

FDA-Regulated Research:

INDs, IDEs, and HUDs

presented by

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Human Research Protections
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<https://hrp.med.cornell.edu>

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



The Federal Drug Administration (FDA)

Oversight of:

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



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**



When Do FDA Regulations Apply?



First, some definitions...

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



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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



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

**PENDING
★ REVIEW ★**



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?

Test Article

Not legally marketed in the US as a drug

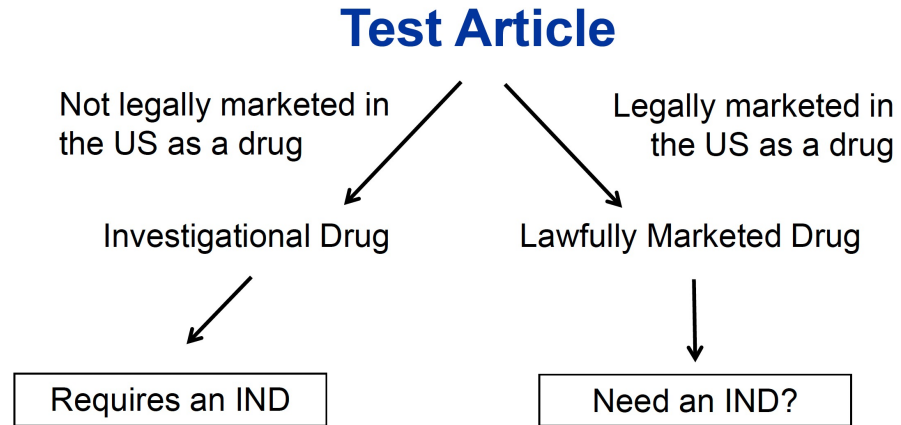
Investigational Drug

Requires an IND

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

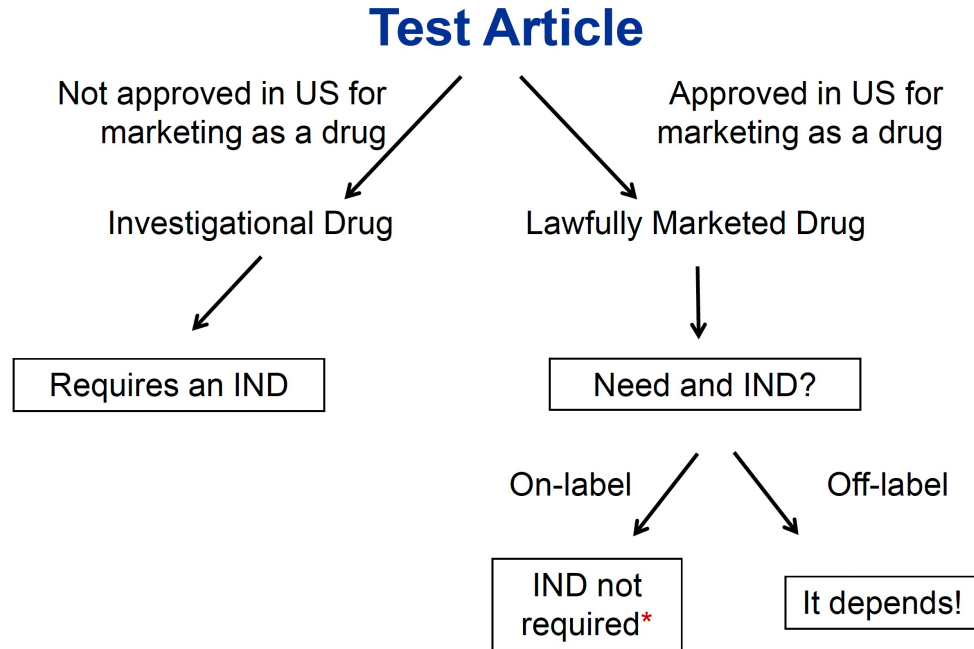


When is an IND Required?



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

When is an IND Required?



** Assuming no marketing application or change in advertising is planned*



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

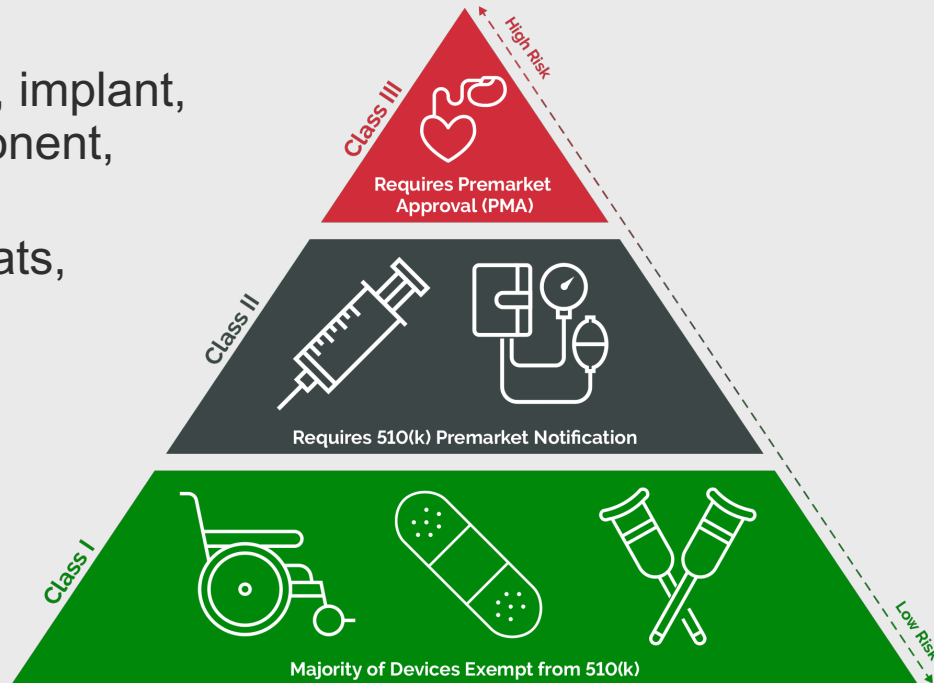


Investigational Device Exemption (IDE)



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**



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: <ol style="list-style-type: none">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

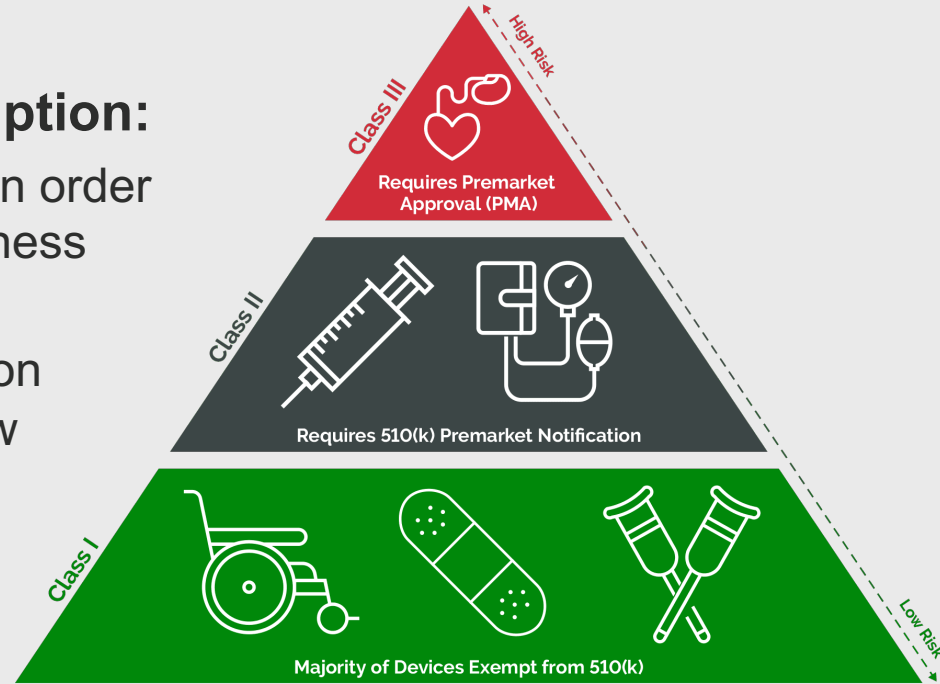
YES, your study involves an investigational device

- **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 assessments in accordance with its labeling – **NOT a device study**



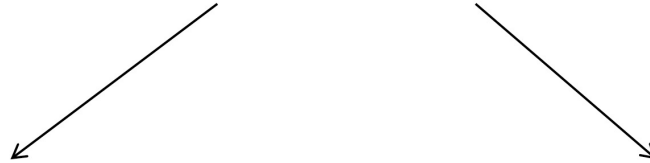
What is an Investigational Device Exemption (IDE)?

- **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))

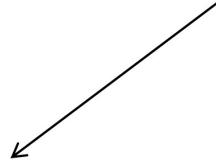
IDE required

- 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))



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)

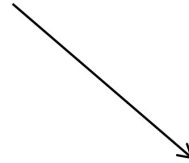
2.	A diagnostic device meeting diagnostic exemption criteria
----	-----------------------------------------------------------

- 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)



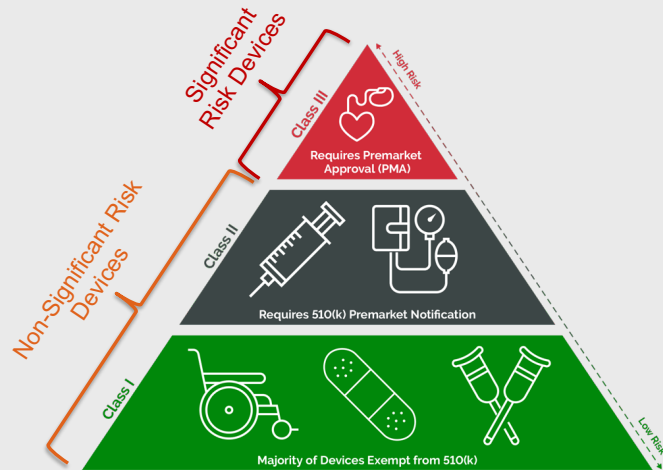
Abbreviated IDE vs. IDE

Abbreviated IDE

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

IDE

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



Device Definitions

Term	Definition
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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**

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



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**



FAQs

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

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FAQs

Below are some answers to the questions we get asked the most about human research protections and the IRB, sorted by type. If there is a question you don't see addressed here, please reach out to us at irb@med.cornell.edu so we can get your answer to you!

ClinicalTrials.gov

FAQs related to this topic are located on our [ClinicalTrials.gov Program](#) web page on our site.

Exempt Research

Does audio/video recording of interviews mean that my study cannot be exempt?	+
What does "normal education practice" mean?	+
Are observations in public schools considered public observations?	+
Can I have prisoners and/or children in my Exempt research?	+

Contact Us

IRB Member Portal

Forms, Templates & Guidelines

Request a Consultation

Weill Cornell Medicine Human Research Protections
575 Lexington Avenue
New York, NY 10022
Phone: (646) 962-8200



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>



FDA-Regulated Research Guidance

To determine whether or not FDA regulations apply to your study, consider the three questions below. Answering 'yes' to **all** three questions indicates FDA regulations do apply.


1. Is your study evaluating what the FDA considers to be a test article?


A **test article** is defined by the FDA as:


- **Drugs or biologics:** Any substance that is described by one of the following:
 - Intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease;
 - Intended to affect the structure or any function of the body (not including food);
 - A substance intended for use as a component of a medicine.


Note: Dietary supplements, foods, and other ingestibles are considered 'drugs' if they are utilized to diagnose, cure, treat, mitigate, or prevent a disease or condition.

- **Devices:** An instrument that can be described by one of the following:
 - Intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease or other conditions;
 - Intended to affect the structure or any function of the body.


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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



Contact us



or

Email:

WCM IRB Office: irb@med.cornell.edu

HRPO team: hrpo@med.cornell.edu





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