



Sponsor and Investigator Obligations

UW Bioen 599

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Sponsor Obligations

21 CFR Part 812



General responsibilities of sponsors {Sec. 812.40 }

- selecting qualified investigators and providing them with the information they need to conduct the investigation properly,
- ensuring proper monitoring of the investigation,
- ensuring that IRB review and approval are obtained,
- submitting an IDE application to FDA, and
- ensuring that any reviewing IRB and FDA are promptly informed of significant new information about an investigation.



FDA and IRB approval.

{21 CFR Sec. 812.42 }

- A sponsor shall not begin an investigation or part of an investigation until an IRB and FDA have both approved the application or supplemental application relating to the investigation or part of an investigation.



Selecting investigators and monitors. [Sec. 812.43]

- (a) *Selecting investigators.* A sponsor shall select investigators qualified by training and experience to investigate the device.
- (b) *Control of device.* A sponsor shall ship investigational devices only to qualified investigators participating in the investigation.
- (c) *Obtaining agreements.* A sponsor shall obtain from each participating investigator a signed agreement that includes:
 - (1) The investigator's curriculum vitae.
 - (2) Where applicable, a statement of the investigator's relevant experience, including the dates, location, extent, and type of experience.
 - (3) If the investigator was involved in an investigation or other research that was terminated, an explanation of the circumstances that led to termination.



Selecting Investigators and Monitors, 2

- (4) A statement of the investigator's commitment to:
- (i) Conduct the investigation in accordance with the agreement, the investigational plan, this part and other applicable FDA regulations, and conditions of approval imposed by the reviewing IRB or FDA;
 - (ii) Supervise all testing of the device involving human subjects; and
 - (iii) Ensure that the requirements for obtaining informed consent are met.



Selecting Investigators and Monitors, 3

- (5) Sufficient accurate financial disclosure information to allow the sponsor to submit a complete and accurate certification or disclosure statement as required under part 54 of this chapter.
- The sponsor shall obtain a commitment from the clinical investigator to promptly update this information if any relevant changes occur during the course of the investigation and for 1 year following completion of the study.
- This information shall not be submitted in an investigational device exemption application, but shall be submitted in any marketing application involving the device.



Selecting Investigators and Monitors, 4

- (d) *Selecting monitors.* A sponsor shall select monitors qualified by training and experience to monitor the investigational study in accordance with this part and other applicable FDA regulations.



Informing investigators

21 CFR Sec. 812.45

- A sponsor shall supply all investigators participating in the investigation with copies of the investigational plan and the report of prior investigations of the device.
- Sometimes referred to as the Investigator's Brochure.



Monitoring Investigations

[21 CFR 812.46]

■ (a) *Securing compliance.*

- A sponsor who discovers that an investigator is not complying with the signed agreement, the investigational plan, the requirements of this part 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.



Monitoring investigations, 2

(b) *Unanticipated adverse device effects.*

(1) A sponsor shall immediately conduct an evaluation of any unanticipated adverse device effect (UADE).

(2) 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.

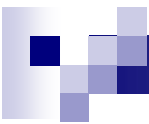


Monitoring investigations, 3

c) Resumption of terminated studies.

If the device is a significant risk device, a sponsor may not resume a terminated investigation without IRB and FDA approval.

If the device is not a significant risk device, a sponsor may not resume a terminated investigation without IRB approval and if the investigation was terminated under paragraph (b)(2) of this section, FDA approval.



Emergency research (under 21 CFR 50.24) {21 CFR Sec. 812.47}

- (a) The sponsor shall monitor the progress of all investigations involving an exception from informed consent under 50.24 of this chapter.
- When the sponsor receives from the IRB information concerning the public disclosures under 50.24(a)(7)(ii) and (a)(7)(iii) of this chapter, the sponsor shall promptly submit to the IDE file and to Docket Number 95S-0158 in the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852, copies of the information that was disclosed, identified by the IDE number.

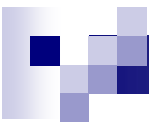


Emergency Research, 2

- b) The sponsor also shall monitor such investigations to determine when an IRB determines that it cannot approve the research because it does not meet the criteria in the exception in 50.24(a) of this chapter or because of other relevant ethical concerns.
- The sponsor promptly shall provide this information in writing to FDA, investigators who are asked to participate in this or a substantially equivalent clinical investigation



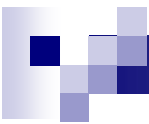
Investigator Obligations



General responsibilities of investigators. [21 CFR Sec. 812.100]

- An investigator is responsible for
 - ensuring that an investigation is conducted according to the signed agreement, the investigational plan and applicable FDA regulations,
 - for protecting the rights, safety, and welfare of subjects under the investigator's care, and
 - for the control of devices under investigation.

An investigator also is responsible for ensuring that informed consent is obtained in accordance with part 50 of this chapter.



Specific Responsibilities of the Investigator (21CFR 812.110)

- (a) *Awaiting approval.* An investigator may determine whether potential subjects would be interested in participating in an investigation, but shall not request the written informed consent of any subject to participate, and shall not allow any subject to participate before obtaining IRB and FDA approval.
- (b) *Compliance.* An investigator shall conduct an investigation in accordance with the signed agreement with the sponsor, the investigational plan, this part and other applicable FDA regulations, and any conditions of approval imposed by an IRB or FDA.



Specific Responsibilities, 2

- (c) *Supervising device use.* An investigator shall permit an investigational device to be used only with subjects under the investigator's supervision. An investigator shall not supply an investigational device to any person not authorized under this part to receive it.
- (d) *Financial disclosure.* A clinical investigator shall disclose to the sponsor sufficient accurate financial information to allow the applicant to submit complete and accurate certification or disclosure statements required under part 54 of this chapter. The investigator shall promptly update this information if any relevant changes occur during the course of the investigation and for 1 year following completion of the study.



Specific Responsibilities, 3

- e) *Disposing of device.*

Upon completion or termination of a clinical investigation or the investigator's part of an investigation, or at the sponsor's request, an investigator shall return to the sponsor any remaining supply of the device or otherwise dispose of the device as the sponsor directs.



Disqualification of an Investigator

(21 CFR 812.119)

- (a) If FDA has information indicating that an investigator has repeatedly or deliberately failed to comply with the requirements of this part, part 50, or part 56 of this chapter, or has repeatedly or deliberately submitted false information either to the sponsor of the investigation or in any required report, the CDRH, the CBER, or the CDER will furnish the investigator written notice of the matter under complaint and offer the investigator an opportunity to explain the matter in writing, or, at the option of the investigator, in an informal conference.

If an explanation is offered and accepted by the applicable Center, the disqualification process will be terminated. If an explanation is offered but not accepted by the Center, the investigator will be given an opportunity for a regulatory hearing under part 16 of this chapter on the question of whether the investigator is entitled to receive investigational devices.



Disqualification, 2

- b) After evaluating all available information, including any explanation presented by the investigator, if the Commissioner determines that the investigator has repeatedly or deliberately failed to comply with the requirements of this part, part 50, or part 56 of this chapter, or has deliberately or repeatedly submitted false information either to the sponsor of the investigation or in any required report, the Commissioner will notify the investigator, the sponsor of any investigation in which the investigator has been named as a participant, and the reviewing IRB that the investigator is not entitled to receive investigational devices. The notification will provide a statement of basis for such determination.



Disqualified Investigators, 3

- c) Each investigational device exemption (IDE) and each cleared or approved application submitted under this part, subpart E of part 807 [510(k)] of this chapter, or part 814 of this chapter [*PMA*] containing data reported by an investigator who has been determined to be ineligible to receive investigational devices will be examined to determine whether the investigator has submitted unreliable data that are essential to the continuation of the investigation or essential to the approval or clearance of any marketing application.



Disqualification, 4

- If the Commissioner determines, after the unreliable data submitted by the investigator are eliminated from consideration, that the data remaining are inadequate to support a conclusion that it is reasonably safe to continue the investigation, the Commissioner will notify the sponsor who shall have an opportunity for a regulatory hearing under part 16 of this chapter. If a danger to the public health exists, however, the Commissioner shall terminate the IDE immediately and notify the sponsor and the reviewing IRB of the determination. In such case, the sponsor shall have an opportunity for a regulatory hearing before FDA under part 16 of this chapter on the question of whether the IDE should be reinstated.



Disqualification, 5

- e) If the Commissioner determines, after the unreliable data submitted by the investigator are eliminated from consideration, that the continued clearance or approval of the marketing application for which the data were submitted cannot be justified, the Commissioner will proceed to withdraw approval or rescind clearance of the medical device in accordance with the applicable provisions of the act.



Disqualification, 6

(f) An investigator who has been determined to be ineligible to receive investigational devices may be reinstated as eligible when the Commissioner determines that the investigator has presented adequate assurances that the investigator will employ investigational devices solely in compliance with the provisions of this part and of parts 50 and 56 of this chapter.



Lists of Investigators

- Financial Disclosure for Investigators

<http://www.fda.gov/oc/guidance/financialdis.html>

- Disqualified Investigators List

http://www.fda.gov/ora/compliance_ref/bimo/dis_res_assur.htm

- Restricted List

http://www.fda.gov/ora/compliance_ref/bimo/rest_removed.htm

- Notice to Explain

<http://www.fda.gov/foi/nidpoe/default.html>