What is an Investigational Device Exemption (IDE)?

Lynn Henley
Investigational Device Exemption Program

Office of Device Evaluation
Center for Devices and Radiological Health
Food and Drug Administration

Outline of Presentation

- The purpose of an IDE submission
- Different types of IDEs
- Study determination or pre-submission
- What an IDE does and does not permit
- When manufacturers or physicians should seek an IDE
- Significant and Non-Significant Risk
- Diagnostic studies
- Roles of sponsors, investigators, and Institutional Review Boards (IRBs)
- IDEs the product development process

Investigational Device Exemption

- An IDE is a **regulatory submission** that permits clinical investigation of devices.
- This investigation is **exempt** from some regulatory requirements.
- The term "IDE" stems from this description in 21 Code of Federal Regulations (CFR) 812.1:

  "An approved investigational device exemption (IDE) permits a device that otherwise would be required to comply with a performance standard or to have premarket approval to be shipped lawfully for the purpose of conducting investigations of that device."

Federal Food, Drug, and Cosmetic Act ⇒ Regulation

Several parts of the Code of Federal Regulations (21 CFR) pertain to IDEs:

- **Part 812 - Investigational Device Exemptions**
- **Part 50 - Protection of Human Subjects and Informed Consent**
- **Part 54 - Financial Disclosure of Investigators**

- **Part 56 - Institutional Review Boards**

Section 520(g) of the Food, Drug, and Cosmetic Act

Purpose of an IDE

"To encourage discovery and development of useful medical devices for human use, to the extent consistent with the protection of the public health and safety and with ethical standards, while maintaining optimum freedom for scientific investigators in their pursuit of that purpose."

Purpose of an IDE

An approved Investigational Device Exemption allows:

- **an investigational device to be used in a clinical study in order to collect safety and effectiveness data required to support a Premarket Approval (PMA) application, a Humanitarian Device Exemption (HDE), or a Premarket Notification [510(k)] submission to FDA.**

- **a device to be shipped lawfully for the purpose of conducting investigations**

Provisions of the IDE Regulation

- All clinical investigations subject to the regulation must be **approved** before they can begin
- **Assigns responsibilities** to all participants in clinical study
- All subjects in the investigation must give **informed consent**

Definitions

Investigational Device

- **Is still in the developmental stage**
- **Object of a clinical investigation is to determine safety and effectiveness**
- **Is not considered to be in commercial distribution**

Investigational Use

- **Clinical evaluation of an already legally marketed device for a new intended use or a new indication for use**

Different Types of IDEs

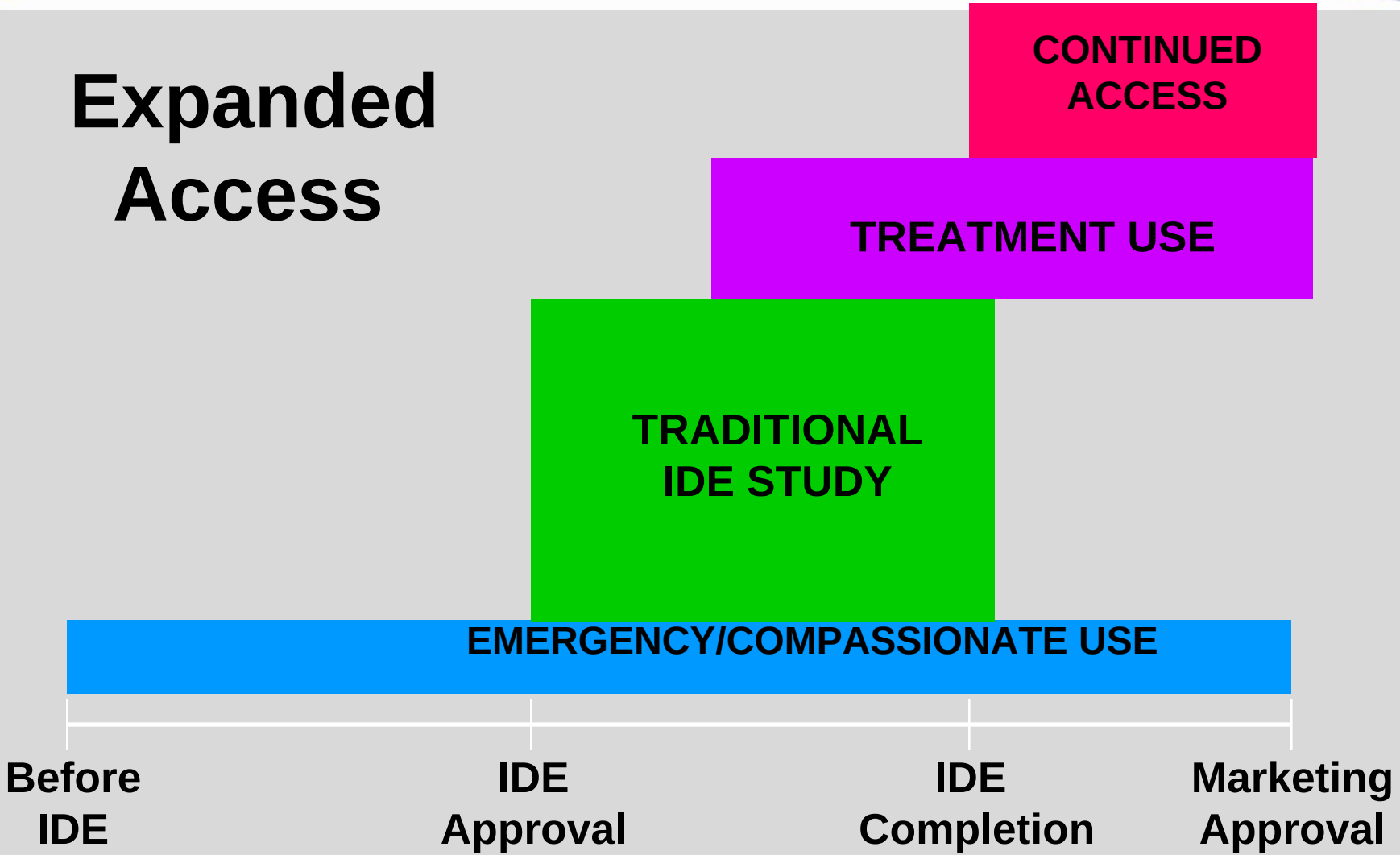
Traditional IDE Studies

- Feasibility Study (Early or Traditional)
- Pivotal Study

Expanded Access Studies

- Emergency Use
- Compassionate Use
- Treatment Use
- Continued Access

Expanded Access



Study Determination or Pre-Submission

- If an IRB is uncertain whether a study is exempt, significant risk or non-significant risk, FDA will make a determination
- Sponsor submits a draft protocol and details about the device to be investigated in the form of a Pre-Submission
- Presents an opportunity for sponsor to get feedback on study from review division
- FDA will issue a letter, usually within 60 days; the **determination is binding** for both sponsor and IRB

Approved IDEs are Exempt from Regulations Pertaining to:

- Misbranding
- Registration
- Pre-Market Notification [510(k)]
- Pre-Market Approvals (PMAs)
- Performance standards
- Good Manufacturing Practices (GMPs) except Design Controls
- Color additive requirements
- Banned devices
- Restricted device requirements

21 CFR 812.1

Approved IDEs are not Exempt from Regulations Pertaining to:

- Adulteration
- Labeling
- Prohibition of: promotion and/or marketing, commercialization, prolonging the investigation, representing the device as safe and effective
- Import/export requirements

FD&C Act, Section 501; 21 CFR 812.5, 812.7, 812.18

Studies Subject to the Regulation

- **To support marketing application [PMA, HDE or 510(k)]**
- **Collection of safety and effectiveness information (e.g., for a new intended use of a legally marketed device)**
- **A sponsor-investigator study of an unapproved device or a new intended use of an approved device (even if no marketing application planned)**

21 CFR 812.2

All Device Investigations

- **Studies Subject to the IDE Regulation**
  - **Significant Risk**
    - **Full Requirements**
  - **Non-Significant Risk**
    - **Abbreviated Requirements**
- **Studies Exempt from the IDE Regulation**

Studies Exempt from Need for an IDE

- Preamendment (pre-1976) devices
- 510(k)-cleared or PMA-approved devices, if used in accordance with approved labeling
- *In vitro* diagnostic devices (most of the time)
- Consumer preference testing
- Combinations of legally marketed devices
- Custom devices (narrowly defined)

21 CFR 812.2(c)

Practice of Medicine

"Nothing in this Act shall be construed to limit or interfere with the authority of a health care practitioner to prescribe or administer any legally marketed device to a patient for any condition or disease within a legitimate health care practitioner-patient relationship…."

From Section 906 of the Food Drug and Cosmetic Act

Practice of Medicine

- Physician should:
  - Be well informed about the product
  - Use firm scientific rationale and sound medical evidence
  - Maintain records on use and effects
- IDE not required; institution may require IRB review, approval and informed consent
- Prohibitions on promotion of unapproved uses of legally marketed devices still apply

FD&C Act, Section 906

Basic Physiological Research

- Investigating a physiological principle
- No intent to develop the device for marketing
- Only using the device to address the research question

⇨ **No IDE needed**; IRB approval and informed consent should be obtained

21 CFR 812.2(a)

If not Exempt from Device Regulation, then…

- Need to assess whether proposed study of device is considered Significant Risk (SR), or Non-significant Risk (NSR)
- IRBs can and do make this assessment most of the time
- If IRBs or sponsors need assistance in making or request that FDA make risk determinations, FDA's determination is final

Significant Risk Study

Presents a potential for serious risk to the health, safety, and welfare of a subject and is:

- **an implant; or**
- **used in supporting or sustaining human life; or**
- **of substantial importance in diagnosing, curing, mitigating, or treating disease or preventing impairment of human health**

Significant Risk Study Examples

- Evaluation of a marketed biliary stent for use in the peripheral vasculature
- Evaluation of an unapproved radiofrequency ablation device for treatment of primary hepatic neoplasia
- Extended wear contact lenses

Significant Risk Studies

- Sponsor submits IDE application to FDA
- FDA **approves, approves with conditions,** or **disapproves** IDE within 30 calendar days
- Sponsor obtains IRB approval
- After **both** FDA and IRB approve the investigation, study may begin

Significant Risk Studies

- Each IDE should include **one indication** only
- If an **additional study** is sent in for a particular IDE, it receives a new 30 day review clock
- **"Approved with Conditions"** signifies that the study may begin, but that certain conditions have been stipulated and must be met by the sponsor
- Most IDE **review decisions** consist of either "approved" or "approved with conditions"

Non-Significant Risk Studies

- Sponsor presents protocol to IRB and a statement why investigation does not pose significant risk
- If IRB approves the investigation as NSR, it may begin
- **Abbreviated** IDE requirements (labeling, IRB, informed consent, monitoring, reporting, prohibition of promotional activities)
- **No IDE** submission to FDA needed

Non-Significant Risk Study Examples

- Most functional MRI studies
- Study of non-invasive blood pressure measuring device
- Electroencephalography studies
- Contact lens studies (daily wear only)

IDEs for In Vitro Diagnostics (IVDs)

- When an **IDE** is required for **IVD studies,** same principles of SR versus NSR apply
- Use of IVD test results to assign different study arms may result in either SR or NSR
- **Correlation studies**, where IVD test results do not impact patient management in those studies, are **generally exempt** from the need for an IDE
- IVD tests (any combination of equipment, disposables, software, procedures, algorithms) used in clinical trials outside their cleared/approved intended uses are investigational devices

- **May submit an IDE to CDRH or device validation information in an IND amendment to the Center for Drug Evaluation and Research (CDER) or Center for Biologics Evaluation and Research (CBER)**

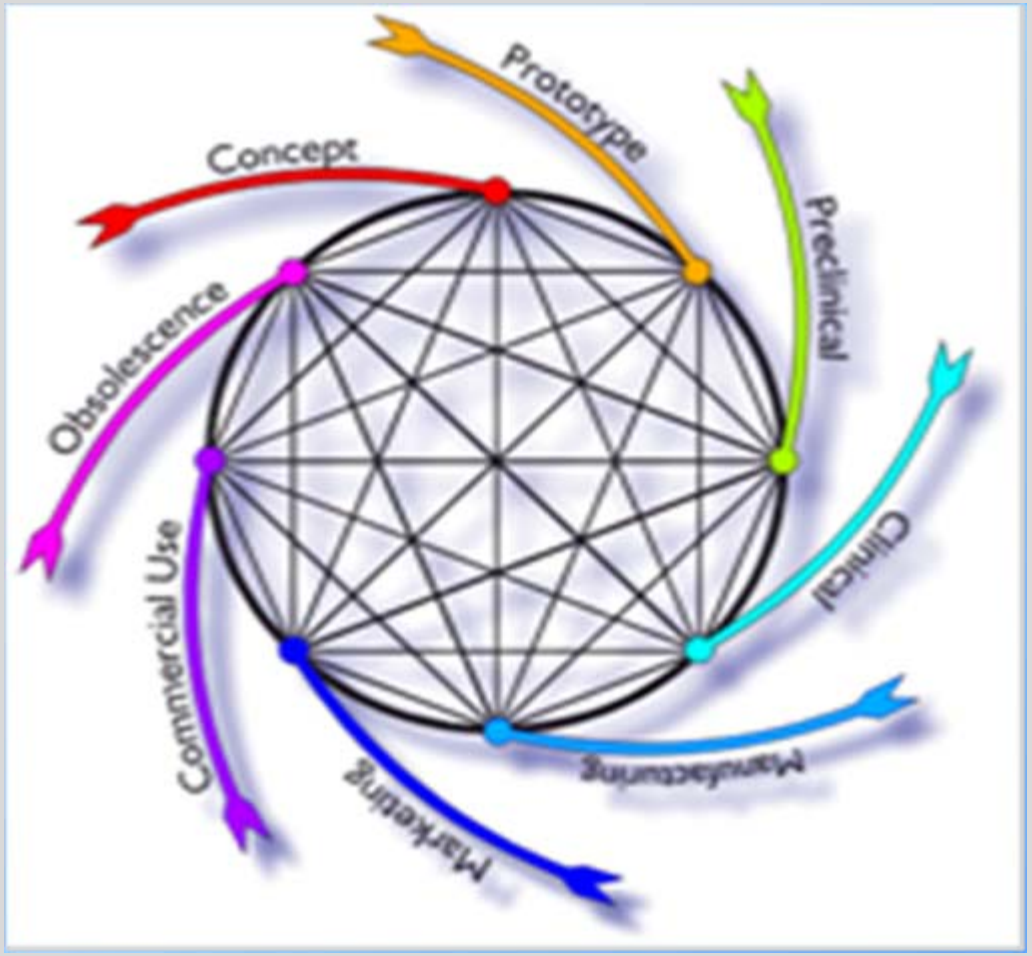
- **No need for both as CDER or CBER will consult CDRH when appropriate**

Clinical Laboratory Improvement Amendments (CLIA)

- **Results reported from human testing are subject to CLIA**

- **CLIA regulates clinical laboratory practice, while the FD&C Act regulates the medical devices used in clinical laboratories**

- **Patient-specific investigational IVD data (e.g., reported and used to select subjects for trials or to assign or alter subjects' clinical management) must be generated in compliance with CLIA**


Concept
Prototype
Preclinical
Clinical
Manufacturing
Marketing
Commercial Use
Obsolescence

Resources

- **Information Sheet Guidance For IRBs, Clinical Investigators, and Sponsors**

  www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126418.pdf

- **Device Advice:**

  www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/default.htm

- **CDRH Learn (including information about sponsor responsibilities, investigator responsibilities, IRBs, and the Bioresearch Monitoring Program):**

  www.fda.gov/Training/CDRHLearn/default.htm

If you have any questions, contact the Division of Small Manufacturers, International and Consumer Assistance (DSMICA)
at:
dsmica@fda.hhs.gov

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