Today’s Topics

- Federal Drug Administration (FDA): Introduction
- When Do FDA Regulations Apply?
- Investigational Drugs
- Investigational Medical Devices
- Expanded Access (Compassionate Use)
- Humanitarian Use Devices (HUD)
- Emergency Use of a Test Article (Drug, Biologic, or Device)
- FAQs
Federal Drug Administration (FDA): Introduction
When Do FDA Regulations Apply?

- Clinical investigation instead of research
- Test article, what’s that?
- Not your typical human subject…
Are you confused yet?

I don't get paid unless you are confused
Investigational Drugs

- Testing of unapproved drugs
- Testing of approved drugs that involves new indications or significant labeling changes
Exemption from IND could be considered for:

- Clinical investigations using marketed drugs
- Bioequivalence/bioavailability studies
- Studies using radiolabeled or cold isotopes
- Studies using dietary supplements or foods
- Studies using endogenous compounds
- Pathogenesis studies using modified organisms
- Studies using wild-type organisms in challenge models
- Studies that do not have a commercial purpose

The FDA has two primary objectives in reviewing an IND:

1. to assure the safety and rights of subjects in all phases of an investigation; and
2. in phases 2 and 3, to help assure that the quality of the scientific evaluation of the drug is adequate to permit an evaluation of the drug’s effectiveness and safety (21 CFR 312.22).
Off-label Use in the Practice of Medicine

Approved products may be used by physicians outside of labeled indications for the practice of medicine

– No IND is needed
Best Practice?

It’s a much safer path to file an IND application and have it deemed exempt than not to file and later be subject to a determination that an IND should have been requested.
Never Forget the IRB

Whether an IND is or is not required, all clinical research must have IRB review and approval.
Let’s Practice!

Is an IND needed?

Pilot Study

How and from where should I start my research?

Conduct a Pilot Study. You will get all the answers.

VS.

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What do you think?

Is an IND needed for this small pilot study?
What do you think?

Is an IND needed for this small pilot study?

No!

A small pilot study is an appropriate first step in determining whether a change in labeling should be sought.
What do you think?

Is an IND needed for this *multi-center randomized study*?
What do you think?

Is an IND needed for this multi-center randomized study?

Yes!

IND Needed
Data could be important and should be considered by the FDA.

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Expanded Access (Compassionate Use)

- Expanded Access: Several parties have a role in an expanded access request
- Institutional Review Board (IRB)
- Licensed Physician
- FDA
- Company (Industry)

Expanded Access
- Single patient
- Intermediate-size patient population
- Large patient population
  - Emergency Use
  - Non-Emergency Use

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Individual Expanded Access Involving Investigational New Drugs (SPINDs)

FDA must determine that:

• Serious/immediately life-threatening disease or condition; no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition;

• Potential benefit justifies the potential risks of the drug; risks are not unreasonable;

• Does not interfere with the initiation/conduct/completion of clinical investigations that could support marketing approval of the expanded access use or otherwise compromise the potential development of the expanded access use; and

• The patient cannot obtain the investigational drug under another IND or protocol.
FDA Form 3296
(Emergency / Non-Emergency SPINDs):
Expedited IRB Review Request
Expanded Access for Intermediate-size Patient Populations and Widespread Use of a Treatment IND

Figure 2: Types of Expanded Access Requests that Occur throughout the Food and Drug Administration’s (FDA) Typical Drug Development and Approval Process

**Clinical Trials**
- **Phase I**: Drugs tested for safety and dosing ranges on 20 to 80 patients
- **Phase II**: Drugs tested for efficacy on a few dozen to hundreds of patients
- **Phase III**: Drugs tested for efficacy on hundreds to thousands of patients

**Review/Approval Process**
- New drug application review
- FDA approval results

- On average, 9.6% of drugs starting at phase I are approved

**Single-patient expanded access requests (emergency and non-emergency) can generally occur during or after phases I, II, or III clinical trials.**

**Intermediate expanded access requests are generally initiated during or after phase II clinical trials.**

**Treatment expanded access requests are generally initiated during phase III clinical trials or once clinical trials are complete when a manufacturer is pursuing FDA’s approval for marketing in the U.S.**

*Source: GAO analysis of FDA data. | GAO-17-564*

Note: According to FDA officials, there can be wide variation in the number of patients involved in the different clinical trial phases, and, when a new drug is being tested for a life-threatening ailment, the drug development process may be expedited by going through only one or two phases of clinical trials before an application is submitted to FDA for marketing approval.
Investigational Medical Devices

Class III
Requires Premarket Approval (PMA)

Class II
Requires 510(k) Premarket Notification

Class I
Majority of Devices Exempt from 510(k)
Let’s Practice!

Which of the following is a medical device?

- Pedometer
- Home blood glucose test
- Breast implants
- Birth control implant
- VR surgery simulator
What do you think?

Is a *pedometer* a medical device?
What do you think?

*Is a pedometer a medical device?*

**No!**

<table>
<thead>
<tr>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is it intended to diagnose, cure, mitigate, treat, or prevent disease?</td>
</tr>
<tr>
<td>Is it intended to affect the structure or any function of the body?</td>
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</tbody>
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<tr>
<th>AND</th>
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<tbody>
<tr>
<td>Primary intended purpose <strong>NOT</strong> achieved by chemical action or by being metabolized?</td>
</tr>
</tbody>
</table>
What do you think?

Is a *blood glucose test kit for home use* a *medical device*?
What do you think?

Is a **blood glucose test kit for home use** a medical device? **Yes!**

| OR | Is it intended to **diagnose, cure, mitigate, treat, or prevent** disease? | ✓ |
|    | Is it intended to **affect the structure** or any **function** of the body? | ✗ |
| AND | Primary intended purpose **NOT** achieved by **chemical action** or by being **metabolized**? | ✓ |
What do you think?

Are silicone breast implants medical devices?
What do you think?

Are silicone breast implants medical devices?

Yes!

<table>
<thead>
<tr>
<th>OR</th>
<th>Intended to <strong>diagnose, cure, mitigate, treat, or prevent</strong> disease?</th>
<th>✗</th>
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<td>✓</td>
</tr>
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</table>
What do you think?

Is a subdermal birth control implant [regulated as] a medical device?
What do you think?

*Is a subdermal birth control implant [regulated as] a medical device?*

No!

| OR | Is it intended to diagnose, cure, mitigate, treat, or prevent disease? | ✗ |
|    | Is it intended to affect the structure or any function of the body?    | ✓ |
| AND| Primary intended purpose **NOT** achieved by chemical action or by being metabolized? | ✗ |
What do you think?

Is a **VR surgical simulator** a medical device?
What do you think?

Is a **VR surgical simulator** a medical device?

**Yes!**

| OR | Is it intended to **diagnose, cure, mitigate, treat, or prevent** disease? | ✓ |
| OR | Is it intended to **affect the structure** or any **function** of the body? | ✗ |
| AND | Primary intended purpose **NOT** achieved by **chemical action** or by being **metabolized**? | ✓ |
Great JOB!!!
Does My Study Need an IDE?

When is an IDE needed?

- Device Study
  - Exempt
  - Not Exempt
    - Significant Risk (SR)
      - Full requirements
    - Non-Significant Risk (NSR)
      - Abbreviated requirements
Who Decides Whether A Device Study is SR or NSR?
Let’s talk about HUDs!

Use is intended to benefit patients with rare conditions or diseases (affecting not more than 8,000 people in the United States per year) and

HUD is exempt from the effectiveness requirements

The use of the device does NOT constitute research; however, federal regulations require the local IRB approve the use of a HUD before it is administered to local patients
Emergency Use of a Test Article (Drug, Biologic or Device)

Life-threatening

- Diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes where the end point of clinical trial analysis is survival.
- The criteria for life-threatening do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the subjects must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.

Severely Debilitating

- Diseases or conditions that cause major irreversible morbidity.
- Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.
What About Informed Consent and IRB Reporting of eINDs?

Informed Consent is waived IF:

- the patient is confronted by a life-threatening situation necessitating the use of the test article;
- informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the patient;
- time is not sufficient to obtain consent from the patient’s legal representative;
- no alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the patient’s life.

IRB reporting

- Reporting of the Emergency Use to the IRB is required of the investigator within five working days after use in a patient.
- This reporting is done via submission of an “Emergency Use of an investigational test article” application form in WRG and contains:
  - Completed form 3926 or 1572/1571
  - Letter of approval from the FDA/sponsor
  - Treatment plan
  - Independent physician concurrence to the proposed treatment plan
  - Consent form (signed if there was time to seek consent from the patient)
FAQs

Q: Can I submit my IRB application before I know if I need an IND?
A: Yes, it is possible to submit an IRB application for a clinical study before an IND submission; however, if the IRB determines an IND may be needed, the study may not proceed until confirmation of IND exemption or acknowledgment of IND receipt is obtained from FDA and the 30-day review period has passed.

Q. I’m using both a drug and a device on my study and I do not qualify for exemption. Do I need both an IND and an IDE?
A: No. Whether you need an IND, or an IDE depends on which product is the primary mode of action in the study. If an investigational drug product is the primary mode of action, you may need an IND. If an investigational device product is the primary mode of action, you may need an IDE. Product accountability and assessment of safety events should still occur for secondary (and other) investigational products.

Q. I submitted an IDE application and 30 days have passed. Can I start my study?
A: No. Unlike an IND, IDEs require approval by the FDA before the study can commence.

Q. If I’m using an approved drug (or device); do I need an IND (or IDE)?
A: If the use of the drug or device product on the protocol is per the approved product labeling, the study may be exempt from IND (or IDE) requirements.
FAQs (continued)

<table>
<thead>
<tr>
<th>Q. How do I obtain a device study risk determination?</th>
<th>Q. Do I need an investigator’s brochure and what should it include?</th>
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<tbody>
<tr>
<td><strong>A:</strong> The Sponsor or Sponsor-Investigator of the study should make and document an initial risk determination. The risk determination should take into account the use of the device on the protocol. This risk determination should be presented to the IRB. The IRB also needs to make a risk determination. If the IRB deems the device to be of non-significant risk, the Sponsor or Sponsor-Investigator will hold an abbreviated IDE. If the IRB determines the device to be of significant risk, the investigator must submit an IDE application to the FDA.</td>
<td><strong>A:</strong> An investigator’s brochure (IB) is a compilation of the clinical and nonclinical data on the investigational product(s) relevant to the IND/IDE. If an IND/IDE includes more than one investigational product, clinical and nonclinical data on each investigational product should be included. A medically qualified person should generally contribute to the authoring of an IB.</td>
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What We Covered

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For More Information on FDA-Regulated Research:

Please visit the WCM IRB website:
https://research.weill.cornell.edu/compliance/human-subjects-research/institutional-review-board/research-team-resources/fda-regulated
FDA Resources


- Expanded Access Contacts:
  - FDA’s Office of Health & Constituent Affairs at 301-796-8460 or PatientNetwork@fda.hhs.gov
  - CDER’s Division of Drug Information at 855-543-3784 or druginfo@fda.hhs.gov
  - CBER at 800-835-4709 or industry.biologics@fda.gov
Other Resources

Email:
WCM IRB Office: irb@med.cornell.edu
HRPO team: hrpo@med.cornell.edu
Questions?