



GENERAL INFORMATION

Principal Investigator: _____

Protocol Number: _____

Protocol Title: _____

PROTOCOL/DEVICE STATUS

1. **RISK Determination:** Significant Risk (SR) → submitted to FDA and CCI/IRB
 Non-significant Risk (NSR) → submitted to CCI/IRB

2. **CCI/IRB Review:** Approved Pending, status: _____ Not Submitted

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

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

4. **EQulP Meeting Date:** _____ **QI Specialist:** _____

MEETING NOTES

SIGNATURES: QUALITY IMPROVEMENT SPECIALIST AND SPONSOR INVESTIGATOR

The responsibilities required by FDA regulations and CH/CCI policies for a Sponsor-Investigator of a non-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 non-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 Non-significant Device

→ Current Good Manufacturing Practices: cGMPs

The Sponsor is responsible for:

- Ensuring the minimum current good manufacturing practice of devices in compliance with 21 CFR 820, Quality System Regulation 21 CFR 820

→ Label the device in accordance with FDA requirements.

The investigational device or its immediate package must have a label that states: [21 CFR 812.5\(a\)](#)

- Name and place of business of the manufacturer, packer or distributor
→ in accordance with [21 CFR 801.1, General Labeling Provisions](#) (see attached) [21 CFR 812.5\(a\)](#)
[21 CFR 801.1\(a-e\)](#)
- Quantity of contents, *if appropriate* [21 CFR 812.5\(a\)](#)
- The statement: “CAUTION – Investigational device. Limited by Federal (or United States) law to investigational use.” [21 CFR 812.5\(a\)](#)
- The label or other labeling must describe all relevant contraindications, adverse effects, hazards, interfering substances or devices, warnings and precautions. [21 CFR 812.5\(b\)](#)
- 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. [21 CFR 812.5\(a\)](#)

→ CCI/IRB Approval

The Sponsor is responsible for:

- Obtain CCI/IRB approval as a non-significant device study, and maintain CCI/IRB approval throughout investigation. 812.2(b)(ii)

→ Informed Consent Process and Documentation

The Sponsor is responsible for:

- Ensuring each participating investigator obtains and documents informed consent for each subject under their care. 812.2(b)(iii)
→ in accordance with [21 CFR 50, Protection of Human Subjects](#) and [21 CFR 56.109\(c\)](#)

**SPONSOR-INVESTIGATOR RESPONSIBILITIES
NON-SIGNIFICANT RISK INVESTIGATIONAL DEVICES**

→Comply with FDA requirements for monitoring the investigation

→ in accordance with [21 CFR 812.46, Monitoring Investigations](#) (see attached)

- 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 812.2\(b\)\(iv\)](#)
[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 non-significant risk devices, the sponsor must obtain CCI/IRB approval before resuming a terminated investigation. [21 CFR 812.46\(c\)](#)

→Maintain Study Records required by FDA

→ in accordance with [21 CFR 812.140\(b\)\(4\)\(5\), Records](#) (see attached).

All records must be accurate, complete and current. The sponsor of non-significant devices must maintain the following records, consolidated in one location and available for FDA inspection and review:

- The name and intended use of the device and the objectives of the investigation [21 CFR 812.140\(b\)\(4\)](#)
- A brief explanation of why the device is not a significant risk device [21 CFR 812.140\(b\)\(4\)](#)
- The name and address of each investigator [21 CFR 812.140\(b\)\(4\)](#)
- The name and address of each IRB that has reviewed the investigation [21 CFR 812.140\(b\)\(4\)](#)
- A statement of the extent to which the good manufacturing regulations will be followed in manufacturing the device: [21 CFR 820, Quality System Regulation](#) [21 CFR 812.140\(b\)\(4\)](#)
- Any other information required by the FDA [21 CFR 812.140\(b\)\(4\)](#)
- Records concerning adverse device effects (whether anticipated or unanticipated) and complaints. [21 CFR 812.140\(b\)\(5\)](#)
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**SPONSOR-INVESTIGATOR RESPONSIBILITIES
NON-SIGNIFICANT RISK INVESTIGATIONAL DEVICES**

→ Makes and Submits Reports as required by FDA

→ in accordance with [21 CFR 812.150\(1-3, 5-10\), Reports](#) (see attached).

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

- Unanticipated Adverse Device Effects:** 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. [21 CFR 812.150\(1\)](#)

Thereafter, the sponsor must submit follow-up reports as the FDA requests.
 - Withdrawal of IRB Approval:** 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. [21 CFR 812.150\(2\)](#)
 - Withdrawal of FDA approval:** 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. [21 CFR 812.150\(3\)](#)
 - Progress Reports:** At least yearly, the sponsor must submit a progress report to all reviewing IRBs [21 CFR 812.150\(5\)](#)
 - Recall and Device Disposition:** 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. [21 CFR 812.150\(6\)](#)
 - Final Report:** for NSR, the sponsor must submit a final report to all reviewing IRB's within 6 months after termination or completion. [21 CFR 812.150\(7\)](#)
 - Informed Consent:** 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. [21 CFR 812.150\(8\)](#)
 - Other:** upon request by a reviewing IRB or FDA, the sponsor must submit accurate, complete and current information about any aspect of the investigation. [21 CFR 812.150\(10\)](#)
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→ Managing Conflicts of Interests: Financial Disclosures

The Sponsor is responsible for:

- | | | |
|--------------------------|---|--------------|
| <input type="checkbox"/> | Maintaining current, complete and accurate records documenting the financial interests of all participating clinical investigators, including sponsor payments | 54.2
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'. | |

→ Ensures that Investigators Maintain Records as required by FDA

→ in accordance with [21 CFR 812.140\(a\)\(3\)\(i\), Records](#) (see attached).

- | | | |
|--------------------------|--|---|
| <input type="checkbox"/> | Investigators must maintain 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. | 21 CFR 812.140(a)(3)(1) |
| <input type="checkbox"/> | 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)(1) |
| | The case history for each individual shall document that informed consent was obtained prior to participation in the study. | |

→ Ensures that Investigators Submit Reports as required by FDA

→ in accordance with [21 CFR 812.150\(a\), Reports](#) (see attached).

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

- | | | |
|--------------------------|--|-----------------------------------|
| <input type="checkbox"/> | <u>Unanticipated adverse device effect</u> : 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) |
| <input type="checkbox"/> | <u>Withdrawal of IRB approval</u> : 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) |
| <input type="checkbox"/> | <u>Informed consent</u> : 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) |
| <input type="checkbox"/> | <u>Other</u> : 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) |

→ 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.
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- Select investigators qualified by training and experience to investigate the device and select monitors qualified by training and experience to monitor the investigational study.**
- in accordance with [21 CFR 812.43. Selecting Investigators and Monitors](#) (see attached)
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ADDITIONAL REFERENCES PROVIDED

1. CH/CCI Policy: Investigational Devices Online Reference: [[Click Here](#)]
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