

Issuing Department: Human Subjects Protection Program
Policy Number: 2011-021.0
Policy Title: Investigational Device Studies

Purpose:

The purpose of this policy is 1) to set forth circumstances under which a Principal Investigator (PI) is not required to obtain an investigational device exemption (IDE) and 2) to set forth the requirements that PIs, sponsors and Institutional Review Boards (IRB) must fulfill when conducting studies that are conducted under an IDE.

Definitions:

See policy 2011-007.0 for definitions of the following terms:

Device | Device, Custom | Device, Non-significant Risk | Device, Significant Risk
Device, Investigational Device Exemption | Device, Unanticipated Adverse Device Effect

Policy:

When research is conducted to determine the safety or effectiveness of a device, one of the following will apply:

- the device has an IDE issued by the FDA,
- the device fulfills the requirements for an abbreviated IDE, or
- the device fulfills one of the IDE exemption categories described below.

The sponsor of the device will make the initial determination of whether the device presents a significant (SR) or non-significant risk (NSR). NSR devices are not necessarily minimal risk studies.

For SR studies, the FDA must approve an investigational device exemption (IDE) application submitted by the sponsor and the IRB must approve the study before it may commence. SR devices studies require review of the convened IRB.

Unless otherwise notified NSR devices are considered to have an approved IDE if the sponsor fulfills the abbreviated requirements set forth below. While exempt from FDA approval, NSR studies must receive IRB approval prior to commencing. NSR studies generally will require full board review but may be approved through the expedited review procedure if the study falls within a designated approvable category and is minimal risk.

NSR device studies may not require submission to the FDA providing they comply with the abbreviated requirements of the regulations as follow:

- The device is not a banned device
- The sponsor labels the device in accordance with the following criteria
 - the investigational device or its immediate package shall bear a label with the following information: the name and place of business of the manufacturer, packer, or distributor, the quantity of contents, if appropriate, and the following statement: “CAUTION –Investigational device. Limited by Federal (or United States) law to investigational use.” The label or other

labeling shall describe all relevant contraindications, hazards, adverse effects, interfering substances or devices, warnings, and precautions.

- The labeling of an investigational device shall not bear any statement that is false or misleading in any particular and shall not represent that the device is safe or effective for the purpose for which it is being investigated.
- The sponsor obtains IRB approval of the investigation after presenting the reviewing IRB with a brief explanation of why the device is not a significant risk device, and maintains such approval.
- The sponsor ensures that each investigator participating in an investigation of the device obtains from each subject under the investigator's care, consent and documents it, unless documentation is waived.
- The sponsor complies with the requirements for monitoring investigations as follows:
 - a sponsor who discovers that an investigator is not complying with the signed investigators agreement, the investigational plan, applicable regulatory requirements, or other applicable FDA regulations, or any conditions of approval imposed by the reviewing IRB or FDA shall promptly either secure compliance, or discontinue shipments of the device to the investigator and terminate the investigator's participation in the investigation. A sponsor shall also require such an investigator to dispose of or return the device, unless this action would jeopardize the rights, safety or welfare of a subject.
 - a sponsor shall immediately conduct an evaluation of any unanticipated adverse device effect
 - a sponsor who determines that an unanticipated adverse device effect presents an unreasonable risk to subjects shall terminate all investigations or parts of investigations presenting that risk as soon as possible. Termination shall occur not later than 5 working days after the sponsor makes this determination and not later than 15 working days after the sponsor first received notice of the effect.
 - a sponsor may not resume a terminated study without IRB and FDA approval
- The sponsor maintains the required records as follows:
 - the name and intended use of the device and the objectives of the investigation
 - a brief explanation of why the device is not a significant risk device
 - the name and address of each investigator
 - the name and address of each reviewing IRB
 - a statement of the extent to which the good manufacturing practice regulation will be followed in manufacturing the device
 - any other information required by the FDA
 - records concerning adverse device effects (whether anticipated or unanticipated) and complaints
- The sponsor makes the required reports as follows;
 - Unanticipated adverse device effects. A sponsor who conducts an evaluation of an unanticipated adverse device shall report the results of such evaluation to FDA and to all reviewing IRB's and participating investigators within 10 working days after the sponsor first receives notice of the effect. Thereafter the sponsor shall submit such additional reports concerning the effect as FDA requests.
 - Withdrawal of IRB approval. A sponsor shall notify FDA and all reviewing IRB's and participating investigators of any withdrawal of approval of an investigation or a part of an investigation by a reviewing IRB within 5 working days after receipt of the withdrawal of approval.

- Withdrawal of FDA approval. A sponsor shall notify all reviewing IRB's and participating investigators of any withdrawal of FDA approval of the investigation, and shall do so within 5 working days after receipt of notice of the withdrawal of approval.
- Progress reports. At regular intervals, and at least yearly, a sponsor shall submit progress reports to all reviewing IRB's. In the case of a significant risk device, a sponsor shall also submit progress reports to FDA. A sponsor of a treatment IDE shall submit semi-annual progress reports to all reviewing IRB's and FDA and annual reports.
- Recall and device disposition. A sponsor shall notify FDA and all reviewing IRB's of any request that an investigator return, repair, or otherwise dispose of any units of a device. Such notice shall occur within 30 working days after the request is made and shall state why the request was made.
- Final report. In the case of a significant risk device, the sponsor shall notify FDA within 30 working days of the completion or termination of the investigation and shall submit a final report to FDA and all reviewing the IRB's and participating investigators within 6 months after completion or termination. In the case of a device that is not a significant risk device, the sponsor shall submit a final report to all reviewing IRB's within 6 months after termination or completion.
- Informed consent. A sponsor shall submit to FDA a copy of any report by an investigator of use of a device without obtaining informed consent, within 5 working days of receipt of notice of such use.
- Significant risk device determinations. If an IRB determines that a device is a significant risk device, and the sponsor had proposed that the IRB consider the device not to be a significant risk device, the sponsor shall submit to FDA a report of the IRB's determination within 5 working days after the sponsor first learns of the IRB's determination.
- Other. A sponsor shall, upon request by a reviewing IRB or FDA, provide accurate, complete, and current information about any aspect of the investigation.
- The sponsor ensures that participating investigators maintain the required records
 - Documents evidencing informed consent and, for any use of a device by the investigator without informed consent, any written concurrence of a licensed physician and a brief description of the circumstances justifying the failure to obtain informed consent. The case history for each individual shall document that informed consent was obtained prior to participation in the study.
- The sponsor ensures that participating investigators makes the required reports;
 - Unanticipated adverse device effects. An investigator shall submit to the sponsor and to the reviewing IRB a report of any unanticipated adverse device effect 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.
 - Withdrawal of IRB approval. An investigator shall report to the sponsor, within 5 working days, a withdrawal of approval by the reviewing IRB of the investigator's part of an investigation.
 - Informed consent. If an investigator uses a device without obtaining informed consent, the investigator shall report such use to the sponsor and the reviewing IRB within 5 working days after the use occurs
 - Other. An investigator shall, upon request by a reviewing IRB or FDA, provide accurate, complete, and current information about any aspect of the investigation.
- The sponsor complies with the prohibitions against promotion and other practices.

- a sponsor, investigator, or any person acting for or on behalf of a sponsor or investigator shall not;
 - promote or test market an investigational device, until after FDA has approved the device for commercial distribution
 - commercialize an investigational device by charging the subjects or investigators for a device a price larger than that necessary to recover costs of manufacture, research, development, and handling.
 - unduly prolong an investigation if data developed by the investigation indicate in the case of a class III device that premarket approval cannot be justified or in the case of a class II device that it will not comply with an applicable performance standard or an amendment to that standard, the sponsor shall promptly terminate the investigation.
 - represent that an investigational device is safe or effective for the purpose for which it is being investigated

In the event that a UConn Health PI is also the sponsor of the IDE, the PI must make arrangements with a Research Compliance Monitor to request a pre-audit of the facilities and to review the additional obligations that the PI assumes when also acting as the sponsor. The audit must occur prior to the submission of the IRB application and the results of the audit must be submitted with the IRB application.

Exemptions from the Requirements of Part 812:

The following types of investigational device studies are exempt from the requirements of Part 812:

- 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.
- 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.
- A diagnostic device, if the sponsor complies with applicable regulatory requirements and if the testing:
 - Is noninvasive
 - Does not require an invasive sampling procedure that presents significant risk.
 - Does not by design or intention introduce energy into a subject.
 - Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure
- 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.
- A device intended solely for veterinary use.
- A device shipped solely for research on or with laboratory animals and labeled in accordance with regulatory requirements
- A custom device, unless the device is being used to determine safety or effectiveness for commercial distribution.

Assessment of Risk

The sponsor makes the initial determination of SR or NSR for the device. However, the IRB will make the final determination for NSR devices. If the IRB disagrees with the sponsor and designates the device as SR, the sponsor will be required to submit to the FDA for an IDE. The study will not be approved by the IRB until the IDE is obtained. The investigator will be informed of the IRB's determination in writing and the investigator must inform the sponsor.

In assessing the risk level of a device the IRB will consider information such as a description of the device and its proposed use, nature of the harm that may result from the use of the device or from procedures required for use of the device, e.g. surgical implants, reports of prior investigations conducted with the device, the proposed investigational plan, a description of subject selection criteria and monitoring procedures. The IRB should be provided with the sponsor's risk assessment and rationale for its determination as NSR. The sponsor must provide the IRB with the FDA's assessment of the device's risk if such an assessment has been made. The IRB may also choose to consult with the FDA.

A clinical study may be exempt from the regulation if the study involves the investigation of a lawfully marketed device.

Investigator Obligations:

The PI of a device study must:

- obtain appropriate approvals (IRB, FDA) prior to obtaining consent and enrolling any subjects;
- maintain control of the device under investigation;
- conduct the study in compliance with the signed agreement with the sponsor, the investigational plan, applicable regulations and policies;
- protect the rights, safety and welfare of subjects under the investigator's care;
- make financial disclosures to the sponsor;
- supervise the device use, the device shall be used only with subjects under the investigator's supervision;
- supply the device to only authorized individuals;
- upon completion or termination of a clinical investigation, or the investigator's part of an investigation, or at the sponsor's request, return to the sponsor any remaining supply of the device or otherwise dispose of the device as the sponsor directs;
- permit authorized persons (e.g. HSPP / IRB staff, FDA staff) to inspect and copy records relating to the investigation;
- if authorized, permit authorized persons (e.g. HSPP / IRB staff, FDA staff) to enter and inspect any establishment where devices are held (manufactured, processed, packed, installed, used, or implanted, or where records of results from use of devices are kept);
- maintain adequate records including:
 - correspondence with another investigator, an IRB, the sponsor, a monitor, or the FDA;
 - records of receipt, use or disposition of a device that relate to the type and quantity of the device, the dates of its receipt, and the batch number or code mark, the names of all persons who received, used, or disposed of each device, why and how many units of the device have been returned to the sponsor, repaired, or otherwise disposed of;
 - each subject's case history and exposure to the device (include the case report forms and supporting data including, for example, the signed and dated consent forms, medical records including progress notes, adverse event reports);

- the protocol and records of any deviations from the protocol; and
- any other records required by the FDA or IRB or relevant to the study;
- submit reports of unanticipated adverse device effects to the IRB in accordance with the Adverse Event reporting policy and to the sponsor as soon as possible but within 10 days of becoming aware of the event;
- submit a report to the sponsor within 5 days of any withdrawal of IRB approval;
- submit progress reports to the IRB, sponsor, and monitor at least annually.

PIs are to retain records for 2 years after the latter of either the date on which the investigation is terminated or completed, or the date that the records are no longer required for purposes of supporting a pre-market approval application or a notice of completion of a product development protocol. Transfer of custody of the records to another person/entity willing to accept responsibility for them may occur but requires that the investigator inform the FDA within 10 days of the transfer.

Names of subjects need not be disclosed unless there is reason to suspect that adequate informed consent was not obtained, or that reports required to be submitted by the investigator to the sponsor or to the IRB have not been submitted or are incomplete, inaccurate, false or misleading.

Procedure

The PI will provide the required information about the device as part of the IRB application process.

- When the PI is also the sponsor of the IDE, the PI will be responsible for arranging a meeting with the Research Compliance Monitor and providing proof that the PI is prepared to meet the additional obligations of the sponsor, as directed to do so in the application checklist

The IRB will conduct its review according to standard practice, evaluating the information provided using the reviewer checklists as a tool in the review process.

Related Policies

2009-005.0 - Monitoring of IRB Approved Studies

2011-007.0 – Definitions Applied to Policies

2011-009.3 – Institutional Review Board – Expedited Reviews

2011-009.5 – Institutional Review Board – Review by Convened Board Full

Basis

21 CFR 50

21 CFR 56.109(c).

21 CFR 812

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