DEVICE DEVELOPMENT PROCESS

FDA's Center for Devices and Radiological Health (CDRH) is responsible for regulating manufacturing and importation of medical devices sold in the United States. In addition, CDRH regulates radiation-emitting electronic products (medical and non-medical) such as lasers, x-ray systems, ultrasound equipment, microwave ovens and color televisions.

Is my device a medical device?

If a product is labeled, promoted or used in a manner that meets the following definitions in section 201(h) of the Federal Food Drug & Cosmetic (FD&C) Act it will be regulated as a medical device. A device is:

"an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is:

- intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals,

or

- intended to affect the structure or any function of the body of man or other animals, and which does not achieve any of it's primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes.

This definition provides a clear distinction between a medical device and other FDA regulated products such as drugs. If the primary intended use of the product is achieved through chemical action or by being metabolized by the body, the product is usually a drug. In cases where it is not clear whether a product is a medical device, Mr. Bryan H. Benesch, Device Determination Officer, Office of Compliance (bryan.benesch@fda.hhs.gov) of the Division of Small Manufacturers, International and Consumer Assistance (DSMICA) can assist in making a determination.

Device Classification

The Food and Drug Administration (FDA) has established classifications for approximately 1,700 different generic types of devices and grouped them into 16 medical specialties referred to as panels. Each of these generic types of devices is assigned to one of three regulatory classes (Class I, Class II and Class III) based on the level of control necessary to assure the safety and effectiveness of the device. The device classification defines the regulatory requirements for an approval of a new device. Regulatory control increases from Class I to Class II to Class III.

Device classification depends on the intended use of the device and also upon indications for use. In addition, classification is risk based, that is, the risk the device poses to the patient and/or the user is a major factor in the class it is assigned. Examples:
To find the classification of your device, as well as whether any exemptions may exist, you need to find the regulation number that is the classification regulation for your device. There are two methods for accomplishing this: go directly to the classification database and search for a part of the device name:

Once you have identified the correct classification regulation go to the device panel (medical specialty) to which the device belongs.

The search will provide you with Device Classification and appropriate CFR regulation. If the device is not classified, you can research similar devices on the FDA website (PMA and 510(k) databases) or use pre-IDE consultation for the FDA determination.

**PMA vs 510(k)**

Premarket approval (PMA) is the FDA process of scientific and regulatory review to evaluate the safety and effectiveness of Class III medical devices. Due to the level of risk associated with Class III devices, FDA needs to see a sufficient valid scientific evidence to assure that the device is safe and effective for its intended use(s). The content of PMA is similar to the NDA for new drugs, and contains manufacturing sections, pre-clinical laboratory studies and clinical investigations.

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*Class I devices*: elastic bandages, examination gloves, and hand-held surgical instruments.

*Class II devices*: powered wheelchairs, infusion pumps, and surgical drapes.

*Class III devices*: implantable pacemaker pulse generators and endosseous implants.
Some devices (from Class I or Class II) may be able to be approved under a different pathway colloquially called **510(k)**. The name refers to requirements outlined in section 510(k) of Food, Drug and Cosmetics Act. If the device is considered substantially equivalent to one or more similarly marketed devices (known as “predicate” devices). A claim of substantial equivalence does not mean the new and predicate devices must be identical. Substantial equivalence is established with respect to intended use, design and other parameters.

**Significant Risk vs Non-significant Risk (FDA Guidance)**

Devices used on human subjects to conduct investigations of safety and effectiveness are considered “Investigational Devices” (Section 520(g) of FDCA). See helpful FDA Guidance for determination of Significant vs Non-Significant Risk

Significant Risk (SR) device presents a potential for **serious risk of health, safety and welfare of a subject**, and:

- Intended to be used as an implant and
- Purported to support or sustain human life
- Is for a use of substantial importance in diagnosing, curing, mitigating or treating disease

Examples of SR devices include sutures, cardiac pacemakers, hydrocephalus shunts, and orthopedic implants. Conversely, non-significant risk (NSR) device study does not pose a significant risk to patients. Non-significant risk should not be confused with “minimal risk”, a term used by the FDA to classify studies. Examples of NSR devices include most daily-wear contact lenses and lens solutions, ultrasonic dental scalers, and foley catheters.

NSR device studies may commence without the FDA approval, based solely on the IRB approval. IRB has to make SR/NSR determination for every device study. The IRB acts as a surrogate overseer for the FDA. If NSR determination is made, the sponsor-investigator must follow abbreviated IDE requirements, which are, in essence, the same requirements as regular IDE only without FDA submission (**21 CFR 812.2 (b)**).

SR devices must meet all regulatory requirements set in **21 CFR 812**, including the requirement for approval by both IRB and the FDA before commencing the study. An investigational device exemption (**IDE**) is a regulatory submission to the CDRH. If approved, it allows the investigational device to be used in a clinical study in order to collect safety and effectiveness data.

**Investigational Device Exemption (IDE)**

**IMPORTANT**: the clinical study of a new indication for an already marketed device falls under the IDE regulation.

IDE requirements:
• Study approved by an institutional review board (IRB). If the study involves a significant risk device, the IDE must also be approved by FDA;
• informed consent from all patients obtained and documented;
• the device is labeled “CAUTION- Investigational Device. Limited to investigational use only”
• Sponsor-investigator complies with monitoring requirements
• Records and reports are maintained

Some studies may be exempt from the IDE regulations (21 CFR 812.2(c)):

1. a legally marketed device when used in accordance with its labeling,
2. a diagnostic device if it is:
   • noninvasive;
   • does not require an invasive sampling procedure that presents significant risk;
   • does not by design or intention introduce energy into a subject;
   • and is not used as a diagnostic procedure without confirmation by another medically established diagnostic product or procedure;
3. consumer preference testing…of legally marketed device(s)
4. a device intended solely for veterinary use;
5. a device shipped solely for research with laboratory animals

**Humanitarian Use Device**

HUD designation requests are the first step in seeking marketing approval of a HUD. The second step is a submission of a Humanitarian Device Exemption (HDE) application to the Center for Devices and Radiological Health (CDRH) or to the Center for Biologics Evaluation and Research (CBER).

HUD is a “medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in fewer than 4,000 individuals in the United States per year.” (21 CFR 814.39(n)). HUD designation request is described in this guidance. The request should be sent to:

Office of Orphan Products Development  
Food and Drug Administration  
10903 New Hampshire Avenue  
WO32-5271 Silver Spring, MD 20993

If the request is granted, the investigator proceeds with the submission of HDE (Investigational Device Exemption). An HDE is similar in both form and content to a premarket approval (PMA) application, but is exempt from the effectiveness requirements of a PMA. An HDE application is not required to contain the results of scientifically valid clinical investigations demonstrating that the device is effective for its intended purpose. The application, however, must contain sufficient information for
FDA to determine that the device does not pose an unreasonable or significant risk of illness or injury, and that the probable benefit to health outweighs the risk of injury or illness from its use, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment. Additionally, the applicant must demonstrate that no comparable devices are available to treat or diagnose the disease or condition, and that they could not otherwise bring the device to market.

**Emergency use of Unapproved device**

An unapproved medical device as a device that is utilized for a purpose, condition, or use for which the device requires, but does not have, an approved application for premarket approval (510(k)) or an approved IDE. Emergency use is permitted if the treating physician determines that:

- The patient has life-threatening condition that needs immediate treatment
- No generally acceptable alternative treatments exist
- Because of an immediate need there is no time to use existing procedures for CDRH approval

Next, the treating physician needs to undertake the following protective measures:

- An independent assessment by an uninvolved physician
- Informed consent from the patient or legal representative
- Approval of the IRB Chair
- Approval from the IDE sponsor, if any
- Prior FDA approval for shipment or emergency use of the investigational device is not required, but the use should be reported to FDA by the IDE sponsor via a supplement within 5 working days from the time the sponsor learns of the use

Note that if a physician, who is faced with an emergency situation contacts FDA to discuss his/her patient’s condition, the FDA will only act in an advisory role, rather than in an approving role. **The responsibility for making the decision as to whether the situation meets the emergency use criteria and whether the unapproved device should be used lies with the physician.**

For guidance on reporting emergency use to the FDA, see CDRH Guidance for the emergency use of unapproved medical devices.

**Compassionate use of Investigational Devices**

This type of use is NOT an emergency use. This request to use investigational device in mitigation, diagnosis and treatment of serious diseases requires an IDE Supplement (see below). The sponsor or investigator has to submit the protocol for use of the device in a single patient or a group of patients. In order to permit this use, CDRH will review the following information:

- No comparable alternative treatment exists
- Sufficient evidence of safety
• Clinical use will not interfere with ongoing clinical investigations

**Treatment Use**

This type of use is NOT an emergency use. This request to use investigational device in mitigation, diagnosis and treatment of serious diseases requires a Treatment IDE Submission. If approved, treatment IDE enables a wider group of patients to receive the investigational device for the same indication as it is being studied under the sponsor IDE. Treatment IDE will remain open even after the sponsor trial has been completed. The following provision have to be met:

• Device is investigated in a controlled clinical trial under IDE for the same use
• Sponsor is actively pursuing market approval
• No comparable alternative treatment exists
• Clinical use will not interfere with ongoing clinical investigations
• Sufficient evidence of safety and effectiveness

**References:**

Arbit, H.M. How to prepare an Investigational Device Exemption (IDE) as a Sponsor-Investigator. SoCRA Source, November 2009, p.58.

How to file an IDE

If the IRB determined that the approval of the protocol with investigational device, the investigator will prepare and submit the IDE application to the FDA. The IDE submission includes:

- Cover Letter
- Application

Content of the Cover Letter:

1. A statement that this is an original IDE application
2. Device information: a brief overview of the device
3. Sponsor-investigator contact information;
4. Device manufacturer information;
5. Applicant information (who submits this application);
6. Other relevant information (e.g. prior discussions with the FDA)

Content of an IDE Application:

1. Table of Contents
2. Report of prior investigations (including animal work)
3. Investigational plan
4. Risk analysis (in table format)
5. Description of the device
6. Monitoring procedures
7. Manufacturing information
8. Sponsor-investigator information, including CV;
9. IRB information;
10. Sales information;
11. Environmental impact statement
12. Labeling
13. Informed Consent materials
14. Other information as pertinent

The template is provided in Appendix 1. The template expands each section in greater details.
**Suggested Format For IDE Submissions**

- Use paper with nominal dimensions of 8 1/2" by 11".
- Use at least a 1 1/2" wide left margin to allow for binding into jackets.
- Use 3-hole punched paper to allow for binding into jackets.
- Clearly and prominently identify submission as original IDE application or, for additional submissions to an IDE application, clearly identify the FDA assigned document number (e.g., G960000) and the reason for the submission (e.g., amendment or supplement) and the type of submission (e.g., Response to FDA letter; Addition of New Institution, etc.).
- Make 3 identical copies of each submission
- Unless the IDE sponsor has provided authorization in writing for another person to submit information on the sponsor's behalf, only the IDE sponsor may amend, supplement, or submit reports to the IDE.
- Sequentially number the pages, providing a detailed table of contents, and use tabs to identify each section.

**Where to mail?**

Mail three copies to:

Food and Drug Administration  
Center for Devices and Radiological Health  
Document Mail Center - WO66-G609  
10903 New Hampshire Avenue  
Silver Spring, Maryland 20993-0002

**Approvals and Disapprovals**

In 2011 the FDA issued a [Guidance on CDRH process](#) for Approval and Disapproval of IDEs. The new Guidance provides provide for three FDA actions on IDE applications:

- Approval
- Approval with Conditions
- Disapproval

The decision is made within 30 days upon receiving the IDE application.

**Supplemental IDE Applications**

Any changes in the Investigational Plan should be approved by the FDA and, when appropriate, IRB, prior to implementing any change to a previously accepted Investigational Plan. The following types of protocol changes would require an approved IDE Supplement because they are likely to have a significant effect on the scientific soundness of the trial design and/or validity of the data resulting from the trial:

- change in indication,
• change in type or nature of study control,
• change in primary endpoint,
• change in method of statistical evaluation, and
• early termination of the study (except for reasons related to patient safety).

In addition, FDA believes that expanding the study by increasing either the number of investigational sites or the number of study subjects participating in a clinical investigation affects the rights, safety, and welfare of the subjects. Therefore, the study may not be expanded without submission and approval of an IDE supplement.

The IDE supplement should be identified with the IDE number on the cover sheet and submitted in triplicate. The outside wrapper of the submission should identify the contents as "Supplemental IDE."

Some exceptions from prior IRB and FDA approval are allowed in the following circumstances

1. **Emergency use.** If PI deviates from the investigational plan to protect the life or physical well-being of a subject in an emergency. Such deviations should be reported to the IRB promptly after its occurrence, and to the FDA within 5-working days after the sponsor becomes aware of it.

2. **Certain changes to the device.** Advanced IRB notification is not required if the changes do not constitute a significant change in design or basic operation and are made in response to information gathered during the course of an investigation. Examples include: creditable data generated under the device control procedures (21 CFR Sec. 820.30), preclinical/animal testing, peer reviewed published literature, and clinical information gathered during a clinical trial or marketing. For a developmental or manufacturing change to a device, the “**Notice of IDE Change**” shall include:
   
   (i) **a summary of the relevant information** gathered during the course of the investigation upon which the change was based;

   (ii) **a description of the change** to the device or manufacturing process (i.e., cross-referenced to the appropriate sections of the original device description or manufacturing process); and

   (iii) if design controls were used to assess the change, a statement that **no new risks were identified by appropriate risk analysis** and that the verification and validation testing, as appropriate, demonstrated that the design outputs met the design input requirements. If another method of assessment was used, the Notice shall include a summary of the information, which served as the creditable information supporting the change.

3. **Certain clinical protocol changes** that do not affect (i) the validity of the data or information resulting from the completion of the approved protocol, or the relationship of the likely patient risk to benefit ratio relied upon to approve the protocol; (ii) the scientific soundness of the investigational plan; or (iii) the rights, safety, or welfare of human subjects
involved in the investigation. For a clinical protocol change, the “Notice of IDE Change” need to include:

(i) a description of the change (cross-referenced to the appropriate sections of the original protocol);

(ii) an assessment supporting the conclusion that the change does not have a significant impact on the study design or planned statistical analysis; and

(iii) a summary of the information that served as the creditable information supporting the sponsor’s determination that the change does not affect the rights, safety, or welfare of the subjects.

4. If changes will be submitted in the annual report. A sponsor may make minor changes to an Investigational Plan without prior FDA approval; provided that the respective changes are reported in the annual progress report for the IDE (see Progress Reports). These minor changes to the purpose of the study, risk analysis, monitoring procedures, labeling, informed consent materials, and IRB information may not affect (i) the validity of the data or information resulting from the completion of the approved protocol, or the relationship of the likely patient risk to benefit ratio relied upon to approve the protocol; (ii) the scientific soundness of the investigational plan; or (iii) the rights, safety, or welfare of human subjects involved in the investigation.

IDE Safety Reports

The Principal Investigator notifies the FDA and all participating investigators in a written IDE safety report of any Unanticipated Adverse Device Effect. The report is also provided to the Sponsor and to the reviewing IRB as soon as possible, but no later than 10 working days after the Investigator first learns of the effect. If an investigator is the sponsor-investigator of the investigational device (IDE holder), the sponsor-investigator must submit Unexpected Device Effect to the FDA per FDA regulations CFR 21 Part 812.150. This report also should be submitted no later than 10 working days. Thereafter the sponsor-investigator shall submit such additional reports concerning the effect as FDA requests.

On an annual basis as part of the update to the study IDE, the Principal Investigator need to submit to the FDA and the IRB:

- A summary of all IDE unanticipated Adverse Device Effect reports submitted during the past year.

- A list of all subjects who died during the participation in the investigation listing cause of death for each.

- A list of subjects who dropped out during the course of the investigation in association with any unanticipated device effect, whether or not thought to be device related.
• IDE Unexpected Device Effect reports should include the following information: Subject identification number and initials, investigator’s name and medical facility, subject’s date of birth, gender, ethnicity, date of implant (if applicable), date/time of onset, a complete description of the event, severity, duration, actions taken and event outcome, e.g. date of resolution or death.

Billing for Investigational devices and procedures during clinical trials

Under 21 CFR 812.7 (b), a sponsor, investigator, or any person acting for or on behalf of a sponsor or investigator shall not 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. This means that in some instances it is possible to bill insurance for investigational device itself. In most cases, however, billing for the device itself may not be possible when the device is Category A or provided free of charge.

For all device clinical studies that include patient services billable to insurance, the sponsor-investigator must submit paperwork to the California Medicare Intermediary, Palmetto GBA, to determine whether the billable expanded costs will be covered for this study. Expanded costs include placement of the investigation device (e.g., implantation), clinically appropriate monitoring and diagnosis, mitigation and treatment of complications.

Please see flowchart below.
INVESTIGATIONAL DEVICE EXEMPTION
APPLICATION

IDE Title

Name of Sponsor Investigator, MD
  X Professor, Department
University of California, Davis

Date of Submission
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Name and the address of the sponsor
Report of Prior Investigations

In this section, sponsor should provide a complete report of prior investigations of the device.

General

The report of prior investigations shall include reports of all prior clinical, animal, and laboratory testing of the device and shall be comprehensive and adequate to justify the proposed investigation.

Specific Content

a) A bibliography of all publications, whether adverse or supportive, that are relevant to an evaluation of the safety or effectiveness of the device, copies of all published and unpublished adverse information, and, if requested by an IRB or FDA, copies of other significant publications.

b) A summary of all other unpublished information (whether adverse or supportive) in the possession of, or reasonably obtainable by, the sponsor that is relevant to an evaluation of safety or effectiveness of the device.

c) If information on nonclinical laboratory studies is provided a statement that all such studies have been conducted in compliance with applicable requirements in the good laboratory practice (GLP) regulation in 21 CRF part 58. If the study was not conducted in compliance with such regulations, a brief statement of the reason for the non compliance.
Investigational Plan

At the beginning of this section, sponsor can give a brief overview of the investigation plan, logic and need for this trial, is it a single-site study, what are the end points etc..

Purpose

The name and intended use of the device and the objectives and duration of the investigations.
Protocol

A written protocol should describe the methodology to be used and an analysis of the protocol demonstrating that the investigation is scientifically sound. Protocol should include objectives and the hypothesis of the trial. Also describe the type of trial (i.e., controlled/open, double-blind/single/blind, etc.). Describe in details how the trial will be conducted and analytical methods that will be used to evaluate the study. If case report forms (CFR) will be used, please attach it to the protocol.
# Risk Analysis

A description and analysis of all increased risks to which subject will be exposed by the investigation; the manner in which these risk will be minimized; a justification for the investigation; and a description of the patient population including the number, age, sex, and condition.

This section is often underdeveloped by sponsor-investigators. Below is a partial example of the risk section for an implantable device. This section may take many pages.

<table>
<thead>
<tr>
<th>Deficiency</th>
<th>Potential Hazard</th>
<th>Resultant Harm</th>
<th>Risk Evaluation Discussion</th>
<th>Mitigation Strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. 5.a.</td>
<td>Surgical Procedure</td>
<td>Pain</td>
<td>The device is placed through a small, minimally invasive skin incision under topical anesthesia. The patient will be brought into the minor procedure room and placed supine. The neck will be prepped and draped in the usual sterile fashion.</td>
<td>Pre-operative clearance from the anesthesia service; routine surgical sedation; notch will be infiltrated with 1% lidocaine.</td>
</tr>
<tr>
<td>2. 5.a.</td>
<td>Surgical Procedure</td>
<td>Bleeding</td>
<td>The implant is secured to the anterior rim of the cricoid cartilage five 2-0 nylon sutures.</td>
<td>Minimally invasive 2 cm skin incision.</td>
</tr>
<tr>
<td>3. 5.a.</td>
<td>Surgical Procedure</td>
<td>Infection</td>
<td>There is increased risk with this surgical procedure as with any other surgical procedure.</td>
<td>Pre-operative prophylactic antibiotics with 1G Cefazolin. Prophylactic antibiotics administered per patients existing PEG tube for 10 days.</td>
</tr>
<tr>
<td>4. 5.a. 21.a. 21.b.</td>
<td>Device dropped or deemed unsterile in some manner</td>
<td>Delay or abort procedure</td>
<td>(Flash sterilization will not be allowed) Additional sterile devices will be available to prevent procedure termination with minimal delay.</td>
<td></td>
</tr>
<tr>
<td>5. 21.a.</td>
<td>Surgical Procedure</td>
<td>Infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. 21.b.</td>
<td>Surgical Procedure</td>
<td>Infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>5.a.</td>
<td>Implanted device</td>
<td>Device rejection</td>
<td></td>
</tr>
<tr>
<td>----</td>
<td>------</td>
<td>-----------------</td>
<td>------------------</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>As with any implant, there is a risk of implant infection and rejection. Titanium is highly biocompatible and magnetic resonance imaging (MRI) compatible. Titanium implants have precedent in head and neck surgery and are commonly used in traumatic and oncologic reconstruction.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>This risk has been included on the patient consent form. Device constructed from ASTM F67-00, grade 2 - unalloyed titanium for surgical implant application. To minimize patient harm associated with rejection, patients will be closely monitored every two weeks for the first two months after implantation. They will then be monitored monthly until two years after device implantation. The implant will be removed if there is any sign of infection that does not resolve with antibiotics or any sign of abscess formation, tissue or cartilage damage, or implant rejection.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>6.</th>
<th>5.b.iii</th>
<th>Implanted device</th>
<th>Seroma</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Titanium is highly biocompatible and magnetic resonance imaging (MRI) compatible. Titanium implants have precedent in head and neck surgery and are commonly used in traumatic and oncologic reconstruction.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>This risk has been included on the patient consent forms.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>7.</th>
<th>5.b.iv</th>
<th>Implanted device</th>
<th>Erosion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Titanium is highly biocompatible and magnetic resonance imaging (MRI) compatible. Titanium implants have precedent in head and neck surgery and are commonly used in traumatic and oncologic reconstruction.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>This risk has been included on the patient consent forms.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>8.</th>
<th>5.b.v</th>
<th>Implanted device</th>
<th>Allergic response</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Device constructed from ASTM F67-00, grade 2 - unalloyed titanium for surgical implant application.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>9.</th>
<th>17.</th>
<th>Endotoxins</th>
<th>Adverse reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Titanium is highly biocompatible and magnetic resonance imaging (MRI) compatible. Titanium implants have precedent in head and neck surgery and are commonly used in traumatic and oncologic reconstruction.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Labeled non-pyrogenic Endotoxin testing less than 0.03EU per QCTL 2300.00 Endotoxin Testing</td>
</tr>
</tbody>
</table>
**Description of Device**

*A description of each important component, ingredient, property and principle of operation of the device and of each anticipated change in the device during the course of investigation*

**Monitoring Plan**

*The sponsor’s written procedures for monitoring the investigation and the name and address of any monitor.*

The ICH Good Clinical Practices Guidelines describe how to monitor the study. Although it applies to drug studies, it also makes sense for device studies *(http://ichgcp.net/518-monitoring)*. The Investigator must develop a monitoring plan, the written procedure for monitoring the study. This section should also include the name, address and qualifications of the monitor.
Manufacturing Information

A description of the methods, facilities, and controls used for the manufacture, processing, storage, and, where appropriate, installation of the device, in sufficient details so that a person generally familiar with good manufacturing practice can make a knowledgeable judgment about the quality control used in the manufacture of the device.

This section often presents the most difficulties for Sponsor-Investigators. We recommend subcontracting the design and manufacturing to an outside party capable of delivering the FDA package for IDE.

Common deficiencies with design and manufacture Section

- **design:** Inadequate characterization or description of the device and its operation due to inadequate or omitted:
  - Design/engineering drawing of device
  - Rationale for device design
  - Device and performance specifications
  - Description of materials (including biocompatibility information)
  - Description of function - how does device and/or components/subsystems work together to achieve desired function
  - Validation testing for subsystems and main system

- **manufacture:** Inadequate or missing description of the controls used to ensure that the devices are produced consistently and as designed.

What are Standards and Controls?

Many domestic and international consensus standards address aspects of safety and/or effectiveness relevant to medical devices. CDRH believes that conformance with recognized consensus standards can support a reasonable assurance of safety and/or effectiveness for many applicable aspects of medical devices. Therefore, information submitted on conformance with such standards should have a direct bearing on safety and effectiveness determinations made during the review of IDEs. When an FDA-recognized consensus standard exists it serves as a complete performance standard for a specific medical device. In these cases, the standard may include specific acceptance criteria that describe the relevant performance characteristics of that specific medical device. Conformance and declarations of conformance to any recognized consensus standard that clearly spells out acceptance criteria is a very effective use of standards in the premarket process.

Some examples of standards for medical devices:
ISO 14937 *Sterilization of health care products - General requirements for characterization of a sterilizing agent and the development, validation and routine control of a sterilization process for medical devices*

DIN-EN-ISO-10993-15 *Biological evaluation of medical devices. Identification and quantification of degradation products from metals and alloys*

It is difficult for an academic sponsor-investigator to know and understand all standards used in development of medical devices. The following table summarizes the most common standards that may need to be considered:

<table>
<thead>
<tr>
<th>Standard Number</th>
<th>Standard Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>IEC 60601-1:1995</td>
<td>Medical Electrical Equipment - Part 1: General Requirements for Basic Safety and Essential Performance</td>
</tr>
<tr>
<td>IEC 60601-1:2007</td>
<td>Medical Electrical Equipment - Part 1: General Requirements for Basic Safety and Essential Performance</td>
</tr>
<tr>
<td>IEC 60601-2-37:2007</td>
<td>Particular Requirements for the Safety of Ultrasonic Medical Diagnostic and Monitoring Equipment</td>
</tr>
<tr>
<td>IEC 60601-1-4:2000</td>
<td>Medical electrical equipment – Part 1-4: General requirements for safety – Collateral Safety - Programmable electrical medical systems</td>
</tr>
<tr>
<td>IEC 61000-3-2:2008</td>
<td>Electromagnetic Compatibility (EMC) - Part 3-2: Limits - Limits for Harmonic Current Emissions (equipment input current &lt;= 16 A per phase)</td>
</tr>
<tr>
<td>IEC 61000-3-3:2008</td>
<td>Electromagnetic Compatibility (EMC) - Part 3-3: Limits – Limitation of Voltage Changes, Voltage Fluctuations and Flicker in Public Low-voltage Supply Systems, for Equipment with Rated Current = 16 A Per Phase and not Subject to Conditional Connection</td>
</tr>
<tr>
<td>IEC 61000-4-4:2007</td>
<td>Electromagnetic Compatibility (EMC) - Part 4-4: Testing and Measurement Techniques - Electrical Fast Transient/burst Immunity Test</td>
</tr>
<tr>
<td>IEC 61000-4-6:2008</td>
<td>Electromagnetic Compatibility (EMC) - Part 4-6: Testing and Measurement Techniques - Immunity to Conducted Disturbances, Induced by Radio-frequency Fields</td>
</tr>
<tr>
<td>IEC 61000-4-8:2001</td>
<td>Electromagnetic Compatibility (EMC) - Part 4-8: Testing and Measurement Techniques - Power Frequency Magnetic Field Immunity Test</td>
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<tr>
<td>ISO-10993-5:1999</td>
<td>Biological Evaluation of Medical Devices - Part 5: Tests for In Vitro Cytotoxicity</td>
</tr>
<tr>
<td>Standard Number</td>
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</tr>
<tr>
<td>-----------------</td>
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<tr>
<td>ISO-10993-7:2008</td>
<td>Biological Evaluation of Medical Devices - Part 7: Ethylene Oxide Sterilization Residuals</td>
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<tr>
<td>ISO 10993-10:2006</td>
<td>Biological Evaluation of Medical Devices - Part 10: Tests for Irritation and Delayed-type Hypersensitivity</td>
</tr>
<tr>
<td>ISO 11135:2008</td>
<td>Medical Devices - Validation and Routine Control of Ethylene Oxide Sterilization</td>
</tr>
<tr>
<td>ISO 11607-1:2006</td>
<td>Packaging of Terminally Sterilized Medical Devices - Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems</td>
</tr>
<tr>
<td>ISO 11607-2:2006</td>
<td>Packaging for Terminally Sterilized Medical Devices - Part 2: Validation Requirements for Forming, Sealing and Assembly Processes</td>
</tr>
<tr>
<td>ISO 13485:2003</td>
<td>Quality Management System - Medical Device - System Requirements for Regulatory Purposes</td>
</tr>
<tr>
<td>ISO 14971:2003</td>
<td>Medical devices – Application of Risk Management to Medical Devices (Note: All new devices shall use the 2007 version of this standard below)</td>
</tr>
<tr>
<td>ISO 14971:2007</td>
<td>Medical devices – Application of Risk Management to Medical Devices</td>
</tr>
<tr>
<td>ISO 15223-1:2007</td>
<td>Medical devices — Symbols to be used with medical device labels, labeling, and information to be supplied</td>
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<tr>
<td>+A1:2008</td>
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<tr>
<td>CSA C22.2 60601-1:2008</td>
<td>Part 1: General Requirements for Basic Safety &amp; Essential Performance, Medical Electrical</td>
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<tr>
<td>BS EN 1041:2008</td>
<td>Information Supplied by the Manufacturer with Medical Devices</td>
</tr>
<tr>
<td>BS EN 550:2007</td>
<td>Sterilization of Medical Devices. Validation and Routine Control of Ethylene Oxide Sterilization</td>
</tr>
<tr>
<td>BS EN 556-1:2001</td>
<td>Sterilization of Medical Devices - Requirements for Devices to be Designed “STERILE” - Part 1: Requirements for Terminally Sterilized Medical Devices</td>
</tr>
<tr>
<td>BS EN 980:2008</td>
<td>Symbols for Use in the Labeling of Medical Devices</td>
</tr>
<tr>
<td>BS EN 60601-1-2:2007</td>
<td>Medical Electrical Equipment, General Requirements for Basic Safety &amp; Essential Performance</td>
</tr>
<tr>
<td>BS EN 60601-1:2006</td>
<td>Medical Electrical Equipment - Part 1: General Requirements for Basic Safety &amp; Essential Performance, Medical Electrical</td>
</tr>
<tr>
<td>BS EN 55011:2007</td>
<td>Limits and Methods of Measurement of Radio Disturbance Characteristics of Industrial, Scientific and Medical (ISM) Radio-frequency Equipment</td>
</tr>
<tr>
<td>BS EN 61000-3-2:2000</td>
<td>Electromagnetic Compatibility (EMC), Part 3: Limits, Section 2: Limits for Harmonic Current Emissions (equipment input current ≤16 A per phase)</td>
</tr>
<tr>
<td>BS EN 61000-3-3:2001</td>
<td>Electromagnetic compatibility (EMC), Part 3: Limits, Section 2: Limitation of Voltage Fluctuations and Flicker in Low-voltage Supply Systems for Equipment with Rated Current ≤16 A</td>
</tr>
<tr>
<td>BS EN 61000-4-2:2001</td>
<td>Testing and Measurement Techniques – Electrostatic Discharge Immunity Test</td>
</tr>
<tr>
<td>BS EN 61000-4-4:2004</td>
<td>Testing and Measurement Techniques – Electrical Fast Transient/Burst Immunity Test</td>
</tr>
<tr>
<td>BS EN 61000-4-5:2006</td>
<td>Testing and Measurement Techniques – Electromagnetic Compatibility</td>
</tr>
<tr>
<td>Standard Number</td>
<td>Standard Name</td>
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<tr>
<td>BS EN 61000-4-6:2007</td>
<td>Test and Measurement Techniques – Immunity to Conducted Disturbances, Induced by Radio Frequency Immunity</td>
</tr>
<tr>
<td>BS EN 61000-4-8:2001</td>
<td>Test and Measurement Techniques - Power Frequency Magnetic Field Immunity Test</td>
</tr>
<tr>
<td>BS EN 61000-4-11:2004</td>
<td>Test and Measurement Techniques - Voltage Dips, Short Interruptions and Voltage</td>
</tr>
<tr>
<td>UL 60601-1:2006</td>
<td>Medical Electrical Equipment - Part 1: General Requirements for Safety</td>
</tr>
<tr>
<td>NEMA UD2-2004</td>
<td>Acoustic Output Measurement Standard for Diagnostic Ultrasound Equipment</td>
</tr>
<tr>
<td>NEMA UD3-2004</td>
<td>Standard for Real-time Display of Thermal &amp; Mechanical Indices on Diagnostic Ultrasound Equipment</td>
</tr>
<tr>
<td>IEC 60601-1-6:2006</td>
<td>Medical electrical equipment - Part 1-6: General requirements for basic safety and essential performance - Collateral standard: Usability</td>
</tr>
<tr>
<td>IEC 62366:2007</td>
<td>Medical devices - Application of usability engineering to medical devices</td>
</tr>
</tbody>
</table>

If a recognized standard describes a test method, but does not specify a performance limit or pass/fail criteria, the manufacturer should submit the test results.

Submissions should include clear documentation of the extent of conformance. FDA recommends that submissions include a matrix that identifies all sections of the consensus standard with an indication of “yes,” “no,” or “not applicable” to indicate conformance. A submission should further specify acceptance criteria that are relevant to the specific medical device and should identify any deviations to the consensus standard. With adequate justification for the acceptance criteria and for any deviations from the standard, FDA can usually accept a declaration of conformance without the need to review test protocols and analyze the raw data.

A declaration of conformity to a recognized consensus standard should do the following:

- identify the applicable recognized consensus standards that were met
- specify, for each consensus standard, that all requirements were met, except for inapplicable requirements or deviations as described below
- identify, for each consensus standard, any way(s) in which the standard may have been adapted for application to the device under review, e.g., identify which of an alternative series of tests were performed
- identify, for each consensus standard, any requirements that were not applicable to the device
- specify any deviations from each applicable standard that was applied (e.g., deviations from international standards that are necessary to meet U.S. infrastructure conventions such as the National Electrical Code (ANSI/NFPA 70)
- specify what differences exist, if any, between the tested device and the device to be marketed and justify the use of test results in these areas of difference
• provide the name and address of each laboratory or certification body that was involved in determining the conformance of the device with the applicable consensus standards and a reference to any accreditations of those organizations, if a test laboratory or certification body was employed

Consensus Standards database is maintained by CDRH staff: [http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm)

The actual standards can be purchased from: [http://www.document-center.com/home.cfm](http://www.document-center.com/home.cfm)

Sometimes the relevant standards can be identified using [Product Classification Database](http://www.document-center.com/home.cfm):

<table>
<thead>
<tr>
<th>Device</th>
<th>Transducer, Blood-Pressure, Extravascular, Extravascular blood pressure transducer, Cardiovascular, Cardiovascular, DRS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regulation Description</td>
<td>510(k)</td>
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<tr>
<td>Regulation Medical Specialty</td>
<td>870.2650</td>
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<tr>
<td>Review Panel</td>
<td>2</td>
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<tr>
<td>Product Code</td>
<td>TRLC Product Code Report</td>
</tr>
<tr>
<td>Total Product Life Cycle (TPLC)</td>
<td>No</td>
</tr>
<tr>
<td>GMP Exempt?</td>
<td>No</td>
</tr>
</tbody>
</table>

**Recognized Consensus Standards**

- IEC 60601-2-34 (2000-10) Medical electrical equipment - Part 2-34: Particular requirements for the safety, including essential performance, of invasive blood pressure monitoring equipment

**Third Party Review**

- Eligible for Accredited Persons Expansion Pilot Program

**Accredited Persons**

- Dekra Certification B.V.
- Intertek Testing Services
- Regulatory Technology Services, LLC
- TÜV Rheinland Of North America, Inc.
- TÜV Sud America Inc.
- Underwriters Laboratories, Inc.

**Quality Systems**

FDA 21 CFR Part 820, also known as the Quality System Regulation (QSR) outlines Current Good Manufacturing Practice cGMP regulations that govern the methods used in, and the facilities and controls used for, the design, manufacture, packaging, labeling, storage, installation, and servicing of all finished devices intended for human use. These requirements are meant to ensure that medical devices are safe and
effective. Medical device manufacturers undergo FDA inspections to ensure FDA 21 CFR Part 820 compliance.

CDRH maintains an extensive Medical Device Quality Systems Manual, which covers the Quality System regulation and the basic Good Manufacturing Practices (GMP) requirements that all manufacturers and distributors must consider when they plan to manufacture medical devices, including medical device kits, trays or packs, for distribution in the United States. Model procedures and sample forms are also included in the manual to assist manufacturers.

When choosing a manufacturer for the investigational device, sponsor-investigator needs to ensure that the manufacturer meets the ends points outlined in the Manual.

Sponsor –investigator typically closely participates in the Design Controls:

**Design input** means the physical and performance requirements of a device that are used as a basis for device design [21 CFR 820.3(f)]. Design input also includes requirements for labeling, packaging, manufacturing, installation, maintenance and servicing. The final device specifications should cover ALL of the device characteristics. At the end, the design input requirements need to be documented, reviewed and approved by a designated individual(s), typically the inventor (PI).

**Design review** means a documented, comprehensive, systematic examination of a design to evaluate the adequacy of the design requirements, to evaluate the capability of the design to meet these requirements, and to identify problems. Typically, design review requires pilot production and validation of initial production units or lots. Subsequent activities are usually design changes. As the development program progresses, the reviews should cover production documentation such as assembly drawings, manufacturing instructions, test specifications, test procedures, etc. Design review is often done by committees in formal meetings. The end of the total design effort has not been reached until it is known that the initial production devices, when transferred to production and produced per the device master record, meet all of the current design specifications

**Design output** (21 CFR 820.3(g) means the results of a design effort at each design phase and at the end of the total design effort. The finished design output is the basis for the device master record. The total finished design output consists of the device, its packaging and labeling, and the device master record. Device master record (DMR) is a compilation of records containing the procedures and specifications for a finished device. This stage includes purchasing of components (with documentation of purchase and validation of the components). Acceptance criteria should be established for each component. Design output is documented, reviewed, and approved before release by a committee

**Design verification and validation** [21 CFR 820.30(f)] confirms that the design output meets the design input requirements. The results of the design verification, including identification of the design, method(s), the date, and the individual(s) performing the verification, are documented in the DHF. Design validation means establishing by objective evidence that device specifications conform with user needs and intended use(s). Verification means confirmation by examination and provision of objective
evidence that specified requirements have been fulfilled. Verification and validation are done according to a written protocol(s). The protocol(s) should include defined conditions for the testing. The protocol(s) should be approved before being used. Test protocol(s) may not be perfect for a new design. Therefore, the designers and other verification personnel carefully annotate any ongoing changes to a protocol. The original design of devices and any subsequent changes should be verified by appropriate and formal laboratory, animal, and in vitro testing. Risk analysis should be conducted to identify possible hazards associated with the design.

**Design transfer** should assure that the section of the design being transferred:

- meets input requirements;
- contains acceptance criteria, where needed;
- contains design parameters which have been appropriately verified;
- is complete and approved for use;
- is fully documented in the DMR or contains sufficient design output information to support the generation of remaining DMR documents; and
- is placed under change control if not already done.

**Design changes** to a device element are controlled per 820.30(i) *Design Changes*, which states that: each manufacturer shall establish and maintain procedures for the identification, documentation, validation or where appropriate verification, review, and approval of design changes before their implementation.

**Design history file** (DHF) means a compilation of records, which describes the design history of a finished device [820.3(e)]. The design controls in 820.30(j) require that each manufacturer shall establish and maintain a DHF for each type of device. Typical documents that may be in, or referenced in, a DHF are listed below:

- design plans;
- design review meeting information;
- sketches;
- drawings;
- procedures;
- photos;
- engineering notebooks;
- component qualification information;
- biocompatibility (verification) protocols and data;
- design review notes;
- verification protocols and data for evaluating prototypes;
- validation protocols and data for initial finished devices;
- contractor / consultants information;
- parts of design output/DMR documents that show plans were followed; and
- parts of design output/DMR documents that show specifications were met.

### ITEMS THAT MAY APPEAR IN A DEVICE SPECIFICATION

<table>
<thead>
<tr>
<th>ITEMS</th>
<th>EXAMPLES</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Name of Product</strong></td>
<td>a. Trade name  d. Chemical name</td>
</tr>
<tr>
<td>b. Trademark</td>
<td>e. Official name</td>
</tr>
<tr>
<td>c. Generic name</td>
<td>f. Common name</td>
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<tr>
<td><strong>2. Performance Characteristics</strong></td>
<td>a. Description/Intended use  e. Contraindications</td>
</tr>
<tr>
<td>b. Accessories</td>
<td>f. Input/Output requirements</td>
</tr>
<tr>
<td>c. Functional parameters</td>
<td>g. Human interface</td>
</tr>
<tr>
<td>d. Limitations</td>
<td>h. Other</td>
</tr>
<tr>
<td><strong>3. Classification</strong></td>
<td>a. Regulatory  c. Functional</td>
</tr>
<tr>
<td>b. Commercial</td>
<td>d. Other</td>
</tr>
<tr>
<td><strong>4. Physical Characteristics</strong></td>
<td>a. Weight  e. Consistency</td>
</tr>
<tr>
<td>b. Size</td>
<td>f. Packaging</td>
</tr>
<tr>
<td>c. Color</td>
<td>g. Power requirements</td>
</tr>
<tr>
<td>d. Form/Shape</td>
<td>h. Other</td>
</tr>
<tr>
<td><strong>5. Environmental Limitations</strong></td>
<td>a. Operating temperature range  f. Moisture protection</td>
</tr>
<tr>
<td>b. Storage temperature range</td>
<td>g. Pressure, altitude limits</td>
</tr>
<tr>
<td>c. Vibration and shock range</td>
<td>h. Electromagnetic interference</td>
</tr>
<tr>
<td>d. Voltage range</td>
<td>i. Electrical transients</td>
</tr>
<tr>
<td>e. Humidity range</td>
<td>j. Shelf life/Other</td>
</tr>
<tr>
<td><strong>6. Important Components</strong></td>
<td>a. Active ingredients  f. Service labeling</td>
</tr>
<tr>
<td>b. Major subsystems</td>
<td>g. Components/items supplied by user</td>
</tr>
<tr>
<td>c. Diagnostic kit materials</td>
<td>h. Software</td>
</tr>
<tr>
<td>d. Accessories</td>
<td>i. Periodic Warranty/Other</td>
</tr>
<tr>
<td>e. Labeling</td>
<td></td>
</tr>
<tr>
<td>b. Electrical</td>
<td>f. Periodic testing</td>
</tr>
<tr>
<td>c. Thermal</td>
<td>g. Maintenance</td>
</tr>
<tr>
<td>d. Mechanical sharp, moving parts</td>
<td>h. Other</td>
</tr>
</tbody>
</table>
DOCUMENTS THAT MAY APPEAR IN A DEVICE MASTER RECORD

1.0 Device Master Record Index (Table of contents)
2.0 Device Specifications
   (Device specifications are described in the chapter text.)
3.0 Manufacturing Information
3.1 Index
   (Optional. See 1.0 above for total table of contents.)
3.2 Formulation or top assembly drawing
3.3 List of components
   1. List of ingredients (including grade or type)
   2. Bill of materials (i.e., component list usually arranged by subassembly or other
      sub-product level or by process steps)
   3. Formula
3.4 Procurement documentation
   1. Specifications
   2. Drawings
   3. Certificate of compliance requirements
   4. Supplier Assessment procedures
3.5 Device documentation
   1. Fabrication drawings
   2. Surface finish procedures
   3. Subassembly drawings
   4. Wiring and piping diagrams
   5. Assembly procedures
   6. Assembly drawings
   7. Reference documentation
      a. Wiring and piping schematics
      b. Test specifications
   8. Sub-batch procedures
   9. Blending or mixing procedures
   10. Solution procedures
   11. Final formulation procedures
   12. Software packages
3.6 Precautions and special notations
   1. Apparel
   2. Cleaning
   3. Storage conditions
   4. Filling, mixing conditions
   5. Hazards and safety precautions
3.7 Equipment, lines, and procedures
   1. Process lines
   2. Assembly lines
   3. Vessels
   4. Mixers, tools
   5. Molds
   6. Machine maintenance procedures
   7. Calibration procedures
   8. Setup procedures
   9. Operating procedures
   10. Process flow charts
3.8 Sterilization procedures
   1. Procedures for ethylene oxide, radiation, filtration, steam, etc.
   2. Handling and flow procedures
   3. Cycle parameter specifications
4. Diagrams for loading products in the chamber

3.9 Production control documentation
1. Inspection procedures
2. Test procedures
3. Blank job travelers
4. Blank inspection/test forms
5. Instrument charts
6. Reporting forms
7. Approved deviations

4.0 Labeling and Packaging
4.1 Index (Optional. see 1.0 above.)
4.2 Labeling
1. Label drawings
2. Labeling drawings
3. Label/labeling review procedures and forms
4. Production control procedures and history record forms
5. Instruction manuals
6. Service manuals
7. Customer software
8. Customer feedback forms

4.3 Packaging
1. Package drawings (usually includes labeling information)
2. Closure drawings
3. Filling and/or packaging procedures
4. Packing procedures
5. Special shipment procedures

4.4 Storage requirements
1. Temperature
2. Humidity
3. Shelf-life

5.0 Control Procedures and Activities
5.1 Index (optional. see 1.0 above.)
5.2 Inspection procedures
1. Incoming
2. In-process
3. Finished devices
4. Process control charts
5. Blank data reporting forms

5.3 Test procedures
1. Incoming
2. In-process
3. Pretest conditioning
4. Finished device
5. Process control charts
6. Blank device history record forms
7. Automated test programs and/or software

6.0 Final Release
6.1 Release document review list
6.2 Distribution procedures
6.3 Blank device history record forms
Example of the Investigators Agreement

An example of the agreement to be entered into by all investigators to comply with investigator obligations stated under part 812, and a list of the names and addresses of all investigators who have signed the agreement.

Investigators CV should be attached as a part of this section. When applicable a statement of the investigator's relevant experience (including the dates, location, extent and type of experience); If the investigator was involved in an investigation or other research that was terminated, an explanation of the circumstances that led to termination; and a statement of the investigator's commitment to:

1. conduct the investigation in accordance with the agreement, the investigational plan, Part 812 and other applicable FDA regulations, and conditions of approval imposed by the reviewing IRB and FDA;
2. supervise all testing of the device involving human subjects; and
3. ensure that the requirements for obtaining informed consent are met
4. Investigator’s commitment to provide sufficient and accurate financial disclosure information and update information if any relevant changes occur during the investigation and for one year following the completion of the study.
Investigator certification

A certification that all investigators who will participate in the investigation have signed the agreement, that the list of investigators includes all the investigators participating in the investigation, and that no investigator will be added to the investigation until they have signed the agreement.
IRB’s Information

A list of the name, address, and chairperson of each IRB that has been or will be asked to review the investigation and a certification of the action concerning the investigation taken by such IRB.
Name and Address of the Investigational Institutions

The name and address of any institution at which a part of the investigation may be conducted.
Financial claims

State if device will be sold. If yes, please state the amount to be charged and an explanation of why sale does not constitute commercialization of the device.
**Environmental assessment**

Per Device Advice on the CDRH Web site, [http://www.fda.gov/cdrh/devadvice/ide/application.shtml](http://www.fda.gov/cdrh/devadvice/ide/application.shtml), an environmental assessment as required under 21 CFR 25.40 or a claim for categorical exclusion under 21 CFR 25.30 or 25.34 is no longer required.
Labeling

Copies of all labeling for the device.

The labeling contain should contain the statement "CAUTION-Investigational Device. Limited by Federal (or United States) Law to Investigational Use." [§ 812.5(a)].

EXAMPLE:

University of California, Davis
UC Davis School of Medicine
Center for Voice and Swallowing
2521 Stockton Blvd., Suite 7200
Sacramento, CA 95817
Phone: 916-734-7470

Contents:
Swallow Expansion Device kit (2 parts):
   One (1)- Swallow Expansion Device Plate/Post Unipart
   One (1) -Swallow Expansion Device Loop

CAUTION: Investigational Device. Limited by Federal (or United States) law to investigational use

WARNING: May interfere with radiation treatment. May not be used in patients with active or chronic infections of cartilage, head and neck or with known allergy to titanium. May not be used in conjunction with tracheotomy.

Labeling should also include directions for use, maintenance labeling etc.
Informed Consent

Copies of all forms and informational materials to be provided to subjects to obtain informed consent.
Additional Information

Any other relevant information FDA requests for review of the application.

This is a good place to include the list any references you are attaching to the application.