



**GENERAL INFORMATION**

**Principal Investigator:** \_\_\_\_\_

**Protocol Number:** \_\_\_\_\_

**Protocol Title:** \_\_\_\_\_

**PROTOCOL/DEVICE STATUS**

1. **CCI/IRB Review:**     Approved     Pending, status: \_\_\_\_\_     Not Submitted

2.  **Protocol registered in IND/IDE Registry**

**If no:**     PI referred to Matt Wladkowski (ext. 4-2777; [Matthew.Wladkowski@childrens.harvard.edu](mailto:Matthew.Wladkowski@childrens.harvard.edu))  
           EQuIP notified Matt Wladkowski via email

3. **EQuIP Meeting Date:** \_\_\_\_\_    **QI Specialist:** \_\_\_\_\_

**MEETING NOTES**

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**SIGNATURES: QUALITY IMPROVEMENT SPECIALIST AND SPONSOR INVESTIGATOR**

The responsibilities required by FDA regulations and CH/CCI policies for a Sponsor-Investigator of a significant risk investigational device in a clinical research trial, were provided to and reviewed with the Sponsor-Investigator of this proposed research trial. The responsibilities and information provided to and reviewed with the Sponsor-Investigator are checked/marked in the attached forms.

**QI Specialist:** \_\_\_\_\_ **Date:** \_\_\_\_\_

The undersigned understands and accepts the responsibilities of the FDA regulations and CH/CCI policies required of the Sponsor-Investigator of a significant risk investigational device clinical research study, as provided by and reviewed with the QI Specialist.

**Sponsor-Investigator:** \_\_\_\_\_ **Date:** \_\_\_\_\_

## SPONSOR RESPONSIBILITIES

### Responsibilities of a Sponsor of a Significant Device

#### → General Responsibilities of Sponsors

- |   |                               |
|---|-------------------------------|
| <input type="checkbox"/> Submit the IDE application to FDA  | <a href="#">21 CFR 812.40</a> |
| <input type="checkbox"/> Obtaining FDA approval and IRB approval for the investigation before beginning an investigation of part of an investigation, and any supplemental application before beginning that portion of the investigation | <a href="#">21 CFR 812.42</a> |
| <input type="checkbox"/> Obtaining FDA approval and IRB approval for any supplemental application before beginning that portion of the investigation  | <a href="#">21 CFR 812.42</a> |
| <input type="checkbox"/> Selecting qualified investigators and providing them with the information they need to conduct the investigation properly  | <a href="#">21 CFR 812.40</a> |
| <input type="checkbox"/> Ensuring proper monitoring   | <a href="#">21 CFR 812.40</a> |

#### → Current Good Manufacturing Practices: cGMPs

##### The Sponsor is responsible for:

- |   |                            |
|---|----------------------------|
| <input type="checkbox"/> Ensuring the minimum current good manufacturing practice of devices in compliance with 21 CFR 820, Quality System Regulation | <a href="#">21 CFR 820</a> |
|---|----------------------------|

#### → Label the device in accordance with FDA requirements.

- |  |  |
|--|--|
| The investigational device or its immediate package must have a label that states:   | <a href="#">21 CFR 812.5(a)</a>                                      |
| <input type="checkbox"/> Name and place of business of the manufacturer, packer or distributor<br>→ in accordance with <a href="#">21 CFR 801.1, General Labeling Provisions</a> (see attached)                    | <a href="#">21 CFR 812.5(a)</a><br><a href="#">21 CFR 801.1(a-e)</a> |
| <input type="checkbox"/> Quantity of contents, <i>if appropriate</i>   | <a href="#">21 CFR 812.5(a)</a>                                      |
| <input type="checkbox"/> The statement: “ <i>CAUTION – Investigational device. Limited by Federal (or United States) law to investigational use.</i> ”   | <a href="#">21 CFR 812.5(a)</a>                                      |
| <input type="checkbox"/> The label or other labeling must describe all relevant contraindications, adverse effects, hazards, interfering substances or devices, warnings and precautions.                          | <a href="#">21 CFR 812.5(b)</a>                                      |
| <input type="checkbox"/> Labeling should not include any statements that may be false or misleading, and should not represent the device as safe or effective for the purposes for which it is being investigated. | <a href="#">21 CFR 812.5(a)</a>                                      |

## SPONSOR-INVESTIGATOR RESPONSIBILITIES SIGNIFICANT RISK INVESTIGATIONAL DEVICES

### → Prohibition of Promotion and Other Practices

A sponsor, investigator, or person acting for or on behalf of a sponsor or investigator shall not: [21 CFR 812.7](#)

- Promote or test market an investigation device, until after FDA has approved the device for commercial distribution [21 CFR 812.7\(a\)](#)
- Charge subjects or investigator for a device a price larger than that necessary to recover costs of manufacturer, research, development and handling [21 CFR 812.7\(b\)](#)
- Prolong an investigation beyond the point needed to collect data required to determine whether the device is safe and effective [21 CFR 812.7\(c\)](#)
- Represent that device is safe or effective for the purposes for which it is being investigated. [21 CFR 812.7\(d\)](#)

### → Comply with FDA requirements for monitoring the investigation

- Selecting Monitors: A sponsor shall select monitors qualified by training and experience to monitor the investigational study in accordance with applicable FDA regulations [21 CFR 812.43 \(d\)](#)
- Securing Compliance: the sponsor must ensure that all participating investigators comply with the signed agreement, investigational plan, applicable FDA regulations, or with the conditions of IRB or FDA approval. [21 CFR 812.46\(a\)](#)  
The sponsor must promptly secure investigator compliance, or discontinue device shipments and terminate that investigator's participation. In such case, the investigator must dispose of or return the device(s), unless the actions would jeopardize the rights, safety or welfare of the subject(s).
- Unanticipated Adverse Device Effects: the sponsor must conduct an evaluation of any unanticipated adverse device effect(s). [21 CFR 812.46\(b.\)](#)  
If it is determined an unanticipated adverse device effect presents an unreasonable risk to subjects, the sponsor must terminate all or parts of the investigation immediately (no later than 5 days after sponsor makes risk determination, and no later than 15 working days after sponsor is first notified of device effect).
- Resumption of Terminated Studies: for significant risk devices, the sponsor may not resume a terminated investigation without IRB and FDA approval. [21 CFR 812.46\(c\)](#)

### → Managing Conflicts of Interests: Financial Disclosures

The Sponsor is responsible for:

- Maintaining current, complete and accurate records documenting the financial interests of all participating clinical investigators, including sponsor payments [21 CFR 54.2](#)  
[21 CFR 54.4](#)
  - Note: sponsors are responsible for developing a method (e.g. form/letter) to ensure adequate disclosure of participating clinical investigators' financial disclosure. Many sponsors develop their own financial disclosure forms.
  - Note: many sponsors obtain financial disclosures from participating investigators at the start of the study, and require updates annually during the study and again before data is 'locked'.

## SPONSOR-INVESTIGATOR RESPONSIBILITIES SIGNIFICANT RISK INVESTIGATIONAL DEVICES

### → Electronic Systems:

The Sponsor is responsible for:

- Ensuring any electronic data and source documentation meets the same fundamental elements of data quality that are expected of paper records [21 CFR 11](#)
  - Reference [21 CFR Part 11 FAQ](#) Guidance from CRIT (Clinical Research Information Technology)
  - Note: CHB sponsor-investigators planning to implement software and electronic systems to collect and maintain study data are recommended to contact the CRP, CTO and CRIT to assist with compliance requirements and evaluating risk.

### → Ensures that Investigators Maintain Records as required by FDA

- All correspondence with another investigator, an IRB, the sponsor, a monitor, or FDA. [21 CFR 812.140\(a\)\(1\)](#)
- Records of receipt, use or disposition of a device that relate to: [21 CFR 812.140\(a\)\(2\)](#)
  - (i) the type and quantity of the device, the dates of its receipt, and the batch number or code mark,
  - (ii) the names of all persons who received, used or disposed of each device
  - (iii) why and how many units of the device have been returned to the sponsor, repaired to otherwise disposed of.
- Investigators must maintain records of each subject's case history and exposure to the device. [21 CFR 812.140\(a\)\(3\)\(1\)](#)

Case histories include the case report forms (CRFs) 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: [21 CFR 812.140\(a\)\(3\)\(i\)](#)

  - (i) Investigators must maintain study 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. [21 CFR 812.140\(a\)\(3\)\(ii\)](#)

The case history for each individual shall document that informed consent was obtained prior to participation in the study.

  - (ii) All relevant observations, including records concerning adverse device effects, information and data on the condition of each subject entering, and during the course of, the investigation, including information about relevant previous medical history and the results of all diagnostic tests
  - (iii) A record of the exposure of each subject to the investigational device, including the date and time of each use and any other therapy.
- The protocol, with documents showing the dates of and reasons for each deviation from the protocol [21 CFR 812.140\(a\)\(4\)](#)
- Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation [21 CFR 812.140\(a\)\(5\)](#)

## SPONSOR-INVESTIGATOR RESPONSIBILITIES SIGNIFICANT RISK INVESTIGATIONAL DEVICES

### → Ensures that Investigators Submit Reports as required by FDA

The Investigator must prepare and submit to the sponsor the following complete, accurate and timely reports:

[21 CFR 812.150\(a\)](#)

- Unanticipated adverse device effect: an investigator must 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 no later than 10 working days after the investigator first learns of the effect. [21 CFR 812.150\(a\)](#)
- Withdrawal of IRB approval: an investigator must report to the sponsor any withdrawal of approval by the reviewing IRB of the investigator's part of an investigation, within 5 working days of notification [21 CFR 812.150\(a\)](#)
- 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. [21 CFR 812.150\(a\)](#)
- Deviations from the investigational plan: An investigator shall notify the sponsor and the reviewing IRB of any deviation from the investigational plan to protect the life or physical well-being of a subject in an emergency. [21 CFR 812.150\(a\)](#)
- Informed consent: in the event an investigator uses a device without obtaining informed consent, the investigator must report such use to the sponsor and the reviewing IRB within 5 working days after the use occurs. [21 CFR 812.150\(a\)](#)
- 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. [21 CFR 812.150\(a\)](#)
- Other: upon request by a reviewing IRB or FDA, an investigator must provide accurate, complete, and current information about any aspect of the investigation. [21 CFR 812.150\(a\)](#)

### → Maintain Study Records required by FDA

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

[21 CFR 812.140\(b\)](#)

- All correspondence with another sponsor, a monitor, an investigator, an IRB or FDA, including required reports. [21 CFR 812.140\(b\)\(1\)](#)
- 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. [21 CFR 812.140\(b\)\(2\)](#)
- Signed investigator agreements including the financial disclosure information required to be collected under 21 CFR 812.43(c)(5) in accordance with part 54. [21 CFR 812.140\(b\)\(3\)](#)
- Records concerning adverse device effects (whether anticipated or unanticipated) and complaints [21 CFR 812.140\(b\)\(5\)](#)
- Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigation or a particular investigation [21 CFR 812.140\(b\)\(6\)](#)

## SPONSOR-INVESTIGATOR RESPONSIBILITIES SIGNIFICANT RISK INVESTIGATIONAL DEVICES

### → Makes and Submits Reports as required by FDA

The sponsor is responsible to prepare and submit the following complete, accurate and timely reports:

[21 CFR 812.150\(1-10\)](#)

- |  |                                      |
|--|--------------------------------------|
| <input type="checkbox"/> <b>Unanticipated Adverse Device Effects:</b> a sponsor must submit to the FDA, all reviewing IRB's and all participating investigators a report with the results from any evaluations conducted for an unanticipated adverse device effect, within 10 working days after the sponsor is first notified of the effect.<br>Thereafter, the sponsor must submit follow-up reports as the FDA requests. | <a href="#">21 CFR 812.150(1)</a>    |
| <input type="checkbox"/> <b>Withdrawal of IRB Approval:</b> a sponsor must notify the 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.   | <a href="#">21 CFR 812.150(20)</a>   |
| <input type="checkbox"/> <b>Withdrawal of FDA approval:</b> a sponsor must notify all reviewing IRB's and participating investigators of any withdrawal of FDA approval of the investigation, and must do so within 5 working days after receipt of notice of the withdrawal of approval.  | <a href="#">21 CFR 812.150(3)</a>    |
| <input type="checkbox"/> <b>Current Investigator List:</b> A sponsor shall submit to the 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 the FDA approval.   | <a href="#">21 CFR 812.150(b)(4)</a> |
| <input type="checkbox"/> <b>Progress Reports:</b> At least yearly, the sponsor must submit a progress report to all reviewing IRBs   | <a href="#">21 CFR 812.150(5)</a>    |
| <input type="checkbox"/> <b>Recall and Device Disposition:</b> a sponsor must notify the FDA and reviewing IRBs of any requests for an investigator to return, repair or otherwise dispose of any units of a device, within 30 working days after the request is made and must state why the request was made.   | <a href="#">21 CFR 812.150(6)</a>    |
| <input type="checkbox"/> <b>Final Report:</b> for SR 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.   | <a href="#">21 CFR 812.150(7)</a>    |
| <input type="checkbox"/> <b>Informed Consent:</b> the sponsor must submit any reports submitted by investigators regarding the use of an investigational device without obtaining consent to the FDA within 5 working days of notification of such use.  | <a href="#">21 CFR 812.150(8)</a>    |
| <input type="checkbox"/> <b>Significant risk device determination:</b> 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.                              | <a href="#">21 CFR 812.150(9)</a>    |
| <input type="checkbox"/> <b>Other:</b> upon request by a reviewing IRB or FDA, the sponsor must submit accurate, complete and current information about any aspect of the investigation.   | <a href="#">21 CFR 812.150(10)</a>   |

### ADDITIONAL REFERENCES PROVIDED

1. CH/CCI Policy: Investigational Devices
2. FDA Regulation, 21 CFR 801: Labeling – General Labeling Provisions
3. FDA Regulation, 21 CFR 812.46: Monitoring Investigations
4. FDA Regulation, 21 CFR 820.1: Quality Systems Regulation
5. FDA Regulation, 21 CFR 812.140: Records
6. FDA Regulation, 21 CFR 812.150: Reports
7. FDA Regulation, 21 CFR 812.43: Selecting Investigators and Monitors

## Definitions

### Investigation Device

A device, including a transitional device that is the object of an investigation.

### Protocol

A document that describes the objectives, design, methodology, statistical considerations, and organization of a trial.

### Standard Operating Procedures (SOPs)

Detailed, written instructions to achieve uniformity of the performance of a specific function

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### Sponsor

An individual, company, institution, or organization which takes responsibility for the initiation, management, and/or financing of a clinical trial, but who does not actually conduct the investigation.

### Sponsor-Investigator

An individual who both initiates and conducts a clinical trial. This term does not include any person other than an individual.

### Investigator

A person responsible for the conduct of the clinical trial at a trial site

### Sub-Investigator

Any individual member of the clinical trial team designated and supervised by the investigator at a trial site to perform critical trial-related procedures and/or to make important trial-related decisions (e.g. associates, residents, fellows)

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### Multi-center Trial

A clinical trial conducted according to a single protocol but at more than one site/investigator

### Monitoring

The act of overseeing the progress of a clinical trial, and of ensuring that it is conducted, recorded, and reported in accordance with the protocol, Standard Operating Procedures (SOPs), GCPs, and applicable regulatory requirements

### Monitoring Report

A written report from the monitor to the sponsor after each site visit and/or other trial-related communication according to the sponsor's standard operating procedures (SOPs).

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### Case Report Form (CRF)

A printed, optical, or electronic document designed to record all of the protocol required information to be reported to the sponsor on each trial subject

### Source Document

The record or location where study data/information is first recorded. This may include original results, certified copies of results, observations or other means to reconstruct and evaluate a study as needed.