



U.S. Food and Drug Administration

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Submitting a PET Drug Investigational New Drug (IND) Application

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CDER

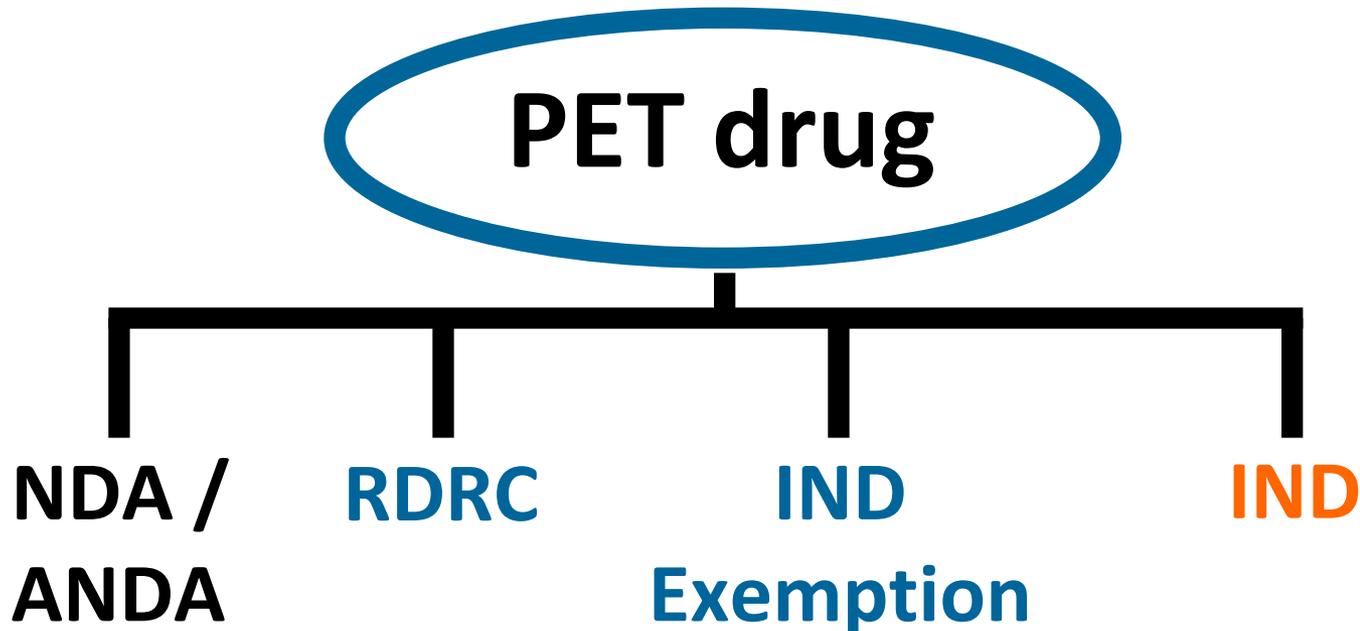
Summary

- **Introduction**
- **When IND Submission Is Not Required**
- **When IND Submission Is Appropriate**
- **IND For Clinical Trial vs. Expanded Access**
- **IND Process**

Uses of PET Drugs

- **“Investigational use” ...**
 - Drug administered within a clinical trial/study or other research project
 - IND or RDRC or exempt from IND
- **“Clinical use” ...**
 - Drug administered as part of clinical care
 - Approved under NDA/ANDA or otherwise legally marketed

Which Submission Is Most Appropriate?



RDRC

**IND not needed if study is approved by a
Radioactive Drug Research Committee (RDRC)**

RDRC research limited to:

- **Basic science**
- **Not for diagnostic or therapeutic purpose**
- **Not an evaluation of drug's safety/efficacy**
- **Dose known not to cause any pharm effect**
- **Radiation dose within specific limits**

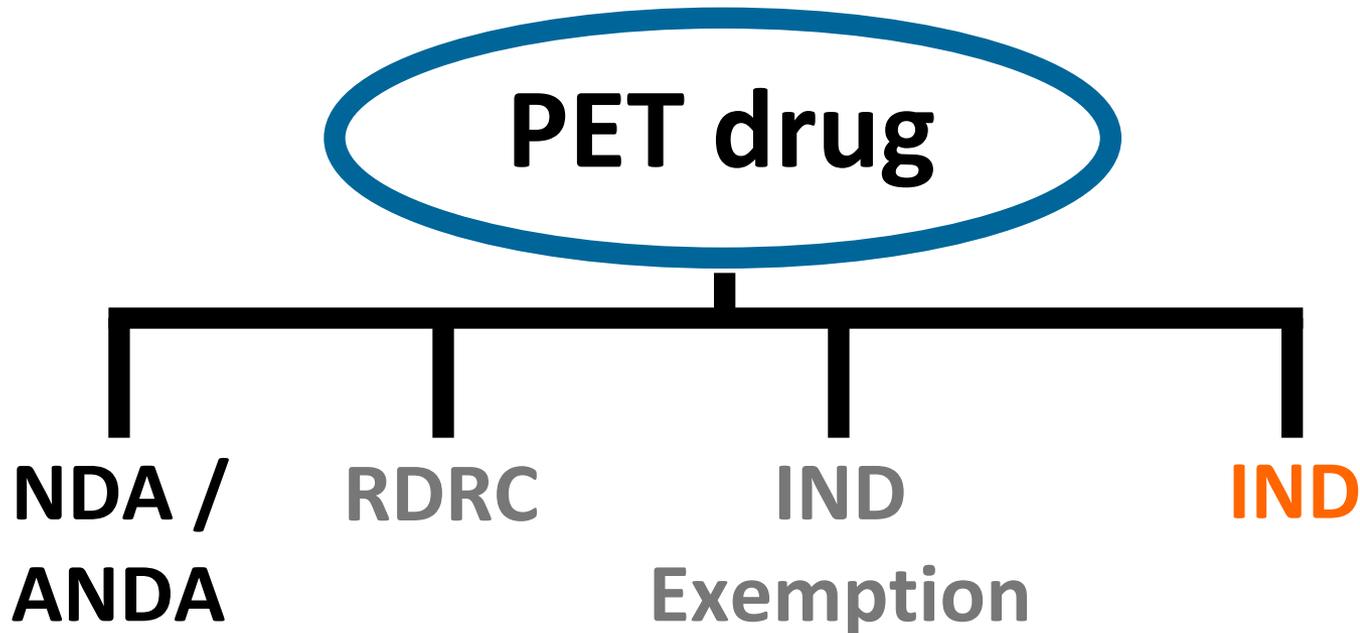
IND Exemption

***Sponsor or sponsor investigator (SI)
determines whether study/trial is exempt***

Criteria:

- Drug lawfully marketed
- Trial/study not intended to support new indication or labeling change
- No intent to support change in advertising
- No significant risk increase (e.g., drug route of administration, dose, patient population)
- Compliant with IRB/consent process
- Trial/study not intended to promote/commercialize the drug

Should I Be Submitting IND?



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What Is an IND?

An IND application is a request for authorization from FDA to:

- **Administer an investigational drug to humans**
- **Obtain exemption from premarket approval requirements**
- **Lawfully ship the drug**

Why Is IND Process Important for PET Drugs?

- Drug development & clinical research
- Patient access to:
 - Investigational PET drugs
 - PET drugs already in clinical use and uncommon usage does not justify submission of NDA/ANDA
- IND process active now and continues beyond Dec 12, 2011

IND Information

www.fda.gov

In search box, "IND"

The screenshot shows the FDA website interface. At the top, there is a navigation bar with the U.S. Department of Health & Human Services logo and the URL www.hhs.gov. Below this is the FDA logo and the text 'U.S. Food and Drug Administration'. A search bar is visible with the text 'A-Z Index' and 'Search' followed by a search input field and a 'go' button. A horizontal menu lists various categories: Home | Food | Drugs | Medical Devices | Vaccines, Blood & Biologics | Animal & Veterinary | Cosmetics | Radiation-Emitting Products | Tobacco Products. Below the menu are social sharing options: Share, Email this Page, Print this page, and Change Font Size.

The main content area is titled 'Drugs' and shows a breadcrumb trail: Home > Drugs > Development & Approval Process (Drugs) > How Drugs are Developed and Approved. The primary heading is 'Investigational New Drug (IND) Application'. To the left is a sidebar with a blue header 'Development & Approval Process (Drugs)' and sub-sections: 'How Drugs are Developed and Approved', 'Types of Applications', and 'Investigational New Drug (IND) Application'. The 'Investigational New Drug (IND) Application' section is expanded, showing a list of links: 'CDER Investigational New Drug (IND) Renumbering' and 'Emergency Investigational New Drug (EIND)'. The main content area contains a list of topics under the heading 'Investigational New Drug (IND) Application':

- Introduction
- Pre-IND Consultation Program
- Guidance Documents for INDs
- Laws, Regulations, Policies and Procedures
 - Code of Federal Regulations
 - Manual of Policies and Procedures (MaPPs)
- Emergency Use of an Investigational Drug or Biologic
 - Physician Request for a Single Patient IND for Compassionate or Emergency Use
- Related Resources

To the right of the main content is a 'Spotlight' box with a blue header and a list of items:

- Final Rule: IND Safety Reporting Requirements for Human Drug and Biological Products and Safety Reporting Requirements for Bioavailability and Bioequivalence Studies in Humans (9/28/2010)

IND Webpage Information

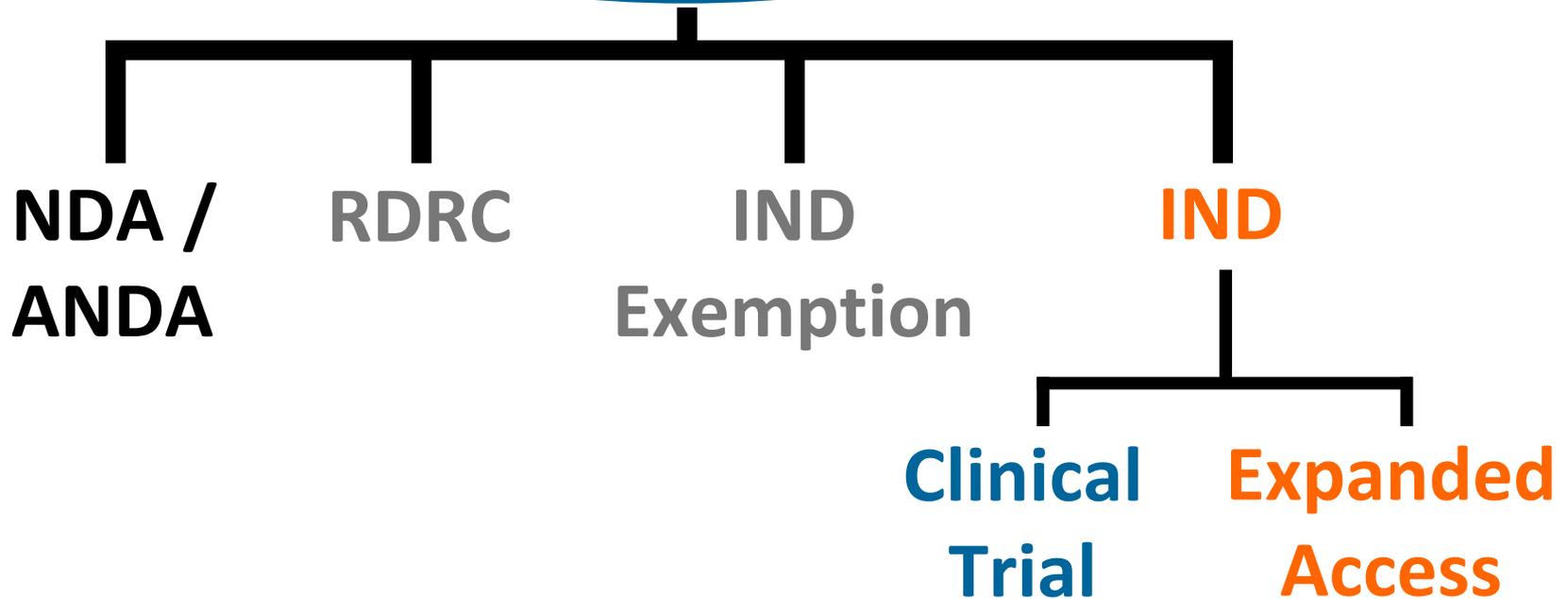
www.fda.gov

- **Pre-IND consultation/meeting program**
- **Guidance documents**
- **Emergency IND options**
- **Multiple related aspects (forms, contacts)**
- **Content and format of IND submissions**

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IND Options



Why Is IND Process Important for PET Drugs?

- Drug development **Clinical Trial**
- Patient access to: **Expanded Access**
 - Investigational PET drugs
 - PET drugs already in clinical use and uncommon usage does not justify submission of NDA/ANDA
- IND process active now and continues beyond Dec 12, 2011

“Access” to Investigational PET Drugs Via:

1. Clinical trial / study:

Primary purpose is to study drug effects

2. “Expanded access”:

Primary purpose is to diagnose or monitor patient’s disease / condition

“Expanded Access”

www.fda.gov

In search box, “expanded access”

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The main content area is titled 'For Consumers' and includes a breadcrumb trail: Home > For Consumers > Consumer Information by Audience > For Patients and Patient Advocates. A sidebar on the left contains a 'Consumer Information by Audience' section with a sub-section for 'For Patients and Patient Advocates', which includes a link to 'Access to Investigational Drugs'. The main content area features a section titled 'Access to Investigational Drugs' with the following text: 'Investigational or experimental drugs are new drugs that have not yet been approved by the FDA or approved drugs that have not yet been approved for a new use, and are in the process of being tested for safety and effectiveness. Patients may decide to seek access to investigational drugs for different reasons. Some patients with serious or life-threatening illnesses seek treatment with investigational drugs if FDA-approved therapies are not working or if their side effects are too severe. Others may have heard about promising early study results for a specific investigational drug, and they might want to learn more.'

A 'Contact Us' sidebar on the right provides information for the Office of Special Health Issues, including the phone number 301-796-8460, the email address OSHI@fda.hhs.gov, and the physical address: 10903 New Hampshire Avenue, Bldg. 32, Room 5367, Silver Spring, MD 20993.

Expanded Access

Patients may need access to investigational PET drugs for clinical use in absence of NDA / ANDA

Criteria:

- **Patient(s) with serious or immediately life-threatening disease / condition**
- **No satisfactory alternative “therapy”**
- **Potential patient benefit justifies potential risks of “treatment” use**
- **Provision of drug will not interfere with drug development**

Expanded Access

Providing access to investigational PET drugs
through IND

Good Clinical Practice:

- **Informed Consent**
- **IRB Approval**
- **Adherence to expanded access protocol**
 - Criteria for patient selection
 - Safety monitoring

Drugs That May Qualify For Expanded Access

Unapproved PET drugs are allowed for clinical use

Low usage may not justify submission of NDA

Modernization Act (comply with USP monograph):

- Carbon monoxide C11
- Fluorodopa F18 injection
- Flumazanil C11 injection
- Mespiperione C11 injection
- Methionine C11 injection
- Raclopride C11 injection
- Sodium acetate C11 injection
- Water O15 injection

Note: Approved drugs not appropriate for Expanded Access:

- Ammonia N13
- Fludeoxyglucose F18
- Sodium fluoride F18
- Rubidium chloride Rb82

Expanded Access

IND Submission Info (p1/2)

Identify category in IND submission:

- **Individual patient**
- **Intermediate-size patient population**
- **Widespread use (treatment IND)**
 - **Actively pursuing marketing approval**
 - **Has on-going or completed clinical trials**

Expanded Access

IND Submission Info (p2/2)

Additional Information Required If

Intermediate-sized Population:

- Is drug under development for marketing approval?
- Preliminary evidence of effectiveness
- Planned size of patient population

Request to Charge

www.fda.gov

In search box, “charging for investigational drug”

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- Expanded Access to Investigational Drugs for Treatment Use (PDF - 216KB)
- Charging for Investigational Drugs (PDF - 204KB)

 Below the list is a link for 'FDA News Release (8/12/2009)'. The text continues: 'The final rule, "Expanded Access to Investigational Drugs for Treatment Use," amends regulations on expanded access to investigational new drugs for treating patients. The final rule clarifies existing regulations and adds new types of expanded access for treatment use. Under the final rule, expanded access to investigational...'

Request to Charge Submissions

- Prominently highlight that IND submission is a “Request to Charge” on the cover letter
- Submit as a component of an original IND application or as an amendment to an existing IND
- Questions?

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(Division of Medical Imaging Products)

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IND Process

- **Submission of IND application to FDA by sponsor or sponsor-investigator (SI)**

- **FDA assigns IND number and issues acknowledgement letter**

- **Clinical trial/study cannot be initiated until 30 days after date of IND receipt, unless otherwise notified by FDA**

- **FDA will notify sponsor or SI of any deficiencies within the 30 day review period**

IND Sponsor or SI

- Submits the IND
- Initiates/conducts the clinical trial/study
- May be an individual, institution or company
- “Sponsor-investigator” is an individual who immediately directs the investigational drug administration

Can I Administer the PET Drug While My IND Is Being Reviewed?

- **Yes, if can provide documentation about current clinical use and the drug has a USP monograph**
- **No, if not in current clinical use or IND is to initiate a trial**
- **If unsure, ask FDA**

IND Content (p1/2)

- 1. Form FDA-1571 (cover sheet)**
- 2. Form FDA-3674 (Clinical trials.gov info)**
- 3. Table of contents**
- 4. Introductory statement, including description of clinical investigation**
- 5. Investigator brochure... *not needed for SI***
- 6. Clinical protocol**
- 7. Informed Consent**
- 8. Background information... *see next slide***

IND Content (p2/2)

7. Background information... *(continued)*

- a. PET drug chemistry, manufacturing & control (CMC) info
- b. Animal and/or clinical pharmacology-toxicology information that supports safety of study/trial
- c. Summary of previous PET drug clinical experience
- d. Estimate of radiation-absorbed dose to body and critical organs, with justification

IND Submission Logistics

- Paper or electronic
- If paper, supply 3 copies
- Electronic submission similar to pathway for NDA / ANDA
- Contact (email) esub@fda.hhs.gov for questions re: electronic submission

IND Submission Logistics

Mail paper submission to:

**US Food and Drug Administration
Central Document Room
5901-B Ammendale Rd.
Beltsville, MD 20705-1266**

***For more info, telephone: 301-796-2050
(Division of Medical Imaging Products)***

IND Review and Maintenance

- **IND is reviewed by multiple disciplines**
 - Project manager, chemistry, pharmacology / toxicology, microbiology, clinical pharmacology, clinical, statistics if appropriate
- **Discussion of IND submissions weekly**

ONCE THE STUDY MAY PROCEED...

- **Submit protocol revisions and new protocols**
- **Report serious and unexpected adverse events**
- **Submit annual progress reports**

Specific Websites

Electronic submission:

<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/default.htm>

IND overview:

<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/default.htm>

Specific Websites

Expanded Access:

<http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/AccessToInvestigationalDrugs/default.htm>

Charging:

<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/ucm172492.htm>

