VIRGINIA COMMONWEALTH UNIVERSITY

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VCU/VCUHS (Significant Risk) IDE Sponsor-Investigator Responsibilities

A sponsor-investigator assumes BOTH investigator and sponsor responsibilities as outlined in the FDA Code of Federal Regulations 21 CFR 812. This means that such investigators have additional responsibilities.

All VCU/VCUHS faculty/employees who apply for an IDE must abide by all relevant federal, state and VCU/VCUHS policies. The Sponsor and Investigator or Sponsor-Investigator (if the same individual), must understand and agree to abide by all responsibilities. This document outlines Federal Regulations regarding responsibilities of Sponsors and Investigators for an IDE.

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Sponsor Responsibilities for Significant Risk Device Studies

A. General Responsibilities 21CFR812.40

Sponsors are responsible for selecting qualified investigators and providing them with the information that they need to conduct the investigation properly. They must also ensure proper monitoring of the investigation and IRB review and approval, submit an IDE application to FDA for Significant Risk (SR) device studies, and inform the IRB and FDA promptly of any significant new information about the investigation.

1. FDA and IRB approval 21 CFR 812.42

A sponsor cannot begin an investigation or any part of an investigation until an IRB and FDA have both approved the application or supplemental application.

2. Investigator Related

a. Selecting Investigators 21 CFR 812.43

A sponsor is responsible for selecting investigators qualified by training and experience to investigate the device.

b. Investigator Agreements 21 CFR 812.43

A sponsor must obtain a signed agreement from each participating investigator that includes:

- The investigator's curriculum vitae,
- A statement of the investigator's relevant experience, including the dates, location, extent, and type of experience, where applicable,
- An explanation of the circumstances that led to termination of a study if the investigator was involved in an investigation or other research that was terminated,
- A statement of the investigator's commitment to: (Investigators Agreement) conduct the investigation in accordance with the agreement, the investigational plan, the IDE and other applicable FDA regulations, and conditions of approval imposed by the reviewing IRB or FDA, supervise all testing of the device involving human subjects and ensure that the requirements for obtaining informed consent are met.
- Sufficient accurate financial disclosure information to allow the sponsor to submit complete and accurate certification or disclosure statement as required under 21 CFR 54, Financial Disclosure by Clinical Investigators. The sponsor shall also 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 one year following completion of the study. This information should be maintained by the Sponsor it does not require submission to the FDA until either the PMA or Premarket Notification 510(k) application is submitted. It is not submitted with the IDE.

- See the Template for the *IDE Investigator Agreement for Clinical Investigation* on the VCU Faculty-Held IND or IDE website.

c. Informing investigators 21 CFR 812.45

A sponsor must supply all investigators participating in the investigation with copies of the investigational plan and a report of prior investigations of the device.

3. Monitoring

a. Selecting Monitors 21 CFR 812.43

A sponsor must select monitors qualified by training and experience to monitor the investigational study in accordance with the IDE and other applicable FDA regulations.

b. Monitoring Plan

The monitoring procedures must be submitted with the IDE application and the name and address of the individual(s) who will monitor the study should be included.

c. Monitoring 21 CFR 812.46

- 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.
- 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.
- 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.

4. Device Control 21 CFR 812.43

A sponsor can ship investigational devices only to qualified investigators participating in the investigation.

5. Sponsor Records 21 CFR 812.140

The sponsor must maintain accurate and complete records relating to the investigation. These records include:

- All correspondence including required reports
- Records of shipment of the device (Including)
    - name and address of the consignee
    - type and quantity of the device, date of shipment, and batch number or code
- Records of disposition of the device (Including)
    - batch number or code of any devices returned to the sponsor, repaired, or disposed of in other ways
    - reasons for and the method of disposal
- Signed investigator agreements including financial disclosure information
- Records concerning complaints and adverse device effects whether anticipated or not
- Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigation or a particular investigation.

6. Sponsor Reports 21 CFR 812.150

The sponsor must provide the following reports in a timely manner to FDA, the IRB's, and/or the investigators. (Time requirements)

- Unanticipated Adverse Device Effects (10 days)
- Withdrawal of IRB Approval (5 days)
- Withdrawal of FDA Approval (5 days)
- Current List of Investigators (Every 6 months)
- Progress Reports (At least annually to the FDA and IRB)
- Recalls and Device Disposition (30 days)
- Final Report (Notify the FDA and IRB within 30 days of completion or termination AND submit a final report within 6 months of completion or termination.)
- Failure to Obtain Informed Consent (5 days)
- Significant Risk Device Determination (5 days)
- Other Reports

See:*http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm046717.htm* for more information regarding required reports.

NOTE: All the reports listed above need to be concurrently submitted to the Clinical Research Compliance Officer through a VCU REDCap at *go.vcu.edu/submit/indide*.

7. Labeling 21 CFR 812.5

Under 21 CFR 812.5 an investigational device or its immediate package must 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 statement, "CAUTION" Investigational device. Limited by Federal (or United States) law to investigational use."

The label must also describe all relevant contraindications, hazards, adverse effects, interfering substances or devices, warnings, and precautions.

The labeling of an investigational device must not contain any false or misleading statements nor imply that the device is safe or effective for the purposes being investigated.

The sponsor should provide detailed information on device labeling in the investigational protocol. This information may vary depending on the device and the nature of the study. Product labeling should be sufficient to ensure stability of the test article for the duration of the study (storage requirements, calibration procedures), bear sufficient directions for proper administration, and detail procedures to follow in the event of patient injury.

8. Promotion of Investigational Devices 21 CFR 812.7

Under 21 CRF 812.7, a sponsor, investigator, or any person acting for or on behalf of a sponsor or investigator cannot:

- 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 a higher price than that necessary to recover costs of manufacture, research, development, and handling.
- Unduly prolong an investigation. If data developed by the investigation indicate that premarket approval (PMA) cannot be justified, the sponsor must promptly terminate the investigation.
- Represent that an investigational device is safe or effective.

However, the sponsor may advertise for research subjects to solicit their participation in a study. Appropriate advertising methods include but are not necessarily limited to: newspaper, radio, TV, bulletin boards, posters, and flyers that are intended for prospective subjects. Advertisements must be reviewed and approved by the IRB to assure that they are not unduly coercive and does not promise a certainty of cure beyond what is outlined in the consent and the protocol. No claims should be made, either explicitly or implicitly, that the device is safe or effective for the purposes under investigation, or that the test article is known to be equivalent or superior to any other device.

FDA considers direct advertising for study subjects to be the start of the informed consent and subject selection process.

Investigator Responsibilities for Significant Risk Device Studies

The investigator is responsible for protecting the rights, safety, and welfare of subjects. An investigator must conduct the investigation in accordance with the signed agreement with the sponsor, the investigational plan, the IDE regulations and other applicable FDA regulations, and any conditions of approval imposed by an IRB and FDA. 21CFR812.100. An investigator must sign an investigators agreement. 21 CFR 812.43

A. IRB Initial and Ongoing Approval

An investigator must await IRB approval and any necessary FDA approval before beginning the study and obtaining written informed consent or permitting subject participation. The investigator is also responsible for maintaining IRB continual approval and reporting while study activities are taking place at his/her site.

B. Informed Consent

An investigator is responsible for obtaining informed consent under 21 CFR Part 50

C. Supervision of Device Use 21 CFR 812.110

An investigator can permit use of the investigational device only with subjects under his/her supervision and cannot not supply an investigational device to any person not authorized under the IDE regulations to receive it.

D. Financial Disclosure 21 CFR 812.110

The clinical investigator must disclose to the sponsor sufficient accurate financial information to allow the IDE applicant (or sponsor) to submit certification or disclosure of financial interests under 21 CFR 54. The investigator must update the information if any relevant changes occur during the course of the investigation and for one year following completion of the study.

E. Device Disposal 21 CFR 812.110

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

F. Records 21 CFR 812.140

The investigator must maintain accurate and complete records relating to the investigation. These records include:

- All correspondence including required reports
- Records of receipt, use, or disposition of the investigational device (Including)
    - type and quantity of device

    - date of receipt
    - batch number or code
    - name of person that 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
- Records of each subject's case history and exposure to the device which must include:
    - signed and dated consent forms
    - condition of each subject upon entering the study
    - relevant previous medical history
    - record of the exposure to the investigational device, including the date and
    - time of each use and any other therapy
    - observations of adverse device effects
    - Medical records (physician and nurse progress notes, hospital charts, etc.)
    - results of all diagnostic tests
    - case report forms
    - any other supporting data
- The protocol and documentation (date and reason) for each deviation from the Protocol
- Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigation or a particular investigation.

See Records for additional information on recordkeeping requirements.

G. Investigator Reports 21 CFR 812.150

The investigator must provide the following reports in a timely manner to the sponsor and/or the IRB.

- Unanticipated Adverse Device Effects
- Withdrawal of IRB Approval
- Progress Reports
- Deviations from the Investigational Plan
- Failure to obtain Informed Consent
- Final Report
- Other Reports

Key References

Code of Federal Regulations Title 21 Part 812
http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=812

ICH E6 Good Clinical Practice Guidelines for Industry
http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM073122.pdf

VCU working manual for VCU/VCUHS investigator initiated IND/IDEs
go.vcu.edu/handbook/indide

VCU Policy on Record Retention (See GS111 for Clinical Research)
http://www.ts.vcu.edu/askit/policies-and-publications/records-management/records-retention--disposition-schedules/

VCUHS Policy Conduct of Clinical Research in Patient Care Areas
http://vcuhspolicy.mcvh-vcu.edu/Policies/zav_PC.CP.004.htm

This document is built from 21 CFR 812 with information from:
http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=812

http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm046702.htm

http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm046722.htm

http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm046706.htm

http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm049864.htm

For specific questions at VCU/VCUHS contact the Clinical Research Compliance Officer:

Betsy Ripley, MD, MS
elizabeth.ripley@vcuhealth.org
804-828-1955, or page 2022.