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Welcome!

- The session will begin shortly; if you are joining us on Zoom, please take a moment to make sure your microphone is muted.
- The presentation portion of this session will be recorded.
- This presentation will include breakout sessions.
- Not registered? Please register now using the QR code.

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FDA-Regulated Research:

INDs, IDEs, and HUDs

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Human Research Protections

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5+ years in human subjects research regulatory compliance.

Former professor of Developmental Psychology at the State University of New York, mentored 41 theses.

15 years of research experience in the area of neurodevelopment, aging, and psycholinguistics, with numerous publications and conference presentations

Joined WCM in 2021

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Jessica Kisenwether, Ph.D., CIP, CCC-SLP

9+ years of experience in human research protections, serves as a regulatory expert for multiple institutions.

Licensed speech-language pathologist in PA and NY.

18 years of research experience in the area of speech science, specifically subjective and objective measures of voice, swallowing, dysfluency, and speech.

Published in numerous journals and presented at state, national, and international conferences

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Today's Topics

- Federal Drug Administration (FDA): Introduction
- When Do FDA Regulations Apply?
- Investigational New Drugs
- Investigational Medical Devices
- Humanitarian Use Devices (HUD)
- Expanded Access
- FAQs

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The Federal Drug Administration (FDA)

Oversight of:

- **Human drugs**
- **Veterinary drugs**
- **Biological products**
- **Medical devices**
- **Tobacco products**

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When Do FDA Regulations Apply?

First, some definitions…

- **Clinical investigation**
- **Test article**
- **Human subject**

If your study meets these definitions, FDA regulations will apply

When Do FDA Regulations Apply?

First, some definitions…

- **Clinical investigation**
  - Any experiment involving a test article and at least one human subject, the results of which are intended to be submitted later to, or held for inspection by, the FDA as part of an application for research or marketing permit
- **Test article**
- **Human subject**

If your study meets these definitions, FDA regulations will apply

When Do FDA Regulations Apply?

First, some definitions…

- **Clinical investigation**
- **Test article**
  - Drugs and medical devices, health apps, additives…
- **Human subject**

If your study meets these definitions, FDA regulations will apply

When Do FDA Regulations Apply?

First, some definitions…

- **Clinical investigation**
- **Test article**
- **Human subject**
  - An individual who is or becomes a research participant, either as a recipient of a test article or control.
  - A subject may be either a healthy human or a patient

If your study meets these definitions, FDA regulations will apply

When Do FDA Regulations Apply?

When a drug or medical device is being used to “cure, treat, mitigate, diagnose, or prevent disease in humans”

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Investigational New Drugs (INDs)

What is a “Drug”?

- **Articles* intended for use in the diagnosis, cure, treatment, mitigation, or prevention of disease (therapeutic component)**
- **Articles* intended to affect structure/any function of the body (pharmacology, MoA)**
- **Biological products**

“Articles” = Drugs

What is an Investigational New Drug (IND)?

- **Investigational New Drug (IND) application is required for:**
  - Non-approved drug or biologic
  - Approved drug that involves NEW indications or NEW patient population
- IND is not required for:
  - Off-labeled use in the practice of medicine

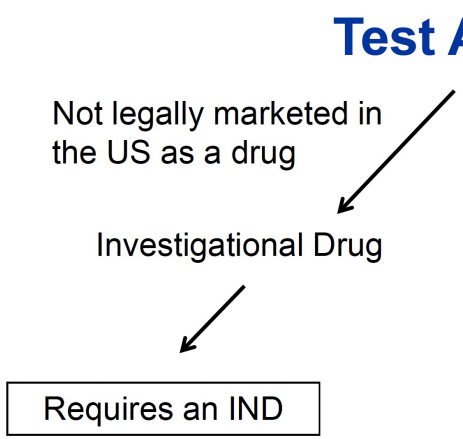
Why Is An IND Necessary?

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).

- **Two General IND Categories:**
  - Commercial
  - Non-Commercial (Research)

When is an IND Required?



- Clinical investigations using a product that is not lawfully marketed in the US as a drug require an IND.

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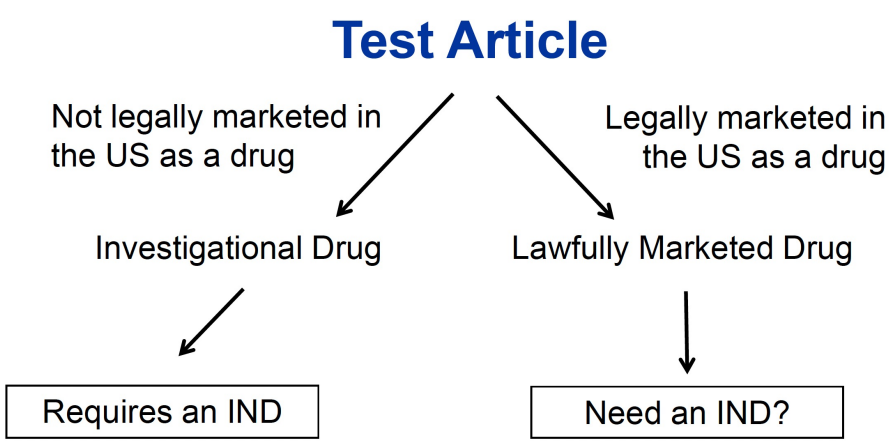
When is an IND Required?



- Clinical investigations using lawfully marketed drugs may or may not require an IND.

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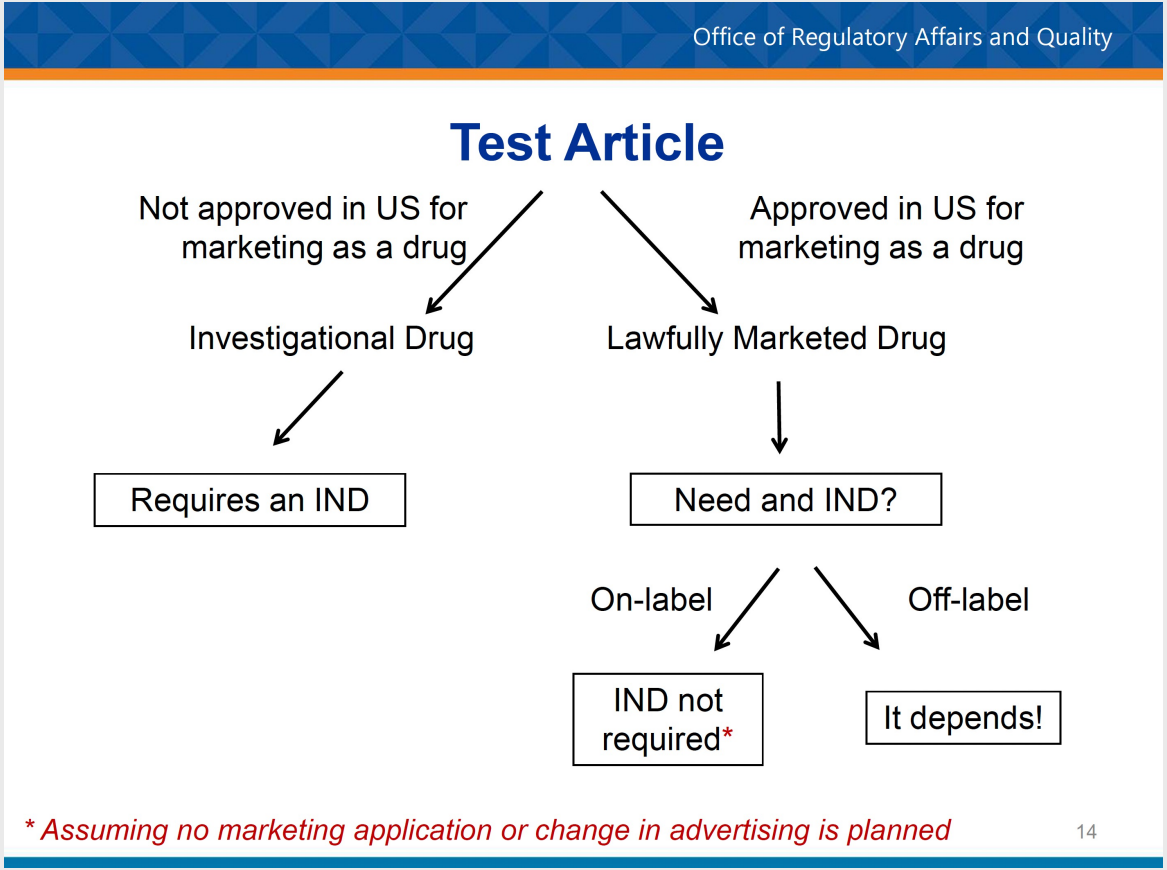
When is an IND Required?



IND Exemption Criteria 312.2(b)

1.	Not designed to support approval of a new indication or change in label.
2.	Not intended to support a significant change in the advertising for a prescription drug product
3.	**Does not involve a route of administration, dosage level, patient population, or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug**
4.	Conducted in compliance with the IRB and informed consent regulations
5.	Conducted in compliance with regulations regarding promotion for investigational drugs

FDA has issued guidance for IND exemption for drugs used to treat cancer, other life-threatening conditions:
https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM071717.pdf

Who Determines IND Exemption?

According to the FDA:

"because the assessment of risks involved in a therapeutic procedure is an everyday part of the practice of medicine, the individual investigator should usually be able to determine the applicability of the exemption."

- this statement is found in both FDA Guidance documents on IND Exemptions

- **Submit your rationale for why the clinical investigation is IND exempt directly to the WCM IRB**
- **If the IRB does not agree – an IND may be necessary**

Who Does What?

Role of the IRB

- Ensuring the protection of human subjects in clinical investigations
- Determination of whether an IND is needed

Role of the Sponsor(s)

- Monitoring progress
- Ensuring Current Good Manufacturing Practices (cGMP)
- Notifying the IRB of any changes
- ClinicalTrials.gov registration
- Maintaining the IND

Role of the PI(s)

- Ensuring the responsible conduct of research
- Ensuring investigation adheres to plan
- Protecting subjects
- Control of test articles
- Informed consent
- IRB maintenance and compliance

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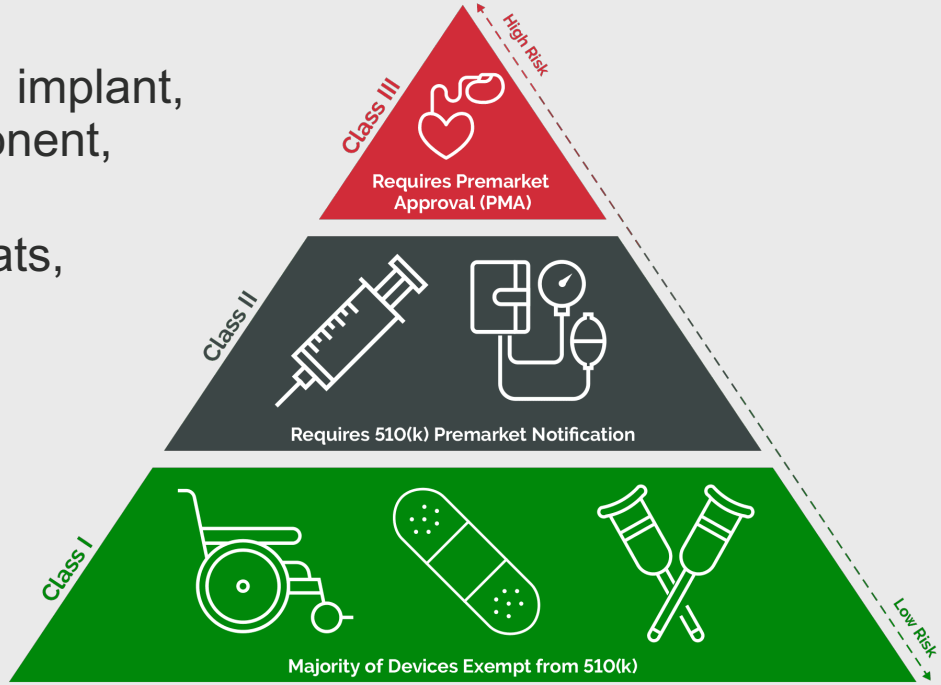
Investigational Device Exemption (IDE)

What is a “Medical Device”?

- **A Medical Device:**
  - Instrument, apparatus, machine, implant, in vitro reagent, including component, part, or accessory
  - Diagnoses, cures, mitigates, treats, or prevents disease or condition
  - Affects structure or function of the body
  - Doesn’t achieve purpose as a drug
- **Classification determines extent of regulatory control**



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Device Definitions

Term	Definition
Investigational Device	A device, including a transitional device, that is the object of an investigation
Transitional Device	A device subject to section 520(l) of the FD&C Act and which FDA previously regulated as a new drug or an antibiotic drug before 5/28/76
Significant Risk Device	A device that: 1. Is intended as an implant and presents a potential for serious risk; 2. Is for use in supporting or sustaining human life and represents a potential for serious risk; 3. Is for use of substantial importance in diagnosing, curing, mitigating, or treating disease or otherwise preventing impairment of human health and presents a potential for serious risk, or; 4. Otherwise presents a potential for serious risk to a subject.
Non-Significant Risk Device	A device that does not pose a significant risk to human subjects

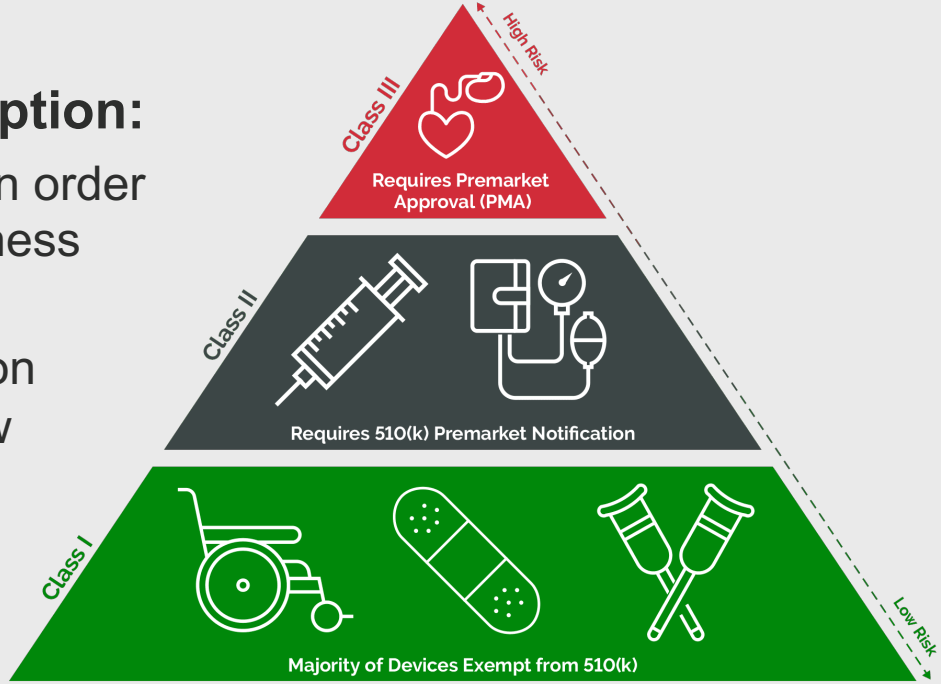
Does My Study Involve an Investigational Device?

- **If the device is the object of the investigation**
- **If you are collecting safety or effectiveness data about the device**

  YES, your study involves an investigational device
- **Examples:**
  - Multi-center clinical trial to collect effectiveness data of an implantable device **- YES**
  - Investigator-initiated study of the effectiveness of commercial VR headsets in pain reduction **- YES**
  - Study utilizing medical device to conduct assesments in accordance with its labeling **– NOT a device study**

What is an Investigational Device Exemption (IDE)?

- **Investigational Device Exemption:**
  - Allows use in a clinical study in order to collect safety and effectiveness data
  - Also includes clinical evaluation of certain modifications or new intended uses of legally marketed devices



When is an IDE Required?

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))

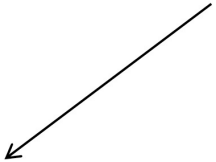
IDE required

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

b) IDE (21 CFR 812.20)

When is an IDE Required?

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))

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IDE Exemption Criteria 812.2(c)

1.	A legally marketed device when used in accordance with its labeling
2.	**A diagnostic device meeting diagnostic exemption criteria**
3.	A device undergoing consumer preference testing, testing of a 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
4.	A device intended solely for veterinary use
5.	A device for research on or with laboratory animals
6.	A custom device, unless the device is being used to determine safety or effectiveness for commercial distribution

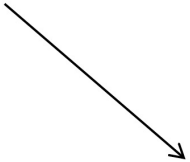
IDE Exemption Criteria 812.2(c)

2.	A diagnostic device meeting diagnostic exemption criteria

- Testing is noninvasive
- Testing does not require an invasive sampling procedure that presents a significant risk
- Testing does not by design or intention introduce energy into a subject
- Testing is not used as a diagnostic procedure without confirmation of the diagnosis by another medically established diagnostic product or procedure

When is an IDE Required?

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



IDE required

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

b) IDE (21 CFR 812.20)

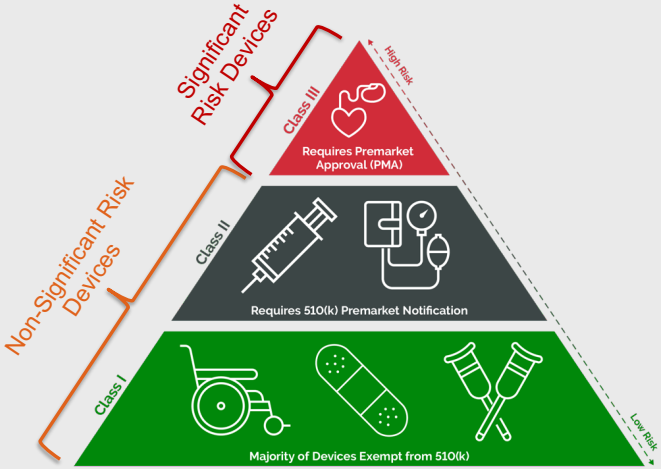
Abbreviated IDE vs. IDE

Abbreviated IDE

- Non-significant risk (NSR) device studies
- Overseen by the IRB

IDE

- Significant risk (SR) device studies
- Overseen by the FDA and IRB



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Non-Significant Risk Device	A device that does not pose a significant risk to human subjects

NSR vs. SR Device Studies: Example

Non-Significant Risk

- A study testing if a sensor pad can detect the electrical activity of the spinal cord
- Surgery/repair of spinal cord is already occurring
- Sensor pad is not implanted

Abbreviated IDE

Significant Risk

- A study testing if a sensor pad can detect the electrical activity of the spinal cord
- Surgery/repair of spinal cord was not already occurring
- Sensor pad is implanted
- Sensor pad otherwise meets definition of a significant risk device

IDE

Role of the IRB: Device Determinations of Risk

Exempt

IRB review is required to confirm that a study meets the criteria for IDE exemption

Non-Significant Risk

Convened IRB review required - If IRB concurs with device risk determination = Abbreviated IDE issued by the IRB

Significant Risk

FDA issues IDE - Convened IRB review required – IDE needed for approval

What the IRB Looks For

- **Risk of the study overall**
- **Explanation of risk determination of device**
  - Include: description of device, reports of prior investigations, proposed plan, inclusion criteria
  - Determination based on the **proposed use** of the device
  - Any procedures subjects must undergo
- **Documentation of IDE, if applicable**

Note: The study risk determination is based on the proposed use of the device in the investigation, not on the device alone.

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Humanitarian Use Devices (HUD)

What is a ”Humanitarian Use Device”?

- **An approved medical device intended to benefit patients in the treatment or diagnosis of a disease/condition affecting <8,000 individuals in the U.S.**
- **FDA approves a HUD by granting a Humanitarian Device Exemption (HDE)**

What is a Humanitarian Device Exemption?

- **Allows for marketing of a Humanitarian Use Device**
  - **Sponsor can ship the device**
  - **Sponsor can bill for use of the device**
- **FDA concludes there is no comparable device available to treat the disease or condition**
- **Fewer requirements than PMA pathway**

Role of the IRB

- **IRB review is required for clinical use of HUDs, even though it is not considered research!**
  - HUD may only be used in a facility after an IRB has approved its use in that facility (except in certain emergencies).
- **IRB approval can be for:**
  - general use
  - a specific patient population
  - for patients under a HUD protocol
  - on a case-by-case basis
- **IRB may have additional requirements**
  - measures of disease progression
  - informed consent

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Expanded Access

What is Expanded Access?

Provides a potential pathway for a patient with an immediately life-threatening condition or serious disease/condition to gain access to an investigational medical product for treatment outside of clinical trials when no comparable or satisfactory alternative therapies are available.

Criteria:

- Patient has **serious disease or condition**
- There is **no comparable or satisfactory alternate**
- Enrollment in **a clinical trial is not possible**
- **Potential benefit justifies the potential risks**
- Provision **will not interfere with investigational trials**

Physician Responsibilities

- Obtain *informed consent* from the patient or legal representative
- Obtain *clearance from the institution* as specified by their policies (e.g. permission from the Department Chair)
- Receive an *independent assessment* from an uninvolved physician; and
- *Authorization* from the device manufacturer
- Involve the IRB:
  - No time for IRB review: Alert the IRB within 5 days of use
  - Time for IRB review: Request review

IRB Review of Expanded Access

- **FDA and IRB approval is required *before* use of product (except in emergency situations in which there is not time for such approval)**
- **Risks are minimized and are reasonable in relation to anticipated benefits**
- **Patient history and treatment plan**
- **Appropriate information in the informed consent**

Specific requirements for IRB review vary by category of treatment use

Take home message:

Never forget the IRB!

Whether an IND, IDE, or HDE is or is not required, **all clinical research must have IRB review and approval**

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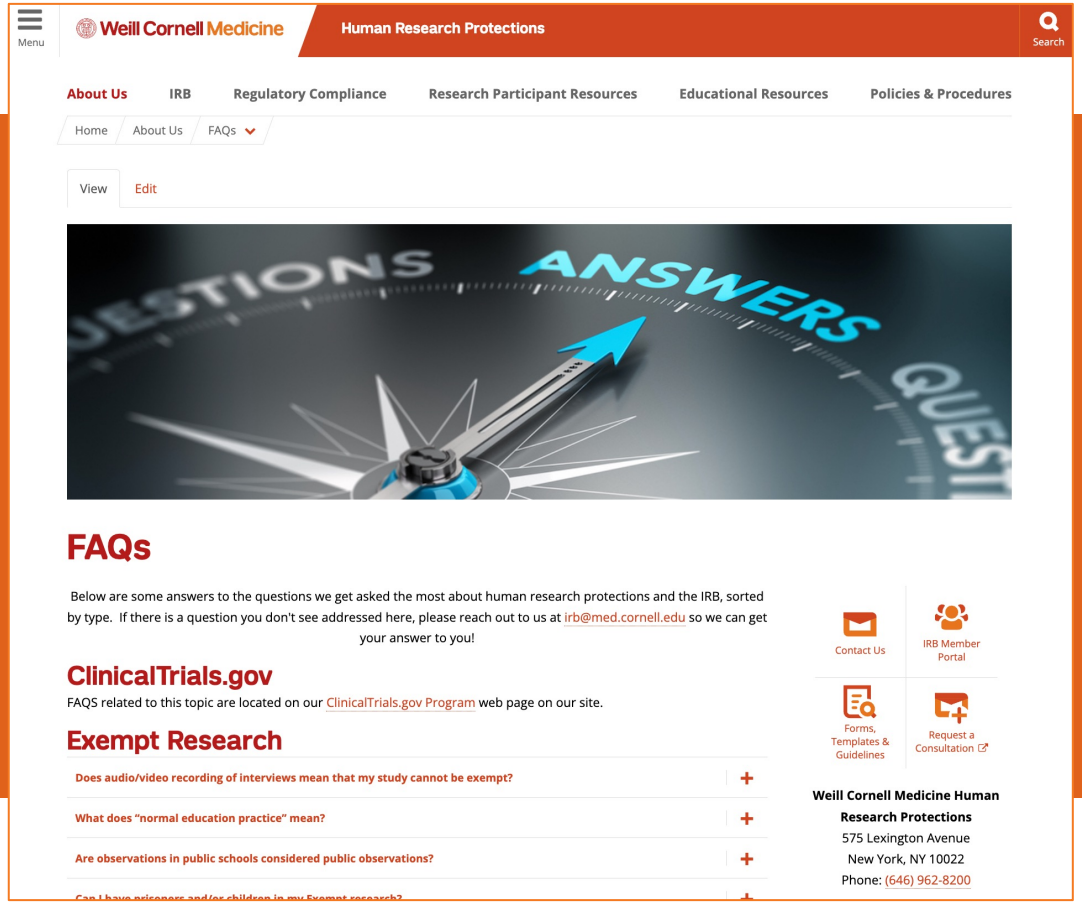
FAQs

https://hrp.weill.cornell.edu/about-us/faqs



Can I submit my IRB application before I know if I need an IND?

***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.*

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?

***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.*

I submitted an IDE application and 30 days have passed. Can I start my study?

***No**. Unlike an IND, IDEs require approval by the FDA before the study can commence.*

How do I obtain a device study risk determination?

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.

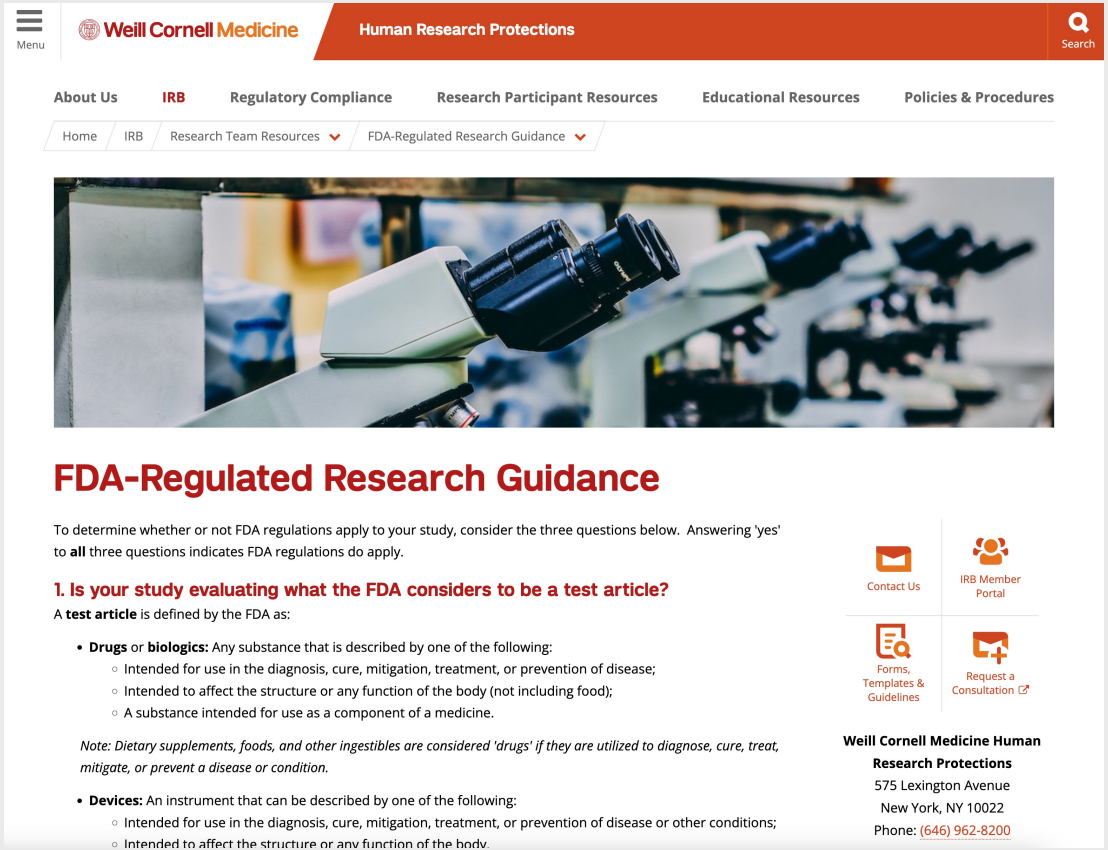
Do I need an investigator's brochure and what should it include?

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.

For More Information on FDA-Regulated Research:

Please visit the WCM IRB website:

https://hrp.weill.cornell.edu/irb/research-team-resources/fda-regulated-research-guidance



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FDA Resources

- **Investigator-Initiated Investigational New Drug (IND) Applications: https://www.fda.gov/drugs/types-applications/investigational-new-drug-ind-application**
- **Individual Patient Expanded Access Applications: https://www.fda.gov/drugs/investigational-new-drug-ind-application/physicians-how-request-single-patient-expanded-access-compassionate-use**
- **Information for Sponsor-Investigators Submitting INDs: https://www.fda.gov/drugs/investigational-new-drug-ind-application/information-sponsor-investigators-submitting-investigational-new-drug-applications-inds**
- **Investigational Device Exemption (IDE): https://www.fda.gov/medical-devices/premarket-submissions-selecting-and-preparing-correct-submission/investigational-device-exemption-ide**
- ***FDA Guidance Document: Humanitarian Device Exemption (HDE) Program Guidance for Industry and Food and Drug Administration Staff*, issued September 6, 2019, **supersedes "*Guidance for HDE holders, Institutional Review Boards (IRBs), Clinical Investigators, and Food and Drug Administration Staff, Humanitarian Device Exemptions (HDE) Regulation: Questions and Answers*," issued July 8, 2010 – https://www.fda.gov/media/74307/download**
- **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

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Contact Us

Scan the QR code to request a consult during our on-site
Tuesday, 1/9 through Thursday 1/11

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IRB Member Portal

Forms, Templates & Guidelines

Request a Consultation

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