDE issued by the FDA;

2.3.2 The device fulfills the requirements for an abbreviated IDE:

2.3.2.1 The device is not a banned device;

2.3.2.2 The sponsor labels the device in accordance with 21 CFR 812.5;

2.3.2.3 The sponsor obtains IRB approval of the investigation after presenting the reviewing IRB with a brief explanation of why the device was not a significant risk device, and maintains such approval;

2.3.2.4 The sponsor ensures that each investigator participating in an investigation of the device obtains from each subject under the investigator’s care, consent under 21 CFR 50 and documents it, unless documentation was waived;

2.3.2.5 The sponsor complies with the requirements of 21 CFR 812.46 with respect to monitoring investigations;
2.3.2.6 The sponsor mains the records required under 21 CFR 812.140(b)(4) and (5) and makes the reports required under 21 CFR 812.150 (a)(1), (2), and (7);

2.3.2.7 The sponsor complies with the prohibitions in 21 CFR 812.7 against promotion and other practices.

2.3.3 The device fulfills one of the IDE exemption categories:

2.3.3.1 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;

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

2.3.3.3 A diagnostic device, if the sponsor complies with applicable requirements in 21 CFR 890.10(c) and if the testing:

2.3.3.3.1 Is noninvasive;

2.3.3.3.2 Does not require an invasive sampling procedure that presents significant risk;

2.3.3.3.3 Does not be designed or intended to introduce energy into a subject;

2.3.3.3.4 Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.

2.3.3.4 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 was not for the purpose of determining safety or effectiveness and does not put participants at risk.

2.3.3.5 A custom device as defined in 21 CFR 812.3(b), unless the device was being used to determine safety or effectiveness for commercial distribution.

2.3.4 The determination of whether the device is SR or NSR. This includes whether or not the IRB agrees with the sponsor's determination of NSR. The risk determination should be based on the proposed use of the device in the investigation and not on the device alone.

2.3.4.1 Devices that are exempt from the IDE requirement are usually NSR and may qualify for waiver of consent. After the Board determines that the study meets requirements for approval (45 CFR 46.111, 21 CFR 56.111) and agrees that
the device is NSR, it considers whether the requirements for a waiver of consent are met. (POLICY: Waivers, Alterations, and Exceptions to Informed Consent or its Written Documentation).

2.3.4.1.1 When the IRB disagrees with sponsor’s determination of NSR, the IRB will table the application and write of letter requesting that the investigator notify the sponsor of the IRB’s decision.

2.3.4.1.2 The sponsor may proceed with submitting a request for an IDE approval from the FDA and when received, the IRB will re-review the application.

2.3.4.1.3 The sponsor or the investigator may withdraw the study and not submit the investigational device to the FDA for consideration of an IDE.

2.3.5 The IRB considers the nature of harm that may result from the device. Studies where the potential harm may be life-threatening to participants, could result in permanent impairment of a body function or permanent damage to a body structure, or could necessitate medical or surgical intervention to preclude permanent impairment or damage should be considered SR.

2.3.5.1 If the participant must undergo a procedure (e.g., a surgical procedure) as part of the investigational study, the IRB must consider the potential harm that might result from the procedure as well as that from the device. Two examples:

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

2.3.5.1.2 A study of an extended wear contact lens is 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.

2.3.6 Determination of the scientific soundness of the study, as it relates to the risk/benefit ratio. This includes design, study population, trial phase, and mechanisms for data analysis and surveillance. (FORM: IRB Checklist for Reviewers and Investigators; GUIDANCE: Evaluating Sound Design.) The criteria for approval are the same for both SR and NSR studies.

2.3.7 Concerns that affect the risk/benefit assessment. This may include prior reviews by the FDA, other institutions, scientific review committees, and funding agents. The Board may seek expert consultation, confer with the FDA, or request a literature review from the medical librarian.
2.3.8 The adequacy of the consent document, whether it meets the criteria for informed consent, including the notification that the FDA may have access to the participants’ study records, and procedures for obtaining informed consent.

2.3.9 AS OF MARCH 7, 2012: FDA requires the following language in all consent forms for drug or device clinical trials that are initiated on or after that date: “A description of this clinical trial will be available on http://www.ClinicalTrials.gov as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.”

2.3.10 The maintenance of the distinction between therapy and research and the investigator’s recognition and management of any conflicts between status as an investigator and the participant’s personal physician. The IRB may require the investigator to inform the participant of this potential conflict.

2.4 At continuing review, NSR and SR devices will be reviewed by the full IRB.

2.5 Modifications of studies will be reviewed by the full board.

2.6 If the FDA rules that a device previously judged NSR is now considered SR, the IRB will suspend the currently approved study, detailing the criteria for suspension. The study may not reopen until an IDE is granted by the FDA and the study is reviewed by the full board following appropriate modifications of the IRB application. The Board may direct the investigator on the issue of re-consenting participants if appropriate.

2.7 The IRB minutes will document the rationale for SR/NSR and other discussions and decisions relevant to approval, continuing review, study modifications, or actions related to suspension.

3.0 REFERENCES

3.1 21 CFR 812.3 (m)

3.2 21 CFR Part 812


3.4 21 CFR §312.61, 62, 69

3.5 21 CFR §812.100, 110, 140 (a)

4.0 RELATED SECTIONS

4.1 GUIDANCE: Regulatory Requirements for Investigators Who Hold INDs or IDEs to be determined.

4.2 POLICY: Continuing Review of Approved IRB Protocols (Title change for policy)

4.3 POLICY: Reportable Events: Protocol Deviations; Unanticipated Problems, and Adverse Events Involving Participants or Others

4.4 POLICY: Waivers, Alterations, and Exceptions to Informed Consent or its Written Documentation

4.5 FORM: IRB Checklist for Reviewers and Investigators

4.6 POLICY: Closure of IRB Protocols (new policy)