FDA Investigational Device Exemption (IDE) Studies

Inna Strakovsky, MPH, CCRC
Sr. Regulatory Affairs Specialist
Office of Clinical Research (OCR)

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Learning Objectives

- Define basic terms related to device research
- Locate applicable regulations
- Determine when an IDE is required
- Describe Sponsor & Investigator responsibilities
- Know contents and submission process for an IDE Application
- Conduct IDE management activities
What is a Medical Device?

- Instrument, apparatus, implement, machine, contrivance, implant, in-vitro reagent, or other similar or related article or component, part, or accessory, which is:
  1) Recognized in the official National Formulary or the United States Pharmacopoeia;
  2) Intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease or other conditions
     OR
     Intended to affect the structure or function of the body
  3) Does not achieve its primary intended purposes through chemical action within or on the body AND is not dependent upon being metabolized for the achievement of any of its primary intended purposes.

Reference: www.fda.gov/aboutfda/transparency/basics/ucm211822.htm
What is an Investigational Device?

- A device that is the object of an investigation.
  - Any investigational phase
  - Device regulations apply regardless of phase
When is an IDE application required?

- Investigational device is not exempt from requirements AND
- Investigational device is a Significant Risk (SR) device

Need to determine

- Is device exempt from IDE requirements?
- Is device a Significant Risk (SR) device?
Devices exempt from IDE requirements

- Legally marketed device when used in accordance with its labeling;
- Diagnostic device if it complies with the labeling requirements and if the testing:
  - 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.

- Consumer preference testing, testing of a modification, or testing of a combination of devices if the device(s) are legally marketed.

Reference: 21 CFR 812.2(c)
Is my device exempt from IDE requirements?

- OCR is able to grant IDE exemptions and provide additional support and guidance

Office of Clinical Research (OCR)
IND/IDE Support Unit
8041 Maloney Building
(215) 746-8334
ocr@exchange.upenn.edu
Significant Risk Device

- Investigational device that presents a potential for serious risk to the health, safety or welfare of a subject due to its intended use AND is used:
  - As an implant OR
  - For supporting or sustaining human life OR
  - Of substantial importance in diagnosing, curing, mitigating, or treating disease or otherwise preventing impairment of human health OR
  - For any other reason.

Does my device present Significant Risk?

- Principal investigator makes the initial determination
- If Significant Risk (SR)
  - Submit IDE application to FDA
  - Submit IRB application to IRB
- If Non-Significant Risk (NSR)
  - Submit determination to the IRB
  - IRB has to agree that device is NSR
  - If IRB disagrees, must submit IDE application to FDA
- Contact IRB or OCR for further guidance
Medical Device

- Investigational Device
  - Exempt from IDE Requirements: May need IRB Approval
  - Non-exempt from IDE Requirements: Significant Risk (SR) Device: FDA Approval (IDE Application)
  - Not Exempt from IDE Requirements: Non-Significant Risk (NSR) Device: IRB Approval
- Non-investigational Device (clinical use): IRB Approval
Investigational Device Exemption (IDE)

- Approval from FDA to use an investigational device in a clinical study in order to collect safety and effectiveness data.

- Types:
  - Traditional
  - Emergency use
  - Compassionate use
  - Treatment use
  - Continued access

IDE Sponsor

- A person who initiates, but does not actually conduct, the investigation. The investigational device is administered, dispensed, or used under the immediate direction of another individual.

Reference: 21 CFR 812.3(n)
IDE Investigator

- The individual who actually conducts a clinical investigation, i.e. under whose immediate direction the test article is administered or dispensed to, or used involving, a subject. If the investigation is conducted by a team of individuals, the investigator is the responsible leader.

- Co-investigator – has same responsibility as investigator

Reference: 21 CFR 812(i)
IDE Sponsor Responsibilities

- Obtain FDA approval to proceed
- Ensure IRB approval is obtained
- Select qualified investigators and vendors
  - Obtain specified information from each investigator before permitting an investigator to begin participation in any studies
  - Obtain periodic updates

IDE Sponsor Responsibilities

- Provide each clinical investigator information necessary to conduct the study
  - Ensure new information provided to investigators, FDA and IRB
- Ensure that the investigation is conducted in accordance with the investigational plan and current protocol
- Monitor the study and evaluate adverse events
- Control the investigational device
- Maintain accurate, complete, and current records

IDE Sponsor Responsibilities

- Register applicable trials on ClinicalTrials.gov
- Ensure timely submissions to the FDA and other applicable agencies
- Withdraw the IDE after the completion of all trials
- Manage investigator noncompliance

PSOM IND/IDE Sponsor Qualifications

- Member of PSOM standing faculty
- Physician/Dentist with current US license or has a licensed individual to review safety
- Experience with FDA-regulated clinical research
- Successful completion of OCR Sponsor training
- Availability of adequate resources
- No continuing non-compliance with clinical trial oversight or conduct
- No significant financial conflict of interest (fCOI) related to the IND/IDE or the clinical trial
- Not a direct report of a Penn faculty member who has a significant fCOI relative to the clinical trial or the IND/IDE

Selecting Qualified Investigators

- Ensure they are not disqualified and/or restricted by the FDA
  - Check the database: www.fda.gov/ICECI/EnforcementActions/UCM321308

- Obtain from each prior to allowing participation:
  - Signed Investigator Agreement
  - CV, additional statement of qualifications
  - Current US professional license (medical, nursing, etc.)
  - Financial disclosure information
  - Ensure each IRB is registered with DHHS

- Document qualifications of each investigator
  - Based on training and experience
  - Ensure each investigator remains qualified throughout the study
IDE Investigator Responsibilities

• Protect rights, safety, welfare of subjects
  • Ensure informed consent is obtained

• Ensure investigation is conducted according to:
  • Signed agreement,
  • Investigational plan,
  • Applicable regulations.

• Follow the Sponsor’s instructions for investigational device use, disposal, or return

Reference: 21 CFR 812.100-119
IDE Investigator Responsibilities

- Control devices under investigation
  - Use only for subjects enrolled in study
- Communicate with the Sponsor, research team, and IRB
- Disclose accurate financial information to the Sponsor
- Maintain accurate, complete, and current records

Reference: 21 CFR 812.100-119
Financial Information

❖ Sponsor
  • Must collect financial information from investigators
    – Before permitting to participate in the study AND
    – At periodic intervals

❖ Investigator
  • Must disclose financial information to the Sponsor
    – Before beginning participation in the study AND
    – At periodic intervals
Pre-IDE Communication

- OCR is available for support and guidance
- FDA has mechanisms for providing feedback before a submission (“Pre-Sub”)
- May be helpful if:
  - New device involves novel technology
  - “First of a kind” indication
  - New indication for existing device
  - New device does not clearly fall within an established regulatory pathway
  - Specific protocol design questions
  - Clarification of how much existing data may be leveraged in future marketing applications
IDE Application Template

- IDE Application template, cover letter template, and application instructions available from OCR

Application for an Investigational Device Exemption

Name of device: [insert full name]
Intended use of the device: [insert brief statement]
Protocol title: [insert full title]
Protocol version number: [insert version number]
Protocol date: [insert version date]

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IDE Application Content

- Cover page
- Table of contents
- Prior investigations of the device
- Investigational plan
- Device manufacturing information
- Example of investigator agreement
- Information for all investigators
- Certification
- IRB information
- Device billing information
- Device labeling
- Informed consent forms
- Other information
Application: Prior investigations

- Allows an evaluation of the safety and effectiveness of the device to justify the proposed study

**Contents**

- All prior clinical, animal, and laboratory testing of the device.
- Both adverse and supportive information, both published and unpublished, from all sources
- Bibliography here or in appendix
Application: Investigational Plan

- Not the same as protocol!
- Describes and justifies the study(ies) in detail

Contents

- Objectives and duration of study(ies)
- Protocol(s)
- Risk analysis
- Description of device
- Monitoring procedures
- Additional records and reports
Application: Device Manufacturing

- Provides detailed information about each device

- Contents
  - Methods, facilities, and controls used for manufacturing, processing, packing, storage, and installation of device
Application: Investigator Information

- Example of Investigator Agreement
  - Contains statements related to investigator responsibilities in conducting a protocol under an IDE
  - Template that principal investigators and sub-investigators will be asked to sign

- List of Investigators who signed Investigator Agreement
  - Names and addresses of all investigators who have signed the investigator’s agreement
Application: Certification

- Section certifies that Sponsor will ensure that
  - All participating investigators signed the agreement;
  - List includes all participating investigators;
  - Investigators will not be added until they sign the agreement.

- OCR’s IDE application template contains standard wording for this section
Application: IRB Information

- Information about each IRB that has or will be asked to review the study
  - Name, address, name of chairperson
  - IRB approval letter

- Some IRBs may not release names of members
  - Obtain memo from the IRB and attach it to the application
  - Penn IRB does not release names of members
    - OCR’s IDE application template includes the memo from Penn’s IRB to this regard
Application: Device Billing

- If you do not plan to charge for the device, state so.
- If you will be charging for the device, indicate:
  - Amount to be charged
  - Explanation of why the sale does not constitute commercialization of the device
Application: Device Labeling

- Include text that will be on the label of the device
- Must include the following statement:
  - CAUTION – Investigational Device. Limited by Federal (or United States) Law to Investigational Use.
- Must also include:
  - Name and address of the manufacturer, packer, or distributor;
  - Quantity;
  - Description of all relevant contraindications, warnings, precautions, adverse effects, and interfering substances or devices.
Application: Informed Consent and Other Information

- **Informed Consent Documents**
  - Include the informed consent form and other materials that will be provided to subjects

- **Other information**
  - Include any other relevant information that the FDA has requested
Submitting the IDE Application

- 1 paper copy + 2 electronic copies
  - eCopy of the paper submission on a CD, DVD, or flash drive

- IDE Sponsor must be located in the U.S.

- IDE Sponsor must submit the IDE application
  - Unless authorization in writing for another to submit on their behalf

FDA Action on IDE Applications

- FDA will notify Sponsor in writing of the date it receives the IDE application

- IDE becomes effective 30 days after the submission has been received by FDA
  - Unless FDA has informed the sponsor prior to 30 days that the IDE is
    - Approved OR
    - Approved with conditions OR
    - Disapproved
FDA Approval of an IDE

- FDA decision letter will include:
  - IDE number
    - May already know, if did Pre-Sub
  - Strict limits on number of subjects and sites
  - Device Categorization (A or B)
    - Important for billing
  - Possible conditions or recommendations that should be addressed or considered
IDE is approved! Now what?
Registration on ClinicalTrials.gov

- Responsible party
  - Sponsor, unless designates another individual

- “Applicable clinical trials” must be registered:

  ![Diagram](http://prsinfo.clinicaltrials.gov/ElaborationsOnDefinitions.pdf)

- Update per regulations

Trial Master File (TMF)

- Sponsor’s records for the IDE and the clinical trial
- Keep all essential documents
  - OCR template
- Best practices
  - Update on a regular basis
  - “If it’s not documented, it hasn’t happened.”
- OCR can assist in developing and/or review your current TMF
Trial Master File (TMF)

- Protocol
- ICF/HIPAA
- Investigational product
- Case Report Forms
- Monitoring
- Adverse Events and Adverse Device Effects
- FDA submissions
- Other agency submissions
- Contractual agreements
- Vendor qualifications
- Sponsor personnel
- Other documents
Investigational Plan Changes

- Investigational plan changes must be prospectively approved by the FDA and the IRB if they affect:
  - Validity of data
  - Risk-benefit ratio
  - Scientific soundness
  - Rights, safety, and welfare of subjects

- Exceptions
  - Emergencies
  - Minor changes
Investigational Device Management

- Allow access only to qualified investigators
- Supervise all use
- Retain all relevant information
- Record accountability
- Document all changes
Monitoring

- Determine approach and method
- Develop a monitoring plan
- Select a qualified monitor
- Manage non-compliance
# FDA Expedited Reporting

## IND/IDE Sponsor FDA Safety and Expedited Reporting Requirements

<table>
<thead>
<tr>
<th>Adverse Event / Adverse Reaction Classification</th>
<th>FDA Reporting Requirements</th>
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<tbody>
<tr>
<td><strong>Serious</strong></td>
<td><strong>Drug/Device Related</strong></td>
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### Other Events

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<tbody>
<tr>
<td><strong>IND Sponsor</strong></td>
<td>≤ 15 calendar days</td>
<td>Findings from clinical, epidemiological, or pooled analyses of multiple studies or any findings from animal or in vitro testing that suggests a significant risk in humans exposed to the drug</td>
</tr>
<tr>
<td><strong>IDE Sponsor</strong></td>
<td>≤ 5 working days</td>
<td>Protocol deviations to protect the life of the subject in emergency, Withdrawal of IRB approval, Lack of Informed Consent</td>
</tr>
</tbody>
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Reference: [https://somapps.med.upenn.edu/pennmanual/secure/pm/reporting#SafetyandExpeditedReportingCharts](https://somapps.med.upenn.edu/pennmanual/secure/pm/reporting#SafetyandExpeditedReportingCharts)
Sponsor Reports

- Current investigator list
- Progress reports
- Unanticipated Adverse Device Effects (UADE)
- Withdrawal of IRB approval
- Withdrawal of FDA approval
- Recall and device dispositions
- Use of device without informed consent
- Final report
- Other reports
Investigator Reports

- Progress report
- Unanticipated Adverse Device Effect (UADE)
- Deviations
- Use of device without informed consent
- Withdrawal of IRB approval
- Final report
- Other reports
Where are these regulations located?

Available Resources

- Penn Manual
  [https://somapps.med.upenn.edu/pennmanual/secure/](https://somapps.med.upenn.edu/pennmanual/secure/)
- Sponsor SOPs
  - Coming soon
- Tools and templates
Office of Clinical Research
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8041 Maloney Building
(215) 746-8334
ocr@exchange.upenn.edu

Inna Strakovsky
Sr. Regulatory Affairs Specialist
(215) 662-4632
innastr@exchange.upenn.edu