Best Practices for the Preparation, Submission, and Maintenance of Sponsor-Investigator INDs and IDEs:

The Investigational Device Exemption (IDE) Workshop

PART 1: Medical Device Studies and the IDE

Kelly Lindblom, PhD, RAC
Regulatory Affairs Scientist

PART 2: IDE Best Practices and Additional Studies

Stephanie Pierce, PhD, RAC
Regulatory Affairs Scientist
Before we get started…

• Please navigate to the following website on your phone/laptop:

  pollev.com/oraq
Office of Regulatory Affairs and Quality

- **Location:** Office of Regulatory Affairs and Quality
  Duke University – Hock Plaza
  2424 Erwin Road, 4th Floor
  Durham, NC 27705

- **Website:** [http://medschool.duke.edu/ORAQ](http://medschool.duke.edu/ORAQ)
  – Includes new and updated template documents
  – Request a speaker
  – Event subscription

- **Contact for Questions:** ORAQ@duke.edu

- **Training Program:** ORAQ-TrainingProgram@duke.edu
ReGARDD

- Regulatory Guidance for Academic Research of Drugs and Devices (ReGARDD) is comprised of regulatory affairs specialists from North Carolina institutions that receive funding from the NIH Clinical and Translational Science Awards (CTSA).
  - UNC and RTI: NC TraCS
  - Wake Forest
  - Duke

- ReGARDD provides academic researchers with the regulatory tools and resources necessary to successfully navigate the pathway from discovery to clinical implementation of new drugs, biologics and medical devices.

- Website: www.regardd.org
ReGARDD Regulatory Contacts

• **NC TraCS:**
  – **Amanda Wood, BS, CCRP**  
    IND/IDE Program Coordinator, TraCS Regulatory Service  
    Amanda_wood@med.unc.edu  
  – **Marie Rape, RN, BSN, CCRC**  
    Associate Director, TraCS Regulatory Service  
    marie_rape@med.unc.edu  
  – **Diana Severynse-Stevens, PhD**  
    Director of Drug Development in Global Health Technologies, RTI International  
    dianastevens@rti.org

  – [https://tracs.unc.edu/index.php/services/regulatory](https://tracs.unc.edu/index.php/services/regulatory)

• **Wake Forest:**
  – **Issis Kelly Pumarol**  
    IND/IDE Navigator  
    ikellypu@wakehealth.edu

  – [https://ctsi.wakehealth.edu/regulatory-guidance](https://ctsi.wakehealth.edu/regulatory-guidance)
PART 1: Medical Device Studies and the IDE

- Introduction and Product Classification
- Medical Device Commercialization
- Clinical Investigations of a Medical Device
- IDE Exemption
- SR/NSR Determination and the IDE
PART 1: Medical Device Studies and the IDE

• Introduction and Product Classification
• Medical Device Commercialization
• Clinical Investigations of a Medical Device
• IDE Exemption
• SR/NSR Determination and the IDE
Food and Drug Administration (FDA)

- Government agencies protect public health by controlling the safety and efficacy of commercialized products including pharmaceuticals, medical devices, veterinary medicines, and cosmetics.

- The United States Food and Drug Administration (FDA) is an agency within the U.S. Department of Health and Human Services that is tasked with protecting public health.
  - FDA is responsible for protecting and advancing public health
Who Regulates Medical Devices?

- Center for Devices and Radiological Health (CDRH) is the center at FDA responsible for overseeing:
  - Medical devices*
  - Radiation-emitting products (medical and non-medical, e.g., lasers, ultrasound equipment, microwave ovens, tanning beds)
  - Combination products, when the primary mode of action is the device component

*Medical devices used to safeguard blood, blood components, and cellular products from infectious agents are regulated by CBER
What is a Medical Device?
Section 201(h) of the FD&C Act

An instrument, apparatus, implement, machine, contrivance, implant, *in vitro* reagent or other similar or related article or 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

- is intended to affect the structure or any function of the body

- does not achieve any of its 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
What is a Medical Device?
What is a Combination Product?

• Combination of drug, biologic, and/or medical device
  – Physically/chemically combined
  – Packaged together
  – Packaged separately but labeled to be used together

• Regulated by their primary mode of action
Primary Mode of Action Example

**Antibiotic with biodegradable delivery device**
- PMOA – drug (kills bacteria)
- Secondary MOA – device delivers drug
- Assigned to CDER

**Wound Dressing with Antimicrobial Agent**
- PMOA – device (acts as a barrier)
- Secondary MOA – drug (kills microorganisms)
- Assigned to CDRH
Uncertainty about the PMOA?

Office of Combination Products (OCP):

• Classifies combination products as drugs, devices, or biological products and assigns an FDA center to have primary jurisdiction for premarket review and postmarket regulation.

• Sponsors can submit a Request for Designation to OCP when the classification/jurisdiction is unclear.
Let’s Practice…

Please open the following website on your phone/tablet:

pollev.com/oraq
Product Classification

For each of the following descriptions, please determine whether the product is a:

- drug
- medical device
- combination product
Facial dermal wrinkle filler

- Calcium hydroxylapatite (CaHA) microspheres suspended in a carboxymethylcellulose gel carrier

- Indicated for subdermal implantation for the correction of moderate to severe facial wrinkles and folds, such as nasolabial folds.

Experience the Radiesse difference.

Radiesse® provides an instant lift by restoring lost volume in areas of the lower face, effectively treating moderate to severe wrinkles and folds. It continues to work over time by stimulating the natural production of collagen for a more refreshed appearance that has been clinically proven to last a year or more in many patients.²

Radiesse® is an ideal option for adding lift to:

- Smile Lines
- Marionette Lines
- Pre-Jowl Folds
- Corners of the Mouth
- Chin Wrinkles

SMILE LINES
Deep smile lines (nasolabial folds) can give your face a tired and aged expression.
Learn More

I found the natural-looking lift I needed.

Andrea, 41 • Midwife & Actual Radiesse® Patient
Facial dermal wrinkle filler is a:

- Drug
- Device
- Combination Product
Abilify MyCite is a:

- Drug
- Device
- Combination product; PMOA drug
- Combination product; PMOA device
Reproductive media used for the culture of reproductive embryos
Reproductive media used in the maintenance of embryos cultured for assisted reproduction procedures would be considered a:
PART 1: Medical Device Studies and the IDE

• Introduction and Product Classification
• Medical Device Commercialization
• Clinical Investigations of a Medical Device
• IDE Exemption
• SR/NSR Determination and the IDE
Medical Device Regulation

Medical Device Amendments (1976):

- Prior to 1976, investigational devices were either not reviewed or reviewed as drugs
- Established device classifications based on risk
- Established the Investigational Device Exemption (IDE)
The FDA has established three regulatory classes of devices based on the level of control necessary to assure the safety and effectiveness of the device:

- **Class I**: General Controls (low risk)
  - Example: dental floss, medical scissors, dental syringe

- **Class II**: General Control & Special Controls (moderate risk)
  - Example: powered wheel chair, MRI, clinical mercury thermometer

- **Class III**: General Controls and Premarket Approval (high risk)
  - Example: external defibrillator, replacement heart valves
General Controls
For All Medical Devices

- Establishment Registration (21 CFR 807.20)
- Medical Device Listing (21 CFR 807.20)
- Manufacturing in accordance with Quality System Regulation (21 CFR 820)
- Labeling (21 CFR 801 or 809)
- Medical Device Reporting (21 CFR 803)
- Submission of a premarket notification (510(k))
- Investigational Device Exemption (21 CFR 812)
Special Controls
For Class II Medical Devices

- Performance standards
- Post-market surveillance
- Patient registries
- Special labeling requirements
- Premarket data requirements
- Guidelines
Premarket Approval
For Class III Medical Devices

- Premarket approval (PMA) is a marketing application for Class III medical devices.
  - Scientific and regulatory review that evaluates the safety and effectiveness of the device.

- Due to the level of risk, FDA has determined that general and special controls are insufficient to assure the safety and effectiveness of Class III devices.
Commercialization Options

- **Exempt** - most Class I (about 95%) and a few Class II (about 9%) devices are exempt from the 510(k) regulations

- **510(k)** - device is at least as safe and effective, or substantially equivalent to, a legally marketed device (predicate) that is not subjected to a PMA
  - 90 day FDA review

- **PMA** - premarket approval is required for all Class III devices. Focus on scientific and regulatory review of safety and effectiveness
  - 180 day FDA review
Commercialization Options

- **Exempt** - most Class I (about 95%) and a few Class II (about 9%) devices are exempt from the 510(k) regulations

- **510(k)** - device is at least as safe and effective, or substantially equivalent to, a legally marketed device (predicate) that is not subjected to a PMA
  - 90 day FDA review

- **PMA** - premarket approval is required for all Class III devices. Focus on scientific and regulatory review of safety and effectiveness
  - 180 day FDA review

**Clinical Studies?**

- Unlikely
- Sometimes (10-15%)
- Almost always
Medical Device Classification

- Device classifications are grouped according to medical specialties.
  - 16 groups
  - Code of Federal Regulations: 21 CFR 862-892

- 862 Clinical Chemistry and Clinical Toxicology
- 864 Hematology and Pathology
- 866 Immunology and Microbiology
- 868 Anesthesiology
- 870 Cardiovascular
- 872 Dental
- 874 Ear, Nose, and Throat
- 876 Gastroenterology and Urology
- 878 General and Plastic Surgery
- 880 General Hospital and Personal Use
- 882 Neurology
- 884 Obstetrical and Gynecological
- 886 Ophthalmic
- 888 Orthopedic
- 890 Physical Medicine
- 892 Radiology
Medical Device Classification

Subpart C—OBSTETRICAL AND GYNECOLOGICAL MONITORING DEVICES

§884.2050 Obstetric data analyzer.
§884.2225 Obstetric-gynecologic ultrasonic imager.
§884.2600 Fetal cardiac monitor.
§884.2620 Fetal electroencephalographic monitor.
§884.2640 Fetal phonocardiographic monitor and accessories.
§884.2660 Fetal ultrasonic monitor and accessories.
§884.2675 Fetal scalp circular (spiral) electrode and applicator.
§884.2685 Fetal scalp clip electrode and applicator.
§884.2700 Intrauterine pressure monitor and accessories.
§884.2720 External uterine contraction monitor and accessories.
§884.2730 Home uterine activity monitor.
§884.2740 Perinatal monitoring system and accessories.
§884.2800 Computerized Labor Monitoring System.
§884.2900 Fetal stethoscope.
§884.2960 Obstetric ultrasonic transducer and accessories.
§884.2980 Telethermographic system.
§884.2982 Liquid crystal thermographic system.
§884.2990 Breast lesion documentation system.
Medical Device Classification

Electronic Code of Federal Regulations

e-CFR data is current as of February 16, 2018

Title 21 → Chapter I → Subchapter H → Part 884 → Subpart C → §884.2900

Browse Previous | Browse Next

Title 21: Food and Drugs
PART 884—OBSTETRICAL AND GYNECOLOGICAL DEVICES
Subpart C—Obstetrical and Gynecological Monitoring Devices

§884.2900  Fetal stethoscope.

(a) Identification. A fetal stethoscope is a device used for listening to fetal heart sounds. It is designed to transmit the fetal heart sounds not only through sound channels by air conduction, but also through the user's head by tissue conduction into the user's ears. It does not use ultrasonic energy. This device is designed to eliminate noise interference commonly caused by handling conventional stethoscopes.

(b) Classification. Class I (general controls). The device is exempt from the premarket notification procedures in subpart E of part 807 of this chapter, subject to the limitations in §884.9.


Need assistance?
Medical Device Classification

§884.2980 Telethermographic system.

(a) Telethermographic system intended for adjunctive diagnostic screening for detection of breast cancer or other uses—

(1) Identification. A telethermographic system for adjunctive diagnostic screening for detection of breast cancer or other uses is an electrically powered device with a detector that is intended to measure, without touching the patient’s skin, the self-emanating infrared radiation that reveals the temperature variations of the surface of the body. This generic type of device may include signal analysis and display equipment, patient and equipment supports, component parts, and accessories.

(2) Classification. Class I (general controls).

(b) Telethermographic system intended for use alone in diagnostic screening for detection of breast cancer or other uses—

(1) Identification. A telethermographic system for use as the sole diagnostic screening tool for detection of breast cancer or other uses is an electrically powered device with a detector that is intended to measure, without touching the patient’s skin, the self-emanating infrared radiation that reveals the temperature variations of the surface of the body. This generic type of device may include signal analysis and display equipment, patient and equipment supports, component parts, and accessories.

(2) Classification. Class III.

(3) Date PMA or notice of completion of a PDP is required. As of the enactment date of the amendments, May 28, 1976, an approval under section 515 of the act is required before the device described in paragraph (b)(1) may be commercially distributed. See §884.3.

Medical Device Classification

A 510(k) is a premarket submission made to FDA to demonstrate that the device to be marketed is at least as safe and effective, that is, substantially equivalent, to a legally marketed device (21 CFR §807.92(a)(2)) that is not subject to premarket approval.

Other Databases
- Device Classification
- Inspections
- Medical Reports
- Premarket Approvals (PMA)
- Post-Approval Studies
- Postmarket Surveillance Studies
- Radiation-Emitting Products
- Radiation-Emitting Electronic Products
- Recalls
- Registration & Listing Standards
- Total Product Life Cycle
- X-Ray Assembler
Office of Regulatory Affairs and Quality

Common Commercialization Options

- **Exempt** - most Class I (about 95%) and a few Class II (about 9%) devices are exempt from the 510(k) regulations.
  - 510(k) - device is at least as safe and effective, or substantially equivalent to, a legally marketed device (predicate) that is not subjected to a PMA
    - 90 day FDA review

- **PMA** - premarket approval is required for all Class III devices. Focus on scientific and regulatory review of safety and effectiveness
  - 180 day FDA review
Alternative Commercialization Option: De Novo Process

- **De Novo Process**: Provides a pathway to market Class I (low risk) and Class II (moderate risk) medical devices for which there is no legally marketed predicate device.

- You must understand and explain all known risks and benefits of the device:
  - How will device risks be mitigated?
  - How will device effectiveness be assured through general/special controls?

- 150 day review by FDA
Alternative Commercialization Option: Humanitarian Device Exemption

• An Humanitarian Use Device (HUD) is a device that is intended to benefit patients by treating or diagnosing a disease or condition that affects or is manifested in fewer than 8,000 individuals in the US per year.

• HDE application is similar to PMA but is exempt from the effectiveness requirements.

• With exception of emergency use, even if used per its approved label, the use of HUD requires IRB approval.
Unique Scenario: General Wellness Products

- FDA does not intend to examine/enforce FD&C requirements
- General wellness products meet the following two factors:
  1. Intended only for general wellness use
  2. Present low risk to the safety of users and other persons

- Categories of products:
  1. Claims do not make reference to diseases or conditions
  2. Claims making reference to diseases or conditions
     - May help to reduce the risk of certain chronic diseases or conditions
     - May help living well with certain chronic diseases or conditions

Unique Scenario:
Mobile Medical Applications

Mobile Medical Application (MMA)

- “. . .is a mobile app that meets the definition of device in section 201(h) of the Federal Food, Drug, and Cosmetic Act (FD&C Act); and either is intended:
  - to be used as an accessory to a regulated medical device; or
  - to transform a mobile platform into a regulated medical device.”
Risk-based Approach for Mobile Applications

MAs that meet the definition of a medical device and are higher risk

MAs that may meet the definition of a medical device but are lower risk

MAs that do not meet the definition of a medical device

Focus of Regulatory Oversight

“Enforcement Discretion”

Not medical devices
Mobile Medical Apps: Focus of FDA Regulatory Oversight

Mobile Apps that meet the definition of a medical device and can pose potential risk to public health:

- Mobile apps that are an extension of one or more medical devices by connecting to such device(s) for purposes of controlling the device(s).
- Mobile apps that transform the mobile platform into a regulated medical device by using attachments, display screens, or sensors or by including functionalities similar to those of currently regulated medical devices.
- Mobile apps that become a regulated medical device (software) by performing patient-specific analysis and providing patient-specific diagnosis, or treatment recommendations.
- Regulated as other non MMA medical devices: based on risk classification requirements (Class I-III).
Enforcement Discretion

Mobile Apps that may meet the definition of a medical device for which the FDA intends to exercise ‘enforcement discretion’:

- Mobile apps that provide or facilitate supplemental clinical care, by coaching or prompting, to help patients manage their health in their daily environment.
- Mobile apps that perform simple calculations routinely used in clinical practice (BMI, APGAR score, delivery date estimator)
Mobile Apps that are NOT Medical Devices

Mobile Apps that could be used in a healthcare environment, in clinical care or patient management, but are NOT considered medical devices:

• Mobile apps that are intended to provide access to electronic “copies” (e.g., e-books, audio books) of medical textbooks or other reference materials.
• Mobile apps that are intended for health care providers to use as educational tools for medical training.
• Mobile apps that are intended for general patient education and facilitate patient access to commonly used reference information.
• Mobile apps that automate general office operations in a health care setting.
• Mobile apps that are generic aids or general purpose products.
Mobile Apps that are NOT Medical Devices

• Mobile apps that provide patients with simple tools to organize and track their health information without providing recommendations to alter or change a previously prescribed treatment or therapy.

• Mobile apps that are specifically marketed to help patients document, show, or communicate to providers potential medical conditions.
Mobile Apps that are NOT Medical Devices

- Mobile apps that meet the definition of Medical Device Data Systems:
  - Apps that are intended to transfer, store, convert format, and display medical device data, without altering the functions or parameters of any connected medical device.
Mobile Apps that are NOT Medical Devices

• Mobile apps that meet the definition of Clinical Decision Support and are not intended to be relied upon to make treatment decisions by a health care professional:
  – Not intended to acquire, process, analyze medical images/signals
  – Intended for the purpose of displaying, analyzing, or printing medical information
  – Intended for the purpose of supporting or providing recommendations to a healthcare professional
Let’s Practice…

Please open the following website on your phone/tablet:

pollev.com/oraq
A mobile app that provides tasks to quantitatively measure impaired attention, hyperactivity, and impulsivity for a particular patient to aid in the diagnosis of ADHD.

When poll is active, respond at PollEv.com/oraq
Text ORAQ to 37607 once to join

- Regulated medical device
- Enforcement discretion
- Not a medical device
<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regulated medical device</td>
<td></td>
</tr>
<tr>
<td>Enforcement discretion</td>
<td></td>
</tr>
<tr>
<td>Not a medical device</td>
<td></td>
</tr>
</tbody>
</table>
A mobile app that coaches breathing techniques and relaxation skills, which, as part of a healthy lifestyle, may help living well with migraine headaches.
PART 1: Medical Device Studies and the IDE

• Introduction and Product Classification
• Medical Device Commercialization
• Clinical Investigations of a Medical Device
• IDE Exemption
• SR/NSR Determination and the IDE
What is a Clinical Investigation?

- A clinical Investigation is any experiment in which a drug or device is administered, dispensed to, or used involving, one or more human subjects, except for the use of a marketed product in the course of medical practice.

  - This would include clinical studies in which a subject is assigned to specific intervention according to a study protocol.
Who Conducts a Clinical Investigation?

- **Sponsor**: An individual, company, academic institution, or other organization that **takes responsibility** for and **initiates** a clinical investigation.

- **Investigator**: An individual who **conducts** a clinical investigation, i.e., under whose **immediate direction** a device is used.

- **Sponsor-Investigator**: An individual who both **initiates** and **conducts** an investigation, and under whose **immediate direction** a device is used.
What is an Investigational Device Exemption (IDE)?

- An IDE is a **regulatory submission** to the FDA that permits the clinical investigation of devices.

- An approved IDE allows:
  - an investigational device to be used in a clinical study in order to collect safety and effectiveness data.
  - a device to be shipped lawfully for the purpose of conducting clinical investigations.
When is a Clinical Investigation Subject to the IDE Regulations?

- If the objective of the clinical investigation is to assess the **safety** and/or **effectiveness** of a medical device, then the study is a device study and is subject to regulatory oversight by the US Food and Drug Administration (FDA).

- 21 CFR 812 (Investigational Device Exemption)
Are all clinical investigations that use devices subject to regulatory oversight by FDA?

- No. If the objective of the study is not to test the safety or effectiveness of the device, then the study would not fall within the scope of 21 CFR 812.

- Devices used as “tools”
In Vitro Diagnostic Device Development

- A research study with one or more objectives to test the safety or effectiveness of an IVDD is a device study and is subject to 21 CFR 812.
- Under FDA guidance documents, this may include determining the performance characteristics of the IVDD, comparing the usefulness of the IVDD to other available tests, and/or validating the utility of the IVDD.
Early Development of IVDDs

1. Collecting samples to determine if there are any biomarkers or signatures that might correlate with a disease, disease risk, or treatment response – “fishing”.

2. Collecting samples to determine if one or more specific biomarkers correlate with a disease, disease risk, or treatment response.

3. In Vitro Diagnostic Multivariate Index Assay – non-transparent “score” to diagnose or predict disease risk.

IDE Regulations Apply?  
No; Basic Research

Yes

Yes

https://irb.duhs.duke.edu/sites/irb.duhs.duke.edu/files/field/attachments/IVD%20development_Final%20Draft-1_0.docx
Clinical Investigation of a Medical Device

Objective of the study is to assess the safety or effectiveness of the device

Be **exempt** of the IDE regulations (21 CFR 812.2 (c))

Have an approved IDE

a) **abbreviated IDE** (21 CFR 812.2 (b))

b) **IDE** (21 CFR 812.20)
PART 1: Medical Device Studies and the IDE

• Introduction and Product Classification
• Medical Device Commercialization
• Clinical Investigations of a Medical Device
• IDE Exemption
• SR/NSR Determination and the IDE
Investigations Exempt from the IDE Regulations

- A legally marketed device when used in accordance with its labeling.
- A **diagnostic device** meeting 4 specified criteria.
- A device undergoing a consumer preference testing, testing of modification or testing of a combination of two or more devices in commercial distribution if the testing is not for the purpose of determining safety or effectiveness and does not put subjects at risk.
- A device intended solely for veterinary use.
- A device for research on or with laboratory animals.
- A custom device. *(21 CFR 812.3(b)) ([http://tinyurl.com/lbxl9k8](http://tinyurl.com/lbxl9k8))**
Diagnostic Exemption Criteria

- Per 21 CFR 812.2 (c), a diagnostic device study is IDE exempt if the testing:
  - Is noninvasive
  - Does not require an invasive sampling procedure that presents a significant risk
  - Does not by design or intention introduce energy into a subject
  - Is not used as a diagnostic procedure without confirmation of the diagnosis by another medically established diagnostic product or procedure
When is a Diagnostic Device Noninvasive?

• “A noninvasive device is one that does not, by design or intention:
  • penetrate or pierce the skin or mucous membranes of the body, the ocular cavity, or the urethra; or
  • enter the ear beyond the external auditory canal, the nose beyond the nares, the mouth beyond the pharynx, the anal canal beyond the rectum, or the vagina beyond the cervical os (21 CFR 812.3(k)).”
How Do I Determine if an Invasive Sampling Procedure Presents a Significant Risk?

“…we recommend that you base your risk determination on the nature of the harm that may result from sampling. For example, FDA considers sampling techniques that require biopsy of a major organ, use of general anesthesia, or placement of a blood access line into an artery or large vein (subclavian, femoral, or iliac) to present a significant risk.”

“Blood sampling that involves simple venipuncture is considered noninvasive, and the use of surplus samples of body fluids or tissues that are left over from samples taken for noninvestigational purposes is also considered noninvasive (21 CFR 812.3(k)).”

http://tinyurl.com/hkjk3fp
What Does Confirmation by another Medically Established Product Mean?

“…test results …should not influence patient treatment or clinical management decisions before the diagnosis is established by a medically established product or procedure”

“…If an investigational test uses a new technology or represents a significant technological advance, established diagnostic products or procedures may not be adequate to confirm the diagnosis provided by the investigational IVD.”

http://tinyurl.com/hkjk3fp
Diagnostic Exemption Criteria

• Per 21 CFR 812.2 (c), a diagnostic device study is IDE exempt if the testing:
  - Is noninvasive
  - Does not require an invasive sampling procedure that presents a significant risk
  - Does not by design or intention introduce energy into a subject
  - Is not used as a diagnostic procedure without confirmation of the diagnosis by another medically established diagnostic product or procedure
PART 1: Medical Device Studies and the IDE

- Introduction and Product Classification
- Medical Device Commercialization
- Clinical Investigations of a Medical Device
- IDE Exemption
- SR/NSR Determination and the IDE
Clinical Investigation of a Medical Device

Objective of the study is to assess the safety or effectiveness of the device

- Be exempt of the IDE regulations (21 CFR 812.2 (c))
- Have an approved IDE
  - a) abbreviated IDE (21 CFR 812.2 (b))
  - b) IDE (21 CFR 812.20)
What is the difference between an abbreviated IDE and an IDE?

Who is overseeing the study:

**IRB (abbreviated IDE)**
- Non-significant risk (NSR) device studies

**FDA and IRB (IDE)**
- Significant risk (SR) device studies
Significant Risk Device Studies

• A **significant risk** device is one that:
  
  • Is intended as an implant and presents a potential for serious risk to the health, safety, and welfare of a subject.
  
  • Is used to support or sustain human life.
  
  • Is of substantial importance in diagnosing, curing, mitigating, or treating disease and/or otherwise preventing impairment of human health.
  
  • Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

  **Note:** The study risk determination is based on the proposed use of a device in an investigation, and not on the device alone.
Example:
NSR vs SR Device Studies

Non-significant risk:
- A study testing if a sensor pad can detect the electrical activity of the spinal cord, if surgery/repair of spinal cord is already occurring, the sensor pad is not implanted

Significant risk:
- A study testing if a sensor pad can detect the electrical activity of the spinal cord, if surgery/repair of spinal cord was not already occurring, or the sensor pad is implanted, or sensor pad otherwise meets definition of a significant risk device
Factors to Consider for Assessing IVD Risk

- Will use of the results from an investigational IVD lead to some study subjects foregoing or delaying a treatment that is known to be effective?
- Will use of the results from an investigational IVD expose study subjects to safety risks (e.g., drug side effects) that exceed the risks encountered with the control arm therapy or non-trial standard of care?
- Is it likely, based on existing knowledge about the relationship between the biomarker and the investigational therapeutic product, that incorrect results from the investigational IVD would present a potential for serious risk to study subjects?
- Does use of the investigational IVD require invasive sampling that is not part of standard of care?

https://tinyurl.com/ydanqyfv
Significant Risk (SR) Device Studies

Information Sheet Guidance For IRBs, Clinical Investigators, and Sponsors

Significant Risk and Nonsignificant Risk Medical Device Studies

http://tinyurl.com/48ywrw8
Study Risk Determination

Sponsor Risk Assessment
(based on clinical protocol, description of device, reports of prior investigations, subject selection criteria, etc.)

Submit to IRB

NSR Agreement

Requires an abbreviated IDE
Non-Significant Risk (NSR) Device Studies

- NSR device studies do not need an IDE application approved by FDA.
- The IRB serves as the FDA’s surrogate for review, approval, and continuing review of NSR device studies.
- NSR device studies must follow the abbreviated requirements at 21 CFR 812.2 (b).
Abbreviated IDE Requirements  
(21 CFR 812.2 (b)(1))

• Label the device properly (21 CFR 812.5)  
  – “CAUTION—Investigational device. Limited by Federal (or United States) law to investigational use.”

• Obtain and maintain IRB approval after presenting why the device study is NSR

• Obtain informed consent (21 CFR 50)

• Monitor the study (21 CFR 812.46)

• Maintain required records and reports

• Comply with prohibitions against promotion (21 CFR 812.7)
Study Risk Determination

Sponsor Risk Assessment
(based on clinical protocol, description of device, reports of prior investigations, subject selection criteria, etc.)

Submit to IRB

NSR Agreement

- Requires an abbreviated IDE
- Unsure of NSR/SR; Request FDA Input
Study Risk Determination

• Q-Submission: Study Risk Determination Request
  • Include device information and clinical protocol
  • Include cover letter and highlight nature of request
  • Response usually within 60 days (binding determination)

• Full IDE Submission
  • Response within 30 days

• Streamlined process for co-development with oncology drugs: https://tinyurl.com/y7rmmabx
Study Risk Determination

Sponsor Risk Assessment
(based on clinical protocol, description of device, reports of prior investigations, subject selection criteria, etc.)

Submit to IRB

NSR Agreement
Requires an abbreviated IDE

SR Determination
Requires submission of IDE to the FDA
Clinical Investigation of a Medical Device

Device Studies

Studies subject to IDE Requirements
- Risk Determination
  - SR
    - Full IDE
      - FDA & IRB Approval
  - NSR
    - Abbreviated IDE
      - IRB Approval

Studies Exempt from IDE Requirements
- IRB Approval

Source: ReGARDD
Let’s Practice…

Please open the following website on your phone/tablet:

pollev.com/oraq
Case Scenario

- A sponsor-investigator is performing a pilot study to investigate whether an algorithm using data from a CT scan can be used to estimate intracranial pressure (ICP) to diagnose patients with headaches due to intracranial hypotension.

- The CT scan images will be analyzed to calculate volume and pressure changes during the cardiac cycle, and this data will be plugged into an Excel spreadsheet-based algorithm. The results of the algorithm will determine whether or not the patient has intracranial hypotension.

- The CT scan will be performed for research purposes, but the physician will not alter the treatment plan based on the information from the algorithm.
<table>
<thead>
<tr>
<th>Are there any medical devices in this study?</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
</tr>
<tr>
<td>Yes. The CT scanner.</td>
</tr>
<tr>
<td>Yes, both the CT scanner and the algorithm.</td>
</tr>
</tbody>
</table>
Is this a device study subject to 21 CFR 812?

No; safety and effectiveness is not being evaluated.

Yes; safety and/or effectiveness of the algorithm is being evaluated.

Yes; safety and/or effectiveness of both devices is being evaluated.
Can this study be exempt of the IDE regulations, or would a NSR/SR assessment need to be made?

Exempt.

NSR/SR assessment needed.
The purpose of a new study is to explore the molecular mechanisms that explain the differences in clinical manifestation between pediatric-onset Lupus (more aggressive) and adult-onset Lupus (less aggressive).

The hypothesis is that plasma levels of the protein LUPA will be higher in pediatric patients with more aggressive disease. This information could be used in the future to diagnose Lupus patients earlier.

Pediatric and adult patients with confirmed Lupus diagnoses will be enrolled for a one-time visit, and blood draws will be performed. LUPA levels will be measured using an ELISA assay.
Is there a medical device in this study?

When poll is active, respond at PollEv.com/oraq
Text ORAQ to 37607 once to join

No medical devices.

Yes, an in vitro diagnostic to measure LUPA levels and correlate them with pSLE.
Is this a device study subject to 21 CFR 812?

No; safety and effectiveness is not being evaluated.

Yes; safety and/or effectiveness of the LUPA IVD is being evaluated.
Can this study be exempt of the IDE regulations, or would a NSR/SR assessment need to be made?

Exempt.

NSR/SR assessment needed.
Case Scenario

- The purpose of a new study is to determine if a strategy for early discharge combined with use of an in-home drug delivery system is superior to typical inpatient care for patients recovering from congestive heart failure.
- The drug and delivery device system, together called the HomeCURE system, are being developed by a local biotech company in RTP and both components are investigational. The device delivers the drug subcutaneously.
- Study participants will be randomized to stay in the hospital for 30 days following heart failure or to receive the HomeCURE system and will have follow-up appointments after 30, 60, and 90 days.
Is there a medical device in this study?

No medical devices.

Yes, a single entity drug delivery device.

Yes, a drug delivery device that is part of a combination product.
Which is the primary mode of action for this combination product?

- Drug component
- Device component
Which regulatory application(s) would be most appropriate for this clinical study?

None; exempt from both IND and IDE regulations.

Only an IND.

Only an IDE.

Both an IND and IDE.
Let’s Take a Break!

The plan to increase productivity by canceling coffee breaks flopped.
Best Practices for the Preparation, Submission, and Maintenance of Sponsor-Investigator INDs and IDEs:

The Investigational Device Exemption (IDE) Workshop

PART 1: Medical Device Studies and the IDE
Kelly Lindblom, PhD, RAC
Regulatory Affairs Scientist

PART 2: IDE Best Practices and Additional Studies
Stephanie Pierce, PhD, RAC
Regulatory Affairs Scientist
PART 2: IDE Best Practices and Additional Studies

- Pre-submission Meetings
- IDE Preparation and Submission
- IDE Maintenance
- Expanded Access Program
PART 2: IDE Best Practices and Additional Studies

- Pre-submission Meetings
- IDE Preparation and Submission
- IDE Maintenance
- Expanded Access Program
Q-Sub Program: Pre-Submission Meeting

- A pre-submission is defined as a formal written request from an applicant for feedback from FDA to be provided in the form of a formal written response or a meeting/teleconference.
- Can be utilized for a wide range of questions
- Meeting will be held 60-75 days after the request is received

Q-Submission Guidance: http://tinyurl.com/kvbf54z
Pre-Submission Meeting

- Can ask questions on predicate devices, planned studies (nonclinical and clinical)
- Best to have a meeting before making costly preclinical decisions
- Can be used even if no clinical study will follow
- Encouraged, but not required, by FDA
- Free
- Can be used more than once
  - Unlike the formal meeting schedule in drug development
Pre-Submission Meeting Package Contents

- Recommended contents of a pre-sub meeting package:
  - Cover letter
  - Table of Contents
  - Device Description
  - Proposed Intended Use
  - Previous Discussions or Submissions
  - Product Development
  - Specific Questions
  - Mechanism for Feedback
  - Other Logistical Information
Pre-Sub Questions

• Identify specific, well-phrased questions

• Bad Questions:
  – Does FDA have any comments on the nonclinical study results?
  – Does the FDA agree that the proposed clinical protocol is adequate to support the safety and effectiveness of the device in a marketing application?
  – What are clinically meaningful outcomes for the device, and what is the best way to analyze them?
Pre-Sub Questions

• Good Questions:
  – Are the nonclinical study protocols sufficient to allow for the collection of data from which conclusions about device safety to support initiation of a clinical study can be drawn?
  – Are the proposed trial design and selected control group appropriate?
  – Is our justification for not conducting carcinogenicity studies adequate?
Pre-Sub Meeting Recommendations

• Before the meeting:
  – Preliminary written responses from FDA will be sent to the applicant ~2-5 days before the meeting
  – Review responses thoroughly and prioritize questions for meeting

• During the meeting:
  – Limit presentation time, don’t present new data, take notes, summarize major decisions at end

• After the meeting:
  – Debrief immediately, draft meeting minutes and submit as an amendment within 15 days
Let’s Practice…

Please open the following website on your phone/tablet:

pollev.com/oraq
Which one of these questions is more appropriate to ask in a pre-sub meeting before submitting an IDE?

Are the proposed sample size calculation method and related elements of the statistical analysis plan appropriate for the proposed clinical study?

How large should the sample size be?
PART 2: IDE Best Practices and Additional Studies

- Pre-submission Meetings
- IDE Preparation and Submission
- IDE Maintenance
- Expanded Access Program
IDE Content (21 CFR 812.20 (b))

Cover Sheet – Form FDA 3514
1. Name and Address of the Sponsor
2. Report of Prior Investigations
3. Investigational Plan
4. Manufacturing Information
5. Investigator Agreement
6. Investigator Certification
7. IRB Information
8. Name and Address of Investigators Institution
9. Financial Claims
10. Environmental Assessment
11. Labeling
12. Informed Consent
13. Additional Information
Cover Sheet – Form FDA 3514

- Used voluntarily
- Same form is used for IDE, 510(k), PMA, meetings, 513(g), etc.
- Captures the following information:
  - original submission, amendment, report or supplement
  - device information (name, intended use, classification)
  - sponsor and manufacturer contact information
  - any previous discussion with the FDA
IDE Content
21 CFR 812.20 (b)

Cover Sheet – Form FDA 3514
1. Name and Address of the Sponsor
2. Report of Prior Investigations
2. Report of Prior Investigations
(21 CFR 812.27)

- 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 Contents:
  - Bibliography of all publications
  - Summary of all unpublished information
  - If nonclinical laboratory studies are referenced, state whether studies were conducted in accordance with good laboratory practice (GLP) regulations (21 CFR 58)
IDE Content
21 CFR 812.20 (b)

Cover Sheet – Form FDA 3514
1. Name and Address of the Sponsor
2. Report of Prior Investigations
3. Investigational Plan
3. Investigational Plan
(21 CFR 812.25)

- Purpose
  - Name and intended use of the device
  - Objectives and duration of the investigation

- Protocol
  - Methodology

- Risk Analysis

- Description of the Device

- Monitoring Procedures

- Additional Records and Reports
IDE Content
21 CFR 812.20 (b)

Cover Sheet – Form FDA 3514
1. Name and Address of the Sponsor
2. Report of Prior Investigations
3. Investigational Plan
4. Manufacturing Information
4. Manufacturing Information

21 CFR 812.20(b)(3)

- FDA-Approved Device – off label and/or modified
  - Refer to the approved product label & describe any changes

- Non-FDA Approved Device – from a company
  - Include manufacturing information provided by the company
  - Refer to a Letter of Authorization (LoA)

- Non-FDA Approved Device – you control manufacturing
  - Methods, facilities, and controls for manufacturing, packaging, storage and installation of the device
What is an LoA?

- This is a letter from a sponsor (company) to their IDE (or IND or MF) stating that confidential information from their submission can be used in support of your submission.

- It gives the FDA “permission” to reference the named materials in support of your IDE application.

- Get copies of the letters to include in your submission!
IDE Content
21 CFR 812.20 (b)

Cover Sheet – Form FDA 3514
1. Name and Address of the Sponsor
2. Report of Prior Investigations
3. Investigational Plan
4. Manufacturing Information
5. Investigator Agreement
5. Investigator Agreement
(21 CFR 812.43)

- **Who is the investigator?**
  - The investigator is the individual who actually conducts a clinical investigation (i.e., under whose immediate direction the investigational device is administered, dispensed to, or used involving human subjects).
  - In the event of an investigation being conducted by a team of individuals, "investigator" refers to the responsible leader of that team.
5. Investigator Agreement
(21 CFR 812.43)

- CV of the investigator
- Statement of investigator’s relevant experience
- If the investigator was involved in an investigation that was terminated, explain the circumstances
- Financial disclosure information
- Statement of investigators commitment to:
  - Conduct the investigation according to the agreement
  - Supervise all testing
  - Ensure that requirements for obtaining IC are met
IDE Content (21 CFR 812.20 (b))

Cover Sheet – Form FDA 3514
1. Name and Address of the Sponsor
2. Report of Prior Investigations
3. Investigational Plan
4. Manufacturing Information
5. Investigator Agreement
6. Investigator Certification
7. IRB Information
8. Name and Address of Investigators Institution
9. Financial Claims
10. Environmental Assessment
11. Labeling
12. Informed Consent
13. Additional Information
Original IDE Submission

- 3 copies of your application are required:
  - 1 Paper copy
  - 2 eCopies with a paper cover letter

Products regulated by CDRH:
U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Control Center- W066-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Products regulated by CBER:
U.S. Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Avenue
WO71, G112
Silver Spring, MD 20993-0002
eCopy Requirements

- eCopy should be an exact duplicate of the paper copy
  - If an identical copy is not feasible, the paper copy must have a placeholder cross-referencing the location of information on the eCopy
  - Cover letter must contain a valid eCopy statement
    - “The eCopy is an exact duplicate of the paper copy.”
    - “The eCopy is an exact duplicate of the paper copy except [specify all differences].”
- Sent on electronic media (CD, DVD, or flash drive)
- All documents need to be in Portable Document Format (PDF) with no security settings
- Use Adobe Acrobat 11 and below
- 50MB or smaller in size
Creating an eCopy

- **Non-Volume Based eCopy**

- **Volume Based eCopy**
  - VOL_001_Administrative Information
    - 001_Cover Letter.pdf
    - 002_Name and address of Sponsor.pdf
  - VOL_002_Report of Prior Investigations
    - 001_Clinical.pdf
    - 002_Animal Testing.pdf

http://tinyurl.com/99jtgle
Ensure eCopy Compliance

- **eSubmitter-eCopies Tool**: a voluntary tool that formats your eCopy content and allows you to download onto a local drive

- **eCopies Validation Module**: a voluntary tool that verifies the format of an eCopy you have already developed on your local drive
FDA Review Process

- Sponsors are notified of the date that FDA receives the original application.

- IDE number is assigned (e.g., G096000)
  - If eCopy is missing, you will be placed on “eCopy Hold”
  - ✓ To lift the hold, send revised eCopy only, with a paper cover letter and an appropriate eCopy statement
FDA Review Process

- Within 30 calendar days of the receipt date, FDA may grant:
  - IDE Approval
  - IDE Approval with Conditions
  - Staged Approval (with Conditions)
  - IDE Disapproval

- An IDE application is considered approved 30 days after it has been received by FDA.

http://tinyurl.com/lxrmd9u
Let’s Practice…

Please open the following website on your phone/tablet:

pollev.com/oraq
If you don't submit an eCopy, when will the review of your IDE be complete?

30 days after FDA receives the initial submission

30 days after you submit a replacement eCopy
Do you need to submit an eCopy if your IDE is reviewed by CBER?

Yes

No
PART 2: IDE Best Practices and Additional Studies

• Pre-submission Meetings
• IDE Preparation and Submission
• IDE Maintenance
• Expanded Access Program
Once you have an active IDE…

- Make sure that you also have IRB approval(s) in place
- Register trial at the ClinicalTrials.gov
ClinicalTrials.gov

- Introduced by FDAAA in 2007
- Do not need to send a 3674 form to the FDA with your IDE submission
- Do need to register “applicable clinical trial” on ClinicalTrials.gov
  - Other reasons to register: publishing, NIH funding
  - DOCR-ctgov@dm.duke.edu
Requirements for IDE Modifications

- Modifications to the Investigational Plan (device or clinical protocol) need to be submitted to FDA:
  - Changes that REQUIRE prior approval (30-day reply from FDA)
  - Changes that DO NOT require prior approval (5-day notice)
  - Changes submitted as a part of annual report

http://tinyurl.com/42wvtncy
IDE Modifications

- Changes that require prior approval (30-day reply from FDA):
  Changes that could impact validity of data, scientific soundness, or the rights/safety/welfare of study subjects:

<table>
<thead>
<tr>
<th>Indication</th>
<th>Type or nature of study control</th>
<th>Primary end point</th>
</tr>
</thead>
<tbody>
<tr>
<td>Significant design changes</td>
<td>Statistical methods evaluation</td>
<td>Expanding the study</td>
</tr>
</tbody>
</table>
# IDE Modifications

- Changes that require **5-day notice** to FDA:
  - Emergency change
  - Changes that do not affect validity of data, scientific soundness, or the rights/safety/welfare of study subjects:

<table>
<thead>
<tr>
<th>Modification of inclusion/exclusion criteria</th>
<th>Increasing frequency at which information is gathered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Design or manufacturing changes that are not significant</td>
<td>Modifying the secondary study endpoints</td>
</tr>
</tbody>
</table>
IDE Modifications

• Changes that can be sent to FDA as part of the annual report:
  • Minor changes that do not affect the validity of data, scientific soundness, or the rights/safety/welfare of study subjects:

<table>
<thead>
<tr>
<th>Monitoring procedures</th>
<th>Labeling</th>
<th>Informed Consent Materials</th>
</tr>
</thead>
<tbody>
<tr>
<td>IRB Information</td>
<td>Purpose of the study</td>
<td>Risk Analysis</td>
</tr>
</tbody>
</table>
## IDE Maintenance

<table>
<thead>
<tr>
<th>IDE Report</th>
<th>Timeline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unanticipated Adverse Device Effects</td>
<td>10 working days</td>
</tr>
<tr>
<td>Withdrawal of IRB approval</td>
<td>5 working days</td>
</tr>
<tr>
<td>Investigator List</td>
<td>Every 6 months</td>
</tr>
<tr>
<td>Progress Report (Annual Report)</td>
<td>At least yearly</td>
</tr>
<tr>
<td>Deviation from Investigational Plan</td>
<td>5 working days or pre-approval</td>
</tr>
<tr>
<td>Failure to Obtain Informed Consent</td>
<td>5 working days</td>
</tr>
<tr>
<td>Recall and Device Disposition</td>
<td>30 working days</td>
</tr>
<tr>
<td>Significant Risk Determination</td>
<td>5 working days</td>
</tr>
<tr>
<td>Final Report</td>
<td>30 working days- notification</td>
</tr>
<tr>
<td></td>
<td>6 months- report</td>
</tr>
</tbody>
</table>
IDE Maintenance - UADEs

- Unanticipated Adverse Device Effect (21 CFR 812.3 (s))
  - Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device if that effect, problem or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application
  - Any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects

- Conduct an evaluation of the UADE and report to the FDA within 10 working days
Progress/Final Report

1. Basic information
2. Study Progress
   - Brief summary of the study progress
   - Number of investigators/investigational sites
   - Number of subjects enrolled
   - Number of devices shipped
   - Disposition of all device shipped
   - Brief summary of results
   - Summary of anticipated and unanticipated adverse effects
   - Description of any deviations from the investigational plan (since last progress report)
Progress/Final Report

3. Risk Analysis
   – Summary of any new adverse information (since the last progress report) that may affect the risk analysis
   – Reprints of any articles published from data collected from this study
   – New risk analysis, if necessary, based on new information and on study progress

4. Other Changes
   – Summary of any changes in manufacturing practices and quality control
   – Summary of all changes in the investigational plan not required to be submitted in a supplemental application

5. Marketing Application or Future Plans
Let’s Practice…

Please open the following website on your phone/tablet:

pollev.com/oraq
Case Scenario

• A sponsor-investigator submits an original IDE application to conduct a 20-subject feasibility study for a permanently implanted device to treat a serious medical condition. The study is intended to provide data to support a future pivotal study.

• FDA’s review of the submission demonstrates that the data provided are sufficient to support a feasibility evaluation under the monitoring plan proposed but finds concerns with the informed consent document, which does not communicate a potential risk relevant for this study.

• FDA determines that this concern should not preclude the sponsor from initiating the feasibility study, provided that the informed consent document is amended.
Case Scenario

• A sponsor-investigator is conducting a pivotal clinical study on a device to treat migraine headaches.
• The original IDE application proposed to test the safety and effectiveness of the device in 180 subjects. An interim analysis of the results suggests that the study may need to enroll more subjects in order to reach statistical significance.
• The sponsor-investigator would like to expand study enrollment to 240 subjects.
This change in the investigational plan is best reported to the FDA as a:

- Emergency Change
- Change Requiring Prior Approval
- Change Submitted as a 5-day Notice
- Change Submitted in the Annual Report
IDE Submission Types

- Supplements
- Reports
- Amendments

http://tinyurl.com/lxrdm9u
Supplements

- Approval for change (prior-approval, 5-day notice)
- Request approval for a new study under the same IDE
- Request study expansion (new sites, more patients)
- Request approval to terminate enrollment/study
- Notify FDA if the study been suspended
- Request approval for the compassionate use
- Request the extension of time to respond to the FDA

The FDA will usually reply to supplements. Reply is similar to the Original IDE submission.
Reports

• Provide biannual investigator/IRB information
• Annual reports
• Failure to obtain ICF
• Notify the FDA of the Emergency Use
• Report the unanticipated adverse device effect
• Report completion of enrollment/study
• Provide final IDE report

The FDA will reply within 30 days only if they have any comments or questions.
Amendments

- Any response to deficiency letter is an amendment.
  - Response to Disapproval
  - Response to Approval with Conditions
  - Response to Refuse to Accept
  - Response to Report Deficient
  - Voluntary Withdrawal by Sponsor

An amendment may be submitted to each of the 3 parent document types: Original IDE submission, IDE Supplement, or an IDE Report.
IDE Tracking System – Supplements and Reports

- IDE Supplements and Reports are tracked independently and are numbered consecutively in the order in which they are submitted.

- Example IDE Tracking
  - Submission 1: Original IDE Submission
  - Submission 2: Supplement 001
  - Submission 3: Report 001
  - Submission 4: Supplement 002
IDE Tracking System – Amendments

• Amendments may be submitted to the original IDE, an IDE supplement, or an IDE report.
  – Each amendment should reference the number of the submission that is being amended.

• Example IDE Tracking
  – Submission 1: Original IDE Submission
  – Submission 2: Supplement 001
  – Submission 3: Report 001
  – Submission 4: Supplement 002
  – FDA Deficiency Letter Received
  – Submission 5: Amendment 001 to Supplement 002
  – FDA Deficiency Letter Received
  – Submission 6: Amendment 002 to Supplement 002
Terminating/Closing an IDE

- If IDE is not yet approved: request a withdrawal
- If you have an active IDE, but no subjects enrolled: request a withdrawal, but state why and account for all the device
- If subjects have been enrolled: you might need to complete follow-up of already enrolled subjects
- If you completed the study: notify FDA within 30-days and send Final Report within 6 months
Let’s Practice…

Please open the following website on your phone/tablet: pollev.com/oraq
Case Scenario

• A sponsor-investigator is developing a novel device to enable ablation of epileptic loci in the brain by a surgical robot.
• The sponsor-investigator has completed an early feasibility study in 5 patients with promising results and would like to perform a larger feasibility study evaluating safety and efficacy endpoints in more subjects.
The submission of this new clinical study protocol is best submitted as:

- An Original IDE Application
- A Supplement to the Existing IDE
- A Report to the Existing IDE
- An Amendment to the Existing IDE
Case Scenario

• The sponsor-investigator developing the novel device to enable ablation of epileptic loci in the brain by a surgical robot received approval to move forward with a larger feasibility study.

• During the feasibility study, the robot malfunctioned in an unexpected manner and ablated untargeted brain tissue, resulting in a study participant’s death.
This unanticipated adverse device effect should be submitted to FDA as:

- A supplement
- An amendment
- A report
PART 2: IDE Best Practices and Additional Studies

- Pre-submission Meetings
- IDE Preparation and Submission
- IDE Maintenance
- Expanded Access Program
Expanded Access for Medical Devices

- Life-threatening or serious condition
- No generally acceptable alternative treatment exists

- Emergency Use
  - Life-threatening situation that needs immediate treatment
  - There is no time to use existing procedures to get FDA approval
  - Must be reported to FDA, IRB within 5 days

- Non-Emergency Use
  - Prior approval of FDA and IRB is required
Expanded Access for Medical Devices

• **Compassionate Use**
  - Individual Patient/Small Group Access
  - Time-frame: during clinical trial

• **Treatment Use IDE**
  - Device is under investigation for the same use under an approved IDE or all clinical trials have been completed
  - Sponsor is pursuing marketing approval/clearance of the investigational device with due diligence
  - Time-frame: late stage clinical trials or after trial completion
Let’s Practice…

Please open the following website on your phone/tablet:

pollev.com/oraq
Case Scenario

• A physician wants to use an investigational ventricular assist device (VAD) on her patient while they are recovering after surgery
• A ventricular assist device (VAD) is a mechanical pump that's used to support heart function and blood flow in people who have weakened hearts
• An early publication showed decreased risk of blood clots compared to approved VADs
Would this patient be eligible for compassionate use of the VAD?

When poll is active, respond at PollEv.com/oraq

Text ORAQ to 37607 once to join

Yes

No
Case Scenario

• A physician wants to use an investigational autologous cell harvesting device to treat a burn victim with life threatening burns
• The patient has insufficient skin for conventional grafting
Would this burn victim be eligible for compassionate use?

Yes

No
Case Scenario

• A patient with moderate hearing loss wants to try an investigational device that may help to prevent additional hearing loss
Would this hearing loss patient be eligible for compassionate use?

Yes

No
Useful Websites:

CDRH Learn Course List
http://www.fda.gov/Training/CDRHLearn/default.htm

Device Advice:
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/default.htm
Thank you!

Questions?
Please contact us at
ORAQ@dm.duke.edu