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IRB REFERENCE MANUAL
SECTION 14
FDA SPONSOR REQUIREMENTS FOR INVESTIGATORS WHO ARE SERVING AS SPONSORS

14.0 FDA SPONSOR REQUIREMENTS FOR INVESTIGATORS WHO ARE SERVING AS SPONSORS

14.1 Sponsors of Investigational Drug or Biologic Studies

A sponsor is an individual, pharmaceutical company, governmental agency, academic institution, private organization, or other organization which takes responsibility for and initiates a clinical investigation. Sponsors of Investigational New Drugs (INDs) are responsible for reviewing the federal regulations before performing any sponsor's duties including, but not limited to, selecting qualified investigators, providing them with the information they need to conduct an investigation properly, ensuring proper monitoring of the investigation(s), ensuring that the investigation(s) is conducted in accordance with the general investigational plan and protocols contained in the Investigational New Drug authorization (IND), maintaining an effective IND with respect to the investigations, and ensuring that FDA and all participating investigators are promptly informed of significant new adverse effects or risks with respect to the drug. (Ref. 21 CFR 312.50)

Sponsors who also serve as investigators of a drug/biologic are individuals who both initiate and conduct an investigation, and under whose immediate direction the investigational drug is administered or dispensed. A sponsor-investigator must meet the requirements for both the sponsor *and* the investigator. Regulatory responsibilities for investigators and sponsors are detailed in Subpart D of 21 CFR 312.

14.1.1 IND Requirements

When research involves the use of a drug other than the use of a marketed drug in the course of medical practice, the IRB must confirm that either:

a. The drug has an IND, or
b. The protocol meets one of the FDA exemptions from the requirement to have an IND (ref. 21 CFR 312.2(b)):

i. **Exemption 1**

The clinical investigation of a drug product that is lawfully marketed in the United States is exempt from the requirements if all the following apply:

1) The investigation is not intended to be reported to FDA as a well-controlled study in support of a new indication for use nor intended to be used to support any other significant change in the labeling for the drug;
2) If the drug that is undergoing investigation is lawfully marketed as a prescription drug product, the investigation is not intended to support a significant change in the advertising for the product;
3) The investigation does not involve a route of administration or dosage level or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product;
4) The investigation is conducted in compliance with the requirements for institutional review set forth in 21 CFR 56 and with the requirements for informed consent set forth in 21 CFR 50; and
5) The investigation is conducted in compliance with the requirements of 21 CRF 312.7.

ii. **Exemption 2**

1) A clinical investigation involving an in vitro diagnostic biological product listed in 14.1.2(b)(ii)(2) below is exempt from the requirements of this part if (a) it is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure, and (b) it is shipped in compliance with 21 CFR 312.160.
2) In accordance with 14.1.2(b)(ii)(1) above, the following products are exempt from the requirements of this part: (*a*) blood grouping serum; (*b*) reagent red blood cells; and (*c*) anti-human globulin.

iii. **Exemption 3**

A drug intended solely for tests in vitro or in laboratory research animals is exempt from the requirements of this part if shipped in accordance with 21 CFR 312.160.

iv. **Exemption 4**
FDA will not accept an application for an investigation that is exempt under the provisions of Exemption 1 above.

v. **Exemption 5**
A clinical investigation involving use of a placebo is exempt from the requirements of this part if the investigation does not otherwise require submission of an IND.

vi. **Exemption 6**
A clinical investigation involving an exception from informed consent under 21 CFR 50.24 is not exempt from the requirements of this part.

14.1.2 Responsibilities of Sponsors with IND Studies

a. **IND Application:** Submits an IND application including Form FDA-1571 and other required documentation to the FDA (ref. 21 CFR 312.23)

b. **Labeling:** Labels the investigational drug in accordance with FDA regulations (ref/ 21 CFR 312.6)

c. **Promotion and Distribution:** Promotes and distributes the drug in accordance with FDA regulations (ref/ 21 CFR 312.7)

d. **Selection of Investigators:** Selects qualified investigators based on training and experience (ref. 21 CFR 312.53(a))

e. **Control of Drug:** Ships investigational drugs only to investigators participating in the investigation (ref. 21 CFR 312.53(b))

f. **Form FDA 1572:** Obtains FDA Form 1572 from the investigator(s) (ref. 21 CFR 312.53(c)(1))

g. **Commitment of Investigator:** Obtains a written statement that the investigator(s) will conduct the study as outlined in the protocol (ref. 21 CFR 312.53(c)(1)(vi)(a))

h. **Financial Disclosure:** Obtains relevant financial information from the investigator(s) (ref. 21 CFR 312.53(c)(4))

i. **Selection of Monitor(s):** Selects a qualified monitor to oversee the progress of the investigation (ref. 21 CFR 312.53(d))

j. **Emergency Research:** Complies with FDA regulations regarding emergency use (ref. 21 CFR 312.54)

k. **Informing Investigators:** Keeps each participating investigator informed on the safety and effectiveness of the drug (ref. 21 CFR 312.55)

l. **Review of Ongoing Investigations**:
   i. Monitors the progress of all IND investigations (ref. 21 CFR 312.56(a))
   ii. Terminates investigator(s) participation when investigator(s) fails to follow protocol (ref. 21 CFR 312.56(b))
   iii. Reviews and evaluates the evidence relating to the safety and effectiveness of the drug as it is obtained from the investigator (ref. 21 CFR 312.56(c))
   iv. Discontinues the study if the investigational drug presents an unreasonable and significant risk to subjects, and notifies the FDA, IRB and the investigator(s) if the study is discontinued (21 CFR 312.56(d))
   v. **Safety Reporting:** Sends safety reports to the FDA (ref. 21 CFR 312.56(c); 21 CFR 312.32)

m. **Sponsor Recordkeeping and Retention** (ref. 21 CFR 312.57)
   i. Maintains adequate records showing the receipt, shipment or other disposition of the investigational drug
   ii. Maintains complete and accurate records of payments made to clinical investigator(s).

n. **Disposition of Unused Supply**: Assures that investigator(s) return all unused investigational drugs 21 CFR 312.59

o. **Investigator Recordkeeping and Retention** (ref. 21 CFR 312.62):
   i. Requires investigator(s) to maintain adequate drug records.
   ii. Requires investigator(s) to keep case histories on each individual administered the investigational drug or employed as a control in the investigation.

p. **Assurance of IRB Review:** Requires investigator(s) to meet local IRB requirements (ref. 21 CFR 312.66)

q. **Investigator Reports:** Collects reports (progress, safety, financial and final reports) from investigator(s) (ref. 21 CFR 312.64)

r. **Handling of Controlled Substances:** Requires investigator(s) to store the investigational drug in a secure area (ref. 21 CFR 312.69)

14.2 Sponsors of Investigational Device or Test Article Studies

A sponsor of an investigational medical device is an individual, pharmaceutical company, governmental agency, academic institution, private organization, or other organization which takes responsibility for and initiates a clinical investigation of an investigational device. Sponsors are responsible for reviewing the federal regulations before performing any sponsor's duties. Sponsors who also serve as investigators of the investigational device are individuals who both initiate and conduct an investigation, and under whose immediate direction the investigation is carried out. A sponsor-investigator must meet the requirements for both the sponsor *and* the investigator.

The following is an overview of the FDA requirements for sponsors, intended to assist sponsors in identifying and complying with their responsibilities in connection with the conduct of clinical investigations of medical devices that are deemed "significant risk" by the reviewing IRB or by the FDA. A significant risk device is an investigational device that: (1) is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject; (2) is for use in supporting or sustaining human life and represents a potential for serious risk to the health, safety, or welfare of a subject; (3) is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or (4) otherwise presents a potential for serious risk to a subject.

In addition, sponsors should be aware that a clinical investigation must be conducted in accordance with any requirements imposed by the reviewing IRB, by institutional policies, or by state law.

14.2.1 Responsibilities of Sponsors with IDE Studies

a. **General Responsibilities** (Ref. 21 CFR 812.40): Sponsors are responsible for 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 Investigational Device Exemption (IDE) application to FDA, and ensuring that any reviewing IRB and FDA are promptly informed of significant new information about an investigation.

An Investigational Device Exemption (IDE) refers to the regulations under 21 CFR 812 Subchapter H. An approved IDE means that the IRB (and FDA for significant risk devices) has approved the sponsor's study application and all the requirements under 21 CFR 812 are met. Additional responsibilities of sponsors are described in subparts B and G.

b. **Application:**
   i. A sponsor shall submit an application to FDA if the sponsor intends to use a significant risk device in an investigation, intends to conduct an investigation that involves an exception from informed consent (ref. 21 CFR 50.24), or if FDA notifies the sponsor that an application is required for an investigation.
   ii. A sponsor A sponsor shall not begin an investigation for which FDA's approval of an application is required until FDA has approved the application.
   iii. A sponsor shall submit a signed "Application for an Investigational Device Exemption" (IDE application), together with accompanying materials in electronic format, to one of the addresses in 21 CFR 812.19, and if eCopy by registered mail or by hand. Subsequent correspondence concerning an application or a supplemental application shall be submitted in electronic format and if eCopy by registered mail or by hand.
   iv. A sponsor shall submit a separate IDE for any clinical investigation involving an exception from informed consent under 21 CFR 50.24 of this chapter. Such a clinical investigation is not permitted to proceed without the prior written authorization of FDA. FDA shall provide a written determination 30 days after FDA receives the IDE or earlier. If the investigation involves an exception from informed consent under 21 CFR 50.24 of this chapter, the sponsor shall prominently identify on the cover sheet that the investigation is subject to the requirements in 21 CFR 50.24.
   v. **Other Contents and Information:** An IDE application shall include all content, additional information, and information previously submitted as outlined under 21 CFR 812.20(b), (c) and (d).

c. **FDA and IRB Approval:** 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. (Ref. 21 CFR 812.42)

d. **Selecting Investigators and Monitors:** A sponsor shall select investigators qualified by training and experience to investigate the device. 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. (Ref. 21 CFR 812.43)

e. **Informing Investigators:** 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. (Ref. 21 CFR 812.45)

f. **Control of Device:** A sponsor shall ship investigational devices only to qualified investigators participating in the investigation. (Ref. 21 CFR 812.43(b))

g. **Obtaining Agreements:** A sponsor shall obtain from each participating investigator a signed agreement that includes:
    i. The investigator's curriculum vitae
    ii. Where applicable, a statement of the investigator's relevant experience, including the dates, location, extent, and type of experience.
    iii. If the investigator was involved in an investigation or other research that was terminated, an explanation of the circumstances that led to termination.
    iv. A statement of the investigator's commitment to: (1) 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; (2) supervise all testing of the device involving human subjects; and (3) ensure that the requirements for obtaining informed consent are met (ref. 21 CFR 50).
    v. Sufficient accurate financial disclosure information to allow the sponsor to submit a complete and accurate certification or disclosure statement as required under 21 CFR 54. 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.

h. **Monitoring** (ref. 21 CFR 812.46):

i. **Securing Compliance:** A sponsor who discovers that an investigator is not complying with the signed agreement, the investigational plan, the IDE requirements, any other applicable FDA regulations, or any conditions of approval imposed by the reviewing IRB or FDA must promptly either secure compliance, or discontinue shipments of the device to the investigator and terminate the investigator's participation in the investigation. A sponsor must also require that the investigator dispose of or return the device, unless this action would jeopardize the rights, safety, or welfare of a subject.

ii. **Unanticipated Adverse Device Effects:** The sponsor must 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 must terminate all investigations or parts of the investigations presenting that risk as soon as possible. Termination 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.

iii. **Resumption of Terminated Studies:** For significant risk device investigations, a sponsor may not resume a terminated investigation without IRB and FDA approval. For a nonsignificant risk device investigation, a sponsor may not resume a terminated investigation without IRB approval. If the nonsignificant risk study was terminated for unanticipated adverse device effects, the sponsor must also obtain FDA approval.

i. **Controlling Distribution and Disposition of Devices**

Although investigators are responsible for ensuring that investigational devices are made available only to persons who are legally authorized to receive them (ref. 21 CFR 812.110(c)), sponsors also bear responsibility for taking proper measures to ensure that devices are not diverted outside of legally authorized channels. Sponsors may ship investigational devices only to

qualified investigators participating in the clinical investigation (ref. 21 CFR 812.43(b)). Sponsors must also maintain complete, current and accurate records pertaining to the shipment and disposition of the investigational device (ref. 21 CFR 812.140(b)). Records of shipment shall include the name and address of the consignee, type and quantity of device, date of shipment, and batch number or code mark. Records of disposition shall describe the batch number or code marks of any devices returned to the sponsor, repaired or disposed of in other ways by the investigator or another person, and the reasons for and method of disposal.

To ensure further compliance with these requirements, sponsors should take appropriate measures to instruct investigators regarding their responsibilities with respect to recordkeeping and device disposition. The specific recordkeeping requirements for investigators are set forth at 21 CFR 812.140(a). Upon completion or termination of a clinical investigation (or the investigator's part of an investigation), or at the sponsor's request, an investigator is required to return to the sponsor any remaining supply of the device or otherwise to dispose of the device as the sponsor directs. (ref. 21 CFR 812.110(e)).

j. **Prohibition of Promotion and Other Practices** (ref. 21 CFR 812.7)

The IDE regulations prohibit the promotion and commercialization of a device that has not been cleared or approved for marketing by the FDA. A sponsor, investigator, or any person acting for or on behalf of a sponsor or investigator shall not:

i. Promote or test market an investigational device, until after FDA has approved the device for commercial distribution;
ii. 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;
iii. 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, or

iv. Represent that an investigational device is safe or effective for the purposes for which it is being investigated.

k. **Supplemental Applications**

Supplemental applications are required to be submitted to, and approved by, the FDA in the following situations:

i. Changes in the investigational plan, changes requiring prior approval including any change that may affect the scientific soundness of the investigation or the rights, safety or welfare of the subjects. IRB approval is also required for changes that may affect the rights, safety or welfare of subjects. The change in the investigational plan may not be implemented until FDA approval (and IRB approval, if required) is obtained.

ii. Addition of New Institutions: IRB approval is also required for new institutions. The investigation at the new institution may not begin until both FDA and IRB approvals are obtained, and certification of IRB approval is submitted to the FDA. Ref. 21 CFR 812.35 for additional information.

l. **Records**

i. **Sponsor Records** (ref. 21 CFR 812.140(b))

A sponsor shall maintain the following accurate, complete and current records relating to an investigation:

1) All correspondence with another sponsor, a monitor, an investigator, an IRB, or FDA, including required reports
2) Records of shipment and disposition. Records of shipment shall include the name and address of the consignee, type and quantity of device, date of shipment, and batch number or code mark. Records of disposition shall describe the batch number or code marks of any devices returned to the sponsor, repaired, or disposed of in other ways by the investigator or another person, and the reasons for and method of disposal.
3) Signed investigator agreements including the financial disclosure information required to be collected under 21 CFR 812.43(c)(5) in accordance with 21 CFR 54.
4) For each investigation subject to 21 CFR 812.2(b)(1) of a device other than a significant

risk device, the records described in 21 CFR 812.140(b)(5) and the following records, consolidated in one location and available for FDA inspection and copying:

- 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 IRB that has reviewed the investigation:
- A statement of the extent to which the good manufacturing practice regulation in 21 CFR 820 will be followed in manufacturing the device; and
- Any other information required by FDA.

5) Records concerning adverse device effects (whether anticipated or unanticipated) and complaints; and
6) Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigation or a particular investigation.

ii. **Investigator Records** (21 CFR 812.140(a))

A participating investigator shall maintain the following accurate, complete, and current records relating to the investigator's participation in an investigation:

1) All correspondence with another investigator, an IRB, the sponsor, a monitor, or FDA, including required reports.
2) 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.
3) Records of each subject's case history and exposure to the device. Case histories include

the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital chart(s), and the nurses' notes. Such records shall include:

- 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.
- All relevant observations, including records concerning adverse device effects (whether anticipated or unanticipated), information and data on the condition of each subject upon entering, and during the course of, the investigation, including information about relevant previous medical history and the results of all diagnostic tests.
- A record of the exposure of each subject to the investigational device, including the date and time of each use, and any other therapy.

4) The protocol, with documents showing the dates of and reasons for each deviation from the protocol.
5) Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation.

Sponsor/Investigator Responsibilities - Records

Records	Maintained by Sponsor	Maintained by Investigator
All correspondence pertaining to the investigation	X	X
Shipment, receipt, disposition	X	X
Device administration & use	-	X
Subject case histories	-	X
Informed consent	-	X
Protocols and reasons for deviations from protocol		X
Adverse device effects and complaints	X	X
Signed investigator agreements	X	-
Conflicts of interest	X	-

m. **Reports**

i. **Sponsor Reports**

A sponsor shall prepare and submit the following complete, accurate and timely reports (ref. 21 CFR 812.150(b)):

1) **Unanticipated Adverse Device Effects:** A sponsor who conducts an evaluation of an unanticipated adverse device effect under 21 CFR 812.46(b) 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.

2) **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.

3) **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.

4) **Current Investigator List*:*** A sponsor shall submit to FDA, at 6-month intervals, a current list of the names and addresses of all investigators participating in the investigation. The sponsor shall submit the first such list 6 months after FDA approval.
5) **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 in accordance with 21 CFR 812.36(f) and annual reports in accordance with this section.
6) **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.
7) **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 IRBs within 6 months after termination or completion.
8) **Informed Consent:** A sponsor shall submit to FDA a copy of any report by an investigator under 21 CFR 812.150(a)(5) of use of a device without obtaining informed consent, within 5 working days of receipt of notice of such use.
9) **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.

10) **Other:** A sponsor shall, upon request by a reviewing IRB or FDA, provide accurate, complete, and current information about any aspect of the investigation.

ii. **Investigator Reports (**21 CFR 812.150(a))
An investigator shall prepare and submit the following complete, accurate, and timely reports:

1) **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.
2) **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.
3) **Progress:** An investigator shall submit progress reports on the investigation to the sponsor, the monitor, and the reviewing IRB at regular intervals, but in no event less often than yearly.
4) **Deviations from the investigational plan:** An investigator shall notify the sponsor and the reviewing IRB (see 21 CFR 56.108(a) (3) and (4)) of any deviation from the investigational plan to protect the life or physical well-being of a subject in an emergency. Such notice shall be given as soon as possible, but in no event later than 5 working days after the emergency occurred. Except in such an emergency, prior approval by the sponsor is required for changes in or deviations from a plan, and if these changes or deviations may affect the scientific soundness of the plan or the rights, safety, or welfare of human subjects, FDA and IRB in accordance with 21 CFR 812.35(a) also is required.
5) **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.

6) **Final report:** An investigator shall, within 3 months after termination or completion of the investigation or the investigator's part of the investigation, submit a final report to the sponsor and the reviewing IRB.
7) **Other:** An investigator shall, upon request by a reviewing IRB or FDA, provide accurate, complete, and current information about any aspect of the investigation.

Sponsor/Investigator Responsibilities - Reporting

Report Type	Sponsors prepare for:	Investigators prepare for:
Unanticipated adverse device events	FDA, IRBs and Investigators	Sponsors and IRBs
Withdrawal of IDE approval	FDA, IRBs and Investigators	Sponsors
Progress Report	FDA and IRBs	Sponsors, Monitors and IRBs
Final Report	FDA, IRBs and Investigators	Sponsors and IRBs
Withdrawal of FDA approval	IRBs and Investigators	N/A
Current Investigator List	FDA	N/A
Recall and device disposition	FDA and IRBs	N/A
Records maintenance transfer	FDA	FDA
Significant risk determinations	FDA	N/A

n. **Inspections** (ref. 21 CFR 812.145):
   i. **Entry and Inspection:** A sponsor or an investigator who has authority to grant access shall permit authorized FDA employees, at reasonable times and in a reasonable manner, to enter and inspect any establishment where devices are held (including any establishment where devices are manufactured, processed, packed, installed, used, or implanted or where records of results from use of devices are kept).
   ii. **Records Inspection:** A sponsor, IRB, or investigator, or any other person acting on behalf of such a person with respect to an investigation, shall permit authorized FDA employees, at reasonable times and in a reasonable manner, to inspect and copy all records relating to an investigation.

iii. **Records Identifying Subjects:** An investigator shall permit authorized FDA employees to inspect and copy records that identify subjects, upon notice that FDA has reason to suspect that adequate informed consent was not obtained, or that reports required to be submitted by the investigator to the sponsor or IRB have not been submitted or are incomplete, inaccurate, false, or misleading.

14.2.2 Additional Guidance: Significant and Nonsignificant Risk Investigational Device Studies

FDA guidance for Sponsors of Nonsignificant Risk Device Studies, Investigators of Significant Risk Device Studies and Investigators of Nonsignificant Risk Device Studies can be found in FDA publication "IDE Responsibilities."