

FDA Updates: Post <212> Deadline

January 27, 2012

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Center for Drug Evaluation and Research
U.S. Food and Drug Administration

If a facility wishes to continue to produce PET drugs for *clinical use* after June 12, 2012, it must have submitted a

- new drug application (**NDA**) or
- abbreviated new drug application (**ANDA**) or
- investigational new drug (**IND**)

by June 12, 2012.

Outline

- **History**
- **Definitions**
- **Clinical Use**
 - Submission options
 - Inspections
- **Research and Investigational Use**
 - RDRC
 - IND exemption
 - PET drugs in therapeutic trials

Why June 12, 2012?



History (page 1 of 2)

1997

Section 121 of Food Drug Administration Modernization Act:

FDA should establish for PET drugs

- Approval procedures and
- Current Good Manufacturing Practice (CGMP) requirements

2009

December 9

Procedures & requirements finalized

- Within 2 years, a NDA or ANDA must be submitted for any PET drug marketed for clinical use in the U.S.

History (page 2 of 2)

2011

December 6

Notice of FDA Exercise of Enforcement Discretion for PET Drugs

- FDA received requests to extend submission deadline
- FDA concerned about creating barrier to access in certain areas
- FDA yet to issue 2 guidances (IND, Q&As)

-
- FDA will not exercise enforcement discretion after **June 12, 2012** (so submit your NDA, ANDA, or IND!).
 - All producers of PET drugs for clinical use must be operating under an approved NDA or ANDA, or effective IND, by **December 12, 2015**.

FDA Notice: PET Drugs

Exercise of Enforcement Discretion

www.fda.gov

Search: “Positron Emission Tomography”
-- 2nd result --

The screenshot shows the FDA website interface. At the top, it says "U.S. Department of Health & Human Services" and "U.S. Food and Drug Administration Protecting and Promoting Your Health". A search bar contains the text "positron emission tomogra" and a red "SEARCH" button. Below the search bar are navigation tabs for Home, Food, Drugs, Medical Devices, Vaccines, Blood & Biologics, Animal & Veterinary, Cosmetics, Radiation-Emitting Products, and Tobacco Products. The "Drugs" tab is selected, and the breadcrumb trail shows "Home > Drugs > Development & Approval Process (Drugs) > Manufacturing". The main content area displays the title "Positron Emission Tomography (PET)" and "Notice of FDA Exercise of Enforcement Discretion for PET Drugs". The text below the title states: "In 1997, Congress passed the Food and Drug Administration Modernization Act (Public Law 105-115) (the Modernization Act). Section 121 of the Modernization Act directed FDA to establish appropriate approval procedures and Current Good Manufacturing Practices (CGMP) for PET drugs. These procedures were published on December 9, 2009, triggering an implementation timeline. Under the requirements of section 121, within 2 years of that publication date, a new drug application (NDA) or abbreviated new drug application (ANDA) must be submitted for any PET drug marketed for clinical use in the United States."

How does *clinical* use differ from *investigational* use and *research* use?



Definitions

Clinical use

- Using as a component of clinical care
- No intent to systematically study safety or effectiveness of the drug

Investigational use

- Use in a study to establish the safety or effectiveness of a new use of the drug to support approval
- Use of certain PET drugs for clinical purposes (expanded access IND)

Research use

- Use in a study of the drug for basic science research
- Not using for immediate therapeutic, diagnostic, or similar purpose
- No intent to determine safety or effectiveness for clinical use

Outline

- **History**
- **Definitions**
- **Clinical Use**
 - Submission options
 - Inspections
- **Research and Investigational Use**
 - RDRC
 - IND exemption
 - PET drugs in therapeutic trials

I have been
producing a PET drug
for *clinical* use.

What should I
submit to FDA to
continue
clinical use?



Submission Options if Currently (before 06/12/12) Producing for *Clinical* Use

FDG, NaF, or
ammonia?

Yes

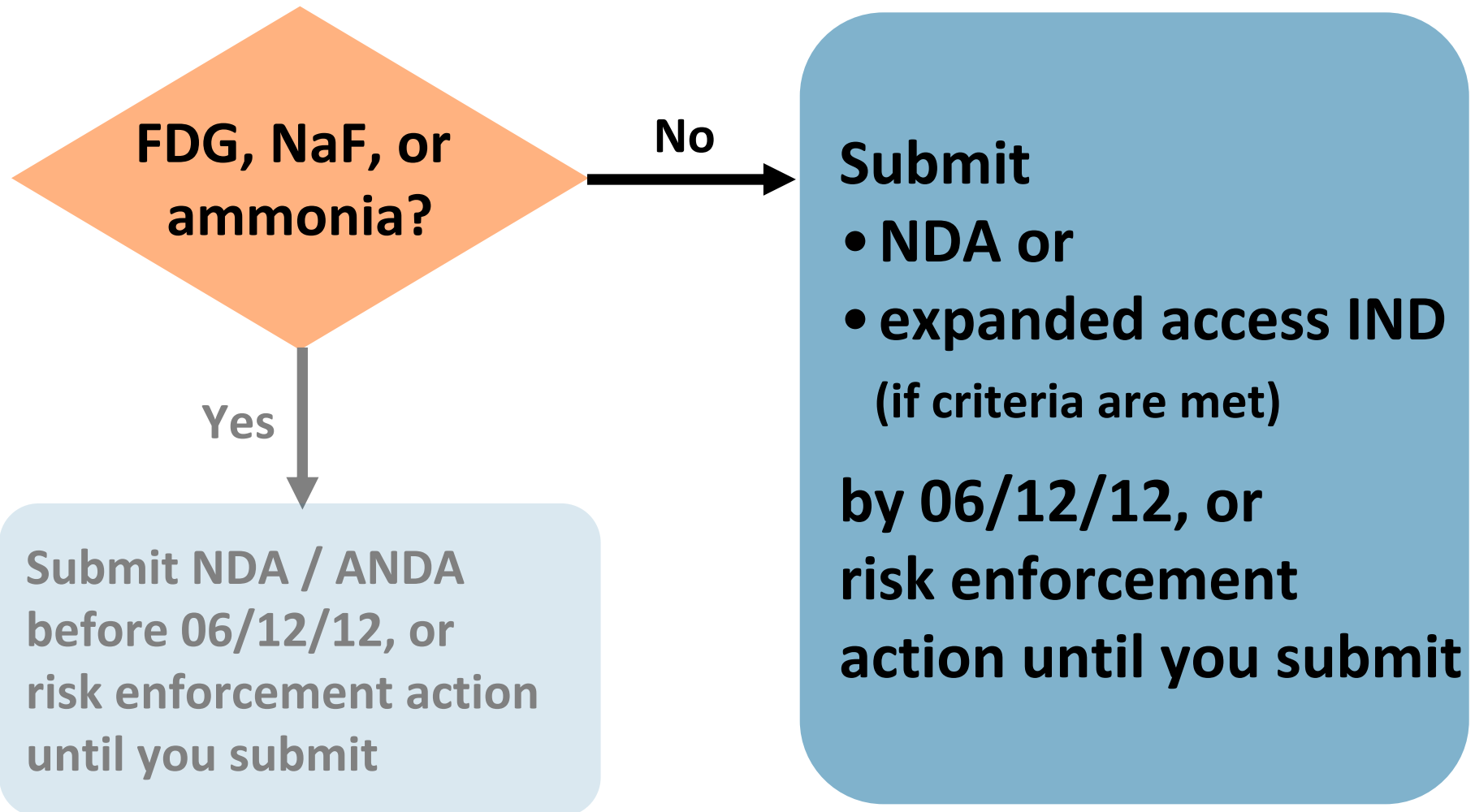
Submit NDA / ANDA
before 06/12/12, or
risk enforcement action
until you submit

What if the PET drug I have been producing for *clinical* use is not FDG, NaF, or ammonia?

What should I submit to FDA to continue *clinical* use?



Submission Options if Currently (before 06/12/12) Producing for *Clinical* Use



Can you tell me more about expanded access IND?



Expanded Access

www.fda.gov

Search: “expanded access”

The screenshot shows the FDA website's search interface. At the top, the FDA logo and name are displayed. A search bar contains the text "expanded access" and a red "SEARCH" button. Below the search bar is a navigation menu with categories like Home, Food, Drugs, Medical Devices, Vaccines, Blood & Biologics, Animal & Veterinary, Cosmetics, Radiation-Emitting Products, and Tobacco Products. The search results section shows "Results 1 - 10 of about 3570 for expanded access. Search took 0.07 seconds." The first result is highlighted in blue and is titled "Access to Investigational Drugs" with the URL <http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/AccessToInvestigationalDrugs/default.htm>. A second result is titled "Final Rules for Expanded Access to Investigational Drugs for ..." with a URL www.fda.gov/.../ApprovalApplications/InvestigationalNewDrugINDApplication/ucm172492.htm. An orange arrow points from the search bar area down to the first search result.

Expanded Access

3rd bullet

The screenshot shows the FDA website's 'For Consumers' section. The main heading is 'Access to Investigational Drugs'. Below the heading is a paragraph explaining that investigational or experimental drugs are new drugs not yet approved by the FDA. This is followed by a paragraph stating that patients may seek access for various reasons, such as serious illnesses or severe side effects. A third paragraph details that these drugs are available through two pathways: clinical trials and expanded access programs (also known as compassionate use). At the bottom of the main content area, there is a list of three bullet points. An orange arrow points to the third bullet point: 'Access to Investigational Drugs Outside of a Clinical Trial (Expanded Access)'. The left sidebar contains a 'Consumer Information by Audience' menu with 'Access to Investigational Drugs' selected. The right sidebar contains 'Contact FDA' information, including a phone number, email address, and office address.

U.S. Food and Drug Administration
Protecting and Promoting *Your* Health

A to Z Index | Follow FDA | Subscribe to Emails

expanded access **SEARCH**

Home | Food | Drugs | Medical Devices | Vaccines, Blood & Biologics | Animal & Veterinary | Cosmetics | Radiation-Emitting Products | Tobacco Products

For Consumers

Home > For Consumers > Consumer Information by Audience > For Patients and Patient Advocates

Consumer Information by Audience

- For Patients and Patient Advocates
- Access to Investigational Drugs**
- Deciding Whether to Seek Access to an Investigational Drug
- Clinical Trials and Investigational Drugs
- Access to Investigational Drugs Outside of a Clinical Trial (Expanded Access)

Access to Investigational Drugs

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.

Investigational drugs are available through two pathways designed to protect patients, because an investigational drug may pose unknown risks to patients and we do not know if it is effective. Patients may be eligible to receive an investigational drug as a participant in a clinical trial or as part of an expanded access program (also known as compassionate use). If you are interested in seeking access to an investigational drug, the information provided here can help guide your decision and your next steps.

- Deciding Whether to Seek Access to an Investigational Drug
- Clinical Trials and Investigational Drugs
- Access to Investigational Drugs Outside of a Clinical Trial (Expanded Access)**

Contact FDA

301-796-8460
OSHI@fda.hhs.gov

Office of Special Health Issues
10903 New Hampshire Avenue
Bldg. 32, Room 367
Silver Spring, MD 20993

Resources for You

- Questions and Answers about

Expanded Access Criteria

www.fda.gov

Search: "21 CFR 312.305"

The screenshot shows the FDA website's search interface. At the top left is the FDA logo and the text "U.S. Food and Drug Administration Protecting and Promoting Your Health". To the right are links for "A to Z Index", "Follow FDA", and "Subscribe to Emails". Below this is a search bar with a red "SEARCH" button. A navigation menu contains buttons for "Home", "Food", "Drugs", "Medical Devices", "Vaccines, Blood & Biologicals", "Animal & Veterinary", "Cosmetics", "Radiation-Emitting Products", and "Tobacco Products".

The search results section shows "Results 1 - 1 of about 1 for 21CFR312.305. Search took 0.02 seconds." Below the search bar, the text "Results for '21CFR312.305' in All of FDA" is displayed. A red arrow points from the search bar area down to the first search result. The result is a link titled "CFR - Code of Federal Regulations Title 21" with a subtext: "... [Code of Federal Regulations]. [Title 21, Volume 5]. [Revised as of April 1, 2011]. [CITE: 21CFR312.305]. TITLE 21--FOOD AND DRUGS. ...". Below the link is the URL "www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.305 - 7k - Cached".

Expanded Access

C R I T E R I A

- **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

C R I T E R I A (in the context of PET drugs)

- **Patient(s) with serious or immediately threatening disease / condition**
 - ◆ **Serious**: Associated with morbidity that has substantial impact on day-to-day functioning
 - ◆ **Life threatening**: Reasonable likelihood of death within months or premature death without treatment
 - ◆ **For a PET drug**: To help detect serious disease / condition in patients without active disease manifestation is considered use for a serious disease or condition

Expanded Access

C R I T E R I A (in the context of PET drugs)

Diagnose, monitor, or treat



- **No satisfactory alternative “therapy”**
 - ◆ **Alternative therapy**: Specified in approved labeling
 - ◆ **For a PET drug**: Unique capability (e.g. assess metabolic activity or identify receptors) might satisfy criteria because information provided is of different nature from that provided by other imaging modalities

Expanded Access

C R I T E R I A (in the context of PET drugs)

- ◆ **Basis of determination:**
 - ✓ Available evidence to support treatment use
 - ✓ Population exposed (size, nature)
 - ✓ Relative seriousness of disease / condition
- **Potential patient benefit justifies potential risks of “treatment” use**
- ◆ **For a PET drug:** FDA anticipates risks of diagnostic use not unreasonable in most patient populations when used to assist in diagnosis of serious conditions (relatively low mass dose & radiation dose)

Expanded Access

C R I T E R I A *(in the context of PET drugs)*

- ◆ **For a PET drug:** FDA anticipates expanded access INDs for PET drugs will generally be used in situations in which it is not feasible to develop the PET drug for marketing approval
- **Provision of drug will not interfere with drug development**

Expanded Access

Good Clinical Practice

- **Informed consent**
- **IRB approval**
- **Safety reports & annual reports**
- **Provide Investigator's Brochure if exists**
- **Adherence to expanded access protocol**
 - Criteria for patient selection
 - Safety monitoring

Drugs That May Qualify For Expanded Access

Low usage may not justify submission of NDA

Modernization Act (comply with USP monograph):

- Carbon monoxide C11
- Fluorodopa F18 injection
- Flumazaniol C11 injection
- Mespiperone C11 injection
- Methionine C11 injection
- Raclopride C11 injection
- Sodium acetate C11 injection
- Water O15 injection

But other PET drugs could potentially qualify.

*Drugs That **DO NOT** Qualify For Expanded Access*

Approved PET drugs

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

SUBMIT

- **ANDA** using the NDA product as the reference product
- OR**
- **505(b)(2) NDA**

Expanded Access IND Content

www.fda.gov

Search: “21 CFR 312.305”

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Expanded Access

IND Content (p1/4)

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 Content (p2/4)

- 1. Form FDA-1571 (cover sheet)**
- 2. “Protocol”**
 - Title, protocol #
 - Rationale for intended use
 - Criteria for patient selection
 - Drug dose, # of doses, route of administration
 - Safety monitoring
 - Drug production site
- 3. Estimate of radiation-absorbed dose to body and critical organs, with justification**

Expanded Access

IND Content (p3/4)

- 4. Chemistry, manufacturing & control (CMC)**
- 5. Pharmacology & toxicology to justify dose and duration of use**
- 6. Satisfaction of Expanded Access criteria**
 - Serious, life threatening condition
 - No alternative diagnostic agent
 - Potential benefit justifies risks
 - Use will not interfere with trials for marketing approval

Expanded Access

IND Content (p4/4)

Additional Information Required If Intermediate-size Population:

- **Is drug under development for marketing approval?**
 - Explain why drug cannot be developed OR
 - Explain why patients cannot be enrolled in clinical study
- **Planned size of patient population**
- **Sufficient evidence for safety of drug at proposed dose and duration to justify # of patients**
- **Preliminary evidence of effectiveness**

Can I recover costs with an expanded access IND?



Request to Charge

www.fda.gov

Search: “charging for investigational drug”

The screenshot shows the FDA website's search results page. At the top, the FDA logo and name are displayed. A search bar contains the text "charging for investigational" and a red "SEARCH" button. Below the search bar is a navigation menu with tabs for Home, Food, Drugs, Medical Devices, Vaccines, Blood & Biologics, Animal & Veterinary, Cosmetics, Radiation-Emitting Products, and Tobacco Products. The "Drugs" tab is selected. The main content area shows a breadcrumb trail: Home > Drugs > Development & Approval Process (Drugs) > How Drugs are Developed and Approved. A large orange arrow points from the "Drugs" tab to the "Development & Approval Process (Drugs)" link in the breadcrumb. The main article title is "Final Rules for Expanded Access to Investigational Drugs for Treatment Use and Charging for Investigational Drugs". The article text states: "FDA is amending its investigational new drug application (IND) regulation with two final rules:" followed by a bulleted list:

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

 Below this is an "FDA News Release (8/12/2009)" section. The text reads: "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 drugs for treatment use will be available to:" followed by another bulleted list:

- individual patients, including in emergencies
- intermediate-size patient populations
- larger populations under a treatment protocol or treatment investigational new drug application (IND)

Recoverable Costs with Expanded Access IND

(typically 1 year authorization)

- **Individual patient**
 - Only direct costs
- **Intermediate-size patient population**
 - Direct costs
 - Indirect administrative costs
 - Including costs associated with monitoring the IND, complying with IND reporting requirements

Request to Charge Submissions

- **Cover letter:**
 - Prominently highlight that IND submission is a “Request to Charge”
- **Submission:**
 - A component of an original IND application, or
 - An amendment to an existing IND
- **Questions?**

Dr. Kaye Kang
kyong.kang@fda.hhs.gov
telephone: 301-796-2050
(Division of Medical Imaging Products)

Request to Charge Submission Content

(Expanded Access--intermediate-size patient population)

- **Provide assurance that charging will not interfere with developing the drug for marketing approval**
 - e.g. Limited use
 - e.g. on-site preparation or limited distribution region (short half-life)
- **Define same number of patients for charging and for expanded access**
- **Describe proposed cost per patient & justification**
(consistent with 21 CFR 312.8(d)(1) and (d)(2))
- **Provide statement by independent certified public accountant**

I have NOT been
producing a PET drug for
clinical use, but I want to start.



**What
should I
submit to
FDA, and
by when?**

Submission Options if NOT Producing for *Clinical* Use Before 06/12/12

**FDG, NaF, or
ammonia?**

Yes

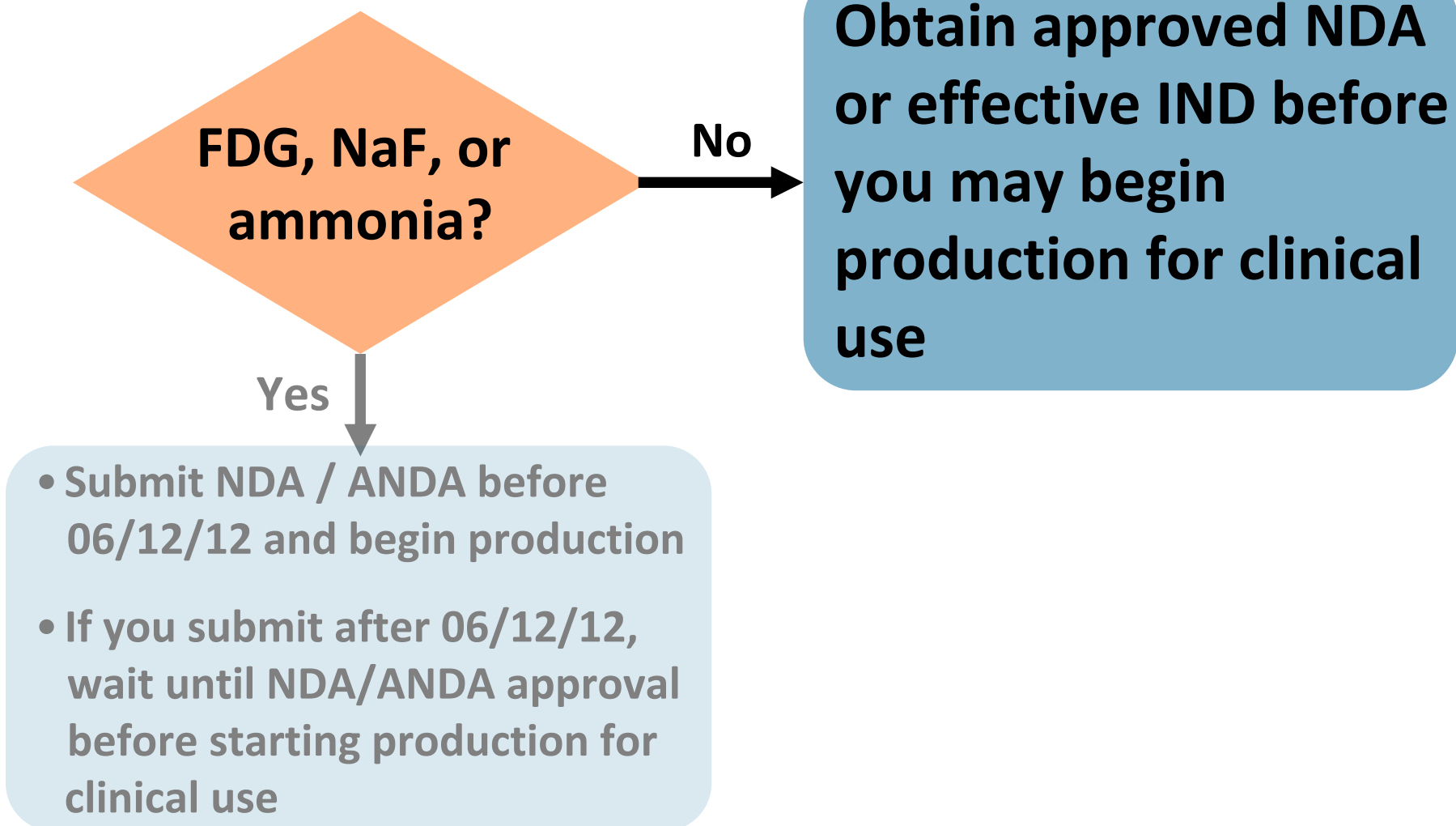
- **Submit NDA / ANDA before 06/12/12 and begin production**
- **If you submit after 06/12/12, wait until NDA/ANDA approval before starting production for clinical use**

What if the PET drug
I want to start producing for
clinical use is not FDG, NaF, or
ammonia?

What should I
submit to
FDA, and by
when?



Submission Options if NOT Producing for *Clinical* Use Before 06/12/12



Can you summarize
what you've said so far
regarding submission
requirements
for *clinical* use
of PET drugs?



See APPENDIX A in:

Guidance

**FDA Regulation of PET Drug
Products**

Questions and Answers

**[Date]
Procedural**

I've submitted my NDA/ANDA.

Any advice regarding inspections?



Answer:

1. Links on Exercise of Enforcement Discretion webpage
2. Info in Q&As Guidance
3. Links on FDA Compliance and Enforcement Actions webpage

Advice on Inspections

- 1. Links on Exercise of Enforcement Discretion webpage**
2. Info in Q&As Guidance
3. Links on FDA Compliance and Enforcement Actions webpage

FDA Notice: PET Drugs

Exercise of Enforcement Discretion

www.fda.gov

Search: “Positron Emission Tomography”
-- 2nd result --

The screenshot shows the FDA website interface. At the top, it displays the U.S. Department of Health & Human Services logo and the FDA logo with the tagline "U.S. Food and Drug Administration Protecting and Promoting Your Health". A search bar contains the text "positron emission tomogra" and a red "SEARCH" button. Below the search bar, there are navigation tabs for Home, Food, Drugs, Medical Devices, Vaccines, Blood & Biologics, Animal & Veterinary, Cosmetics, Radiation-Emitting Products, and Tobacco Products. The "Drugs" tab is selected, and the breadcrumb trail shows: Home > Drugs > Development & Approval Process (Drugs) > Manufacturing. The search results show a link for "Positron Emission Tomography (PET)" with the subtitle "Notice of FDA Exercise of Enforcement Discretion for PET Drugs".

And scroll down...

Middle of the page...

1a →

CGMP for PET Drugs

- Small Entity Compliance Guide: PET Drugs - Current Good Manufacturing Practice (CGMP) (PDF - 228KB)
- Federal Register Notice: Final Rule - CGMP for PET Drugs
- PET Drug Products - Current Good Manufacturing Practice (CGMP) (PDF - 399KB)
Guidance document issued 12/9/2009
- Positron Emission Tomography (PET): Questions and Answers about CGMP Regulations for PET Drugs (12/9/2009)
- Positron Emission Tomography (PET): Additional Questions and Answers Based on December 9, 2009 Stakeholder Call (4/8/2010)

1b →

2 →

Compliance Program Guidance Manual

FDA has posted the Compliance Program Guidance Manual for PET CGMP drug inspections. FDA's Compliance Programs provide instructions to FDA personnel for inspecting facilities, sampling and analyzing FDA-regulated products, and initiating and implementing regulatory follow up, when appropriate. FDA personnel who will be involved in evaluating PET production facilities are being trained to use the PET Compliance Program, to know the PET CGMP regulations and guidance, and to understand the unique aspects of PET production. FDA will offer webinars to the PET community to explain this program and provide general information about FDA inspection practices beginning in 2012.

- [CPGM: PET CGMP Drug Process and Pre-approval Inspections/Investigations \(PDF - 182KB\)](#)

Historical Information

- [Historical Information on Positron Emission Tomography \(PET\)](#)

Contact Us

For more information contact the PET working group, by e-mail at: PETDrugs@fda.hhs.gov.

3 →

Public Meeting Information

- [Preparing NDAs or ANDAs for fludeoxyglucose \(FDG\) 18 injection, ammonia N 13 injection, and sodium fluoride F 18 injection used in PET imaging; Public Meeting](#)
- [Webinar on CGMP for PET Drugs](#)

1a

Guidance

PET Drugs — Current Good Manufacturing Practice (CGMP)

(Small Entity Compliance Guide)

August 2011
Compliance

1b

Guidance

PET Drugs — Current Good Manufacturing Practice (CGMP)

December 2009
Compliance

2

FOOD AND DRUG ADMINISTRATION
COMPLIANCE PROGRAM GUIDANCE MANUAL

PROGRAM

7356.002P

CHAPTER 56 - DRUG QUALITY ASSURANCE

SUBJECT: POSITRON EMISSION TOMOGRAPHY (PET) CGMP DRUG PROCESS AND PRE-APPROVAL INSPECTIONS/INVESTIGATIONS REF: 7356.002 (2/01/2002) and 7346.832 (5/10/2010)		IMPLEMENTATION DATE 12/12/2011
		COMPLETION DATE 12/11/2014
DATA REPORTING		
PRODUCT CODES	PROGRAM ASSIGNMENT CODES	
All PET Drugs Industry code: 65 Profile Class code: PET	56002P Drug Process Inspections (PET) 46832P Positron Emission Tomography (PET) Pre-Approval Inspections/Investigations (NDA) 52832P Positron Emission Tomography (PET) Pre-Approval Inspections/Investigations (ANDA)	

10/5/2011

3



U.S. Food and Drug Administration
Protecting and Promoting *Your* Health

Home | Food | **Drugs** | Medical Devices | Vaccines, Blood & Biologics | Animal & Veterinary | Cosmetics

Drugs

Home > Drugs > Development & Approval Process (Drugs) > Manufacturing

Development & Approval Process (Drugs)

Manufacturing

Drug Applications and Current Good Manufacturing Practice (CGMP) Regulations

Positron Emission Tomography (PET)

Questions and Answers on Current Good Manufacturing Practices (CGMP) for Drugs

Webinar on CGMP for PET Drugs

FDA is presenting a webinar on CGMPS for PET Drugs.

Date: January 19, 2012

Time: 1:00 p.m. - 3:00 p.m. EST

Link: <https://collaboration.fda.gov/cderpet/>

Conference number: (866) 771-2454, and participant code: 84786087

Advice on Inspections

1. Links on Exercise of Enforcement Discretion webpage
- 2. Info in Q&As Guidance**
3. Links on FDA Compliance and Enforcement Actions webpage

See General Questions & Inspections in:

Guidance

FDA Regulation of PET Drug Products

Questions and Answers

[Date]

Procedural

Are inspections required before continuing production at a site included in an NDA / ANDA submitted by 06/12/12?

Answer:

The facility does not need to be inspected before production of PET drugs can continue.



Can academic sites schedule the initial FDA inspection in advance?

Answer:

Yes.

**Note: For-cause inspections
are not scheduled in
advance.**



For an NDA / ANDA submitted before 06/12/12, can the production method be changed before the initial inspection of the facility?



Answer:

Yes. Submit an amendment to the application. Include:

- supporting data;
- description of all changes & controls required;
- assessment of effect on identity, strength, purity, & quality

*For Changes in Equipment or
Facilities, See **APPENDIX B** in:*

Guidance

**FDA Regulation of PET Drug
Products**

Questions and Answers

**[Date]
Procedural**

Advice on Inspections

1. Links on Exercise of Enforcement Discretion webpage
2. Info in Q&As Guidance
- 3. Links on FDA Compliance and Enforcement Actions webpage**

FDA Compliance and Enforcement Actions

www.fda.gov

Search: “FDA compliance and enforcement actions”

The screenshot shows the FDA website's search results page. At the top, the FDA logo and name are displayed. A search bar contains the text "FDA compliance and enfor" with a red "SEARCH" button. Below the search bar is a navigation menu with links for Home, Food, Drugs, Medical Devices, Vaccines, Blood & Biologics, Animal & Veterinary, Cosmetics, Radiation-Emitting Products, and Tobacco Products. The main content area is titled "About FDA" and includes a breadcrumb trail: Home > About FDA > Transparency > Transparency Initiative. A sidebar on the left has a "Transparency" button and a "Transparency Initiative" link. The main content area features a section titled "Information about FDA Compliance and Enforcement Actions" with links for "Phase II Progress Report" and "Phase III Progress Report". An orange arrow points from the text "Link to Inspections Database" to a link in the main content area. Below the link is a photograph of two FDA inspectors in blue uniforms examining products in a warehouse. The text below the photo states: "FDA has responsibility for enforcing a broad range of statutory and regulatory requirements. FDA is taking steps to make its enforcement activities more transparent. For example, FDA has posted a searchable database that includes the name and address of inspected facilities, the date(s) of inspection, type of FDA-regulated products involved, and final inspectional classification, as well as a summary of the most common inspectional observations. FDA has also placed a number of enforcement-related datasets on the Data.gov website. These include datasets for major food recalls."

Lower down, see link to “Warning letters” (section III.A.)

Switch Gears

From:

Clinical
Use



To:

Research
&
Investigational
Use

Outline

- **History**
- **Definitions**
- **Clinical Use**
 - Submission options
 - Inspections
- **Research and Investigational Use**
 - RDRC
 - IND exemption
 - PET drugs in therapeutic trials

Definitions

Clinical use

- Using as a component of clinical care
- No intent to systematically study safety or effectiveness of the drug

Investigational use

- Use in a study to establish the safety or effectiveness of a new use of the drug to support approval
- Use of certain PET drugs for clinical purposes (expanded access IND)

Research use

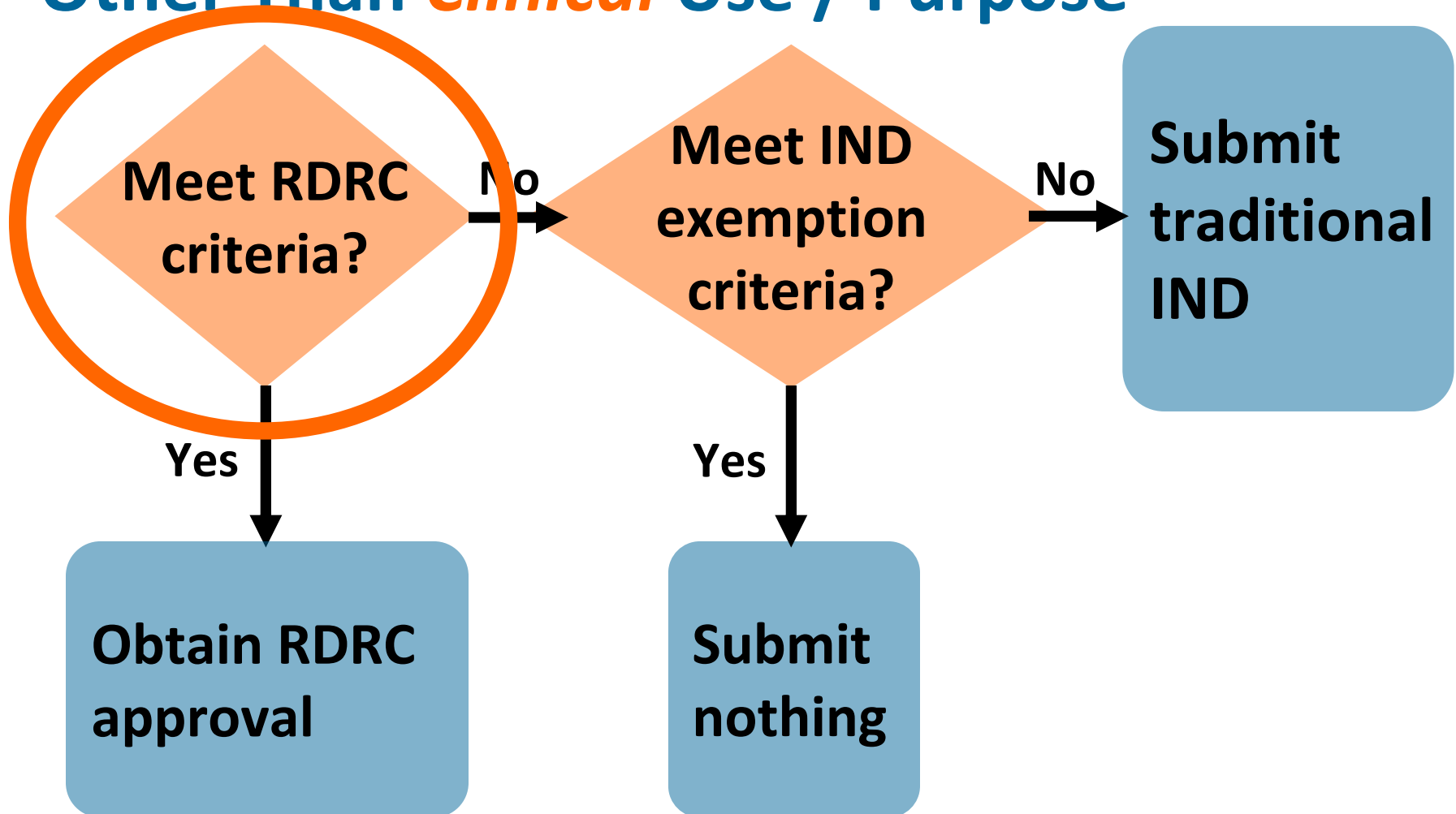
- Use in a study of the drug for basic science research
- Not using for immediate therapeutic, diagnostic, or similar purpose
- No intent to determine safety or effectiveness for clinical use

I'm administering PET drugs to humans, but **NOT** for a **clinical** use/purpose.

What
should I
submit to
FDA, and
by when?



Submission Options for PET Drug Uses Other Than *Clinical* Use / Purpose



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 pharmacologic effect**
- **Radiation dose within specific limits**

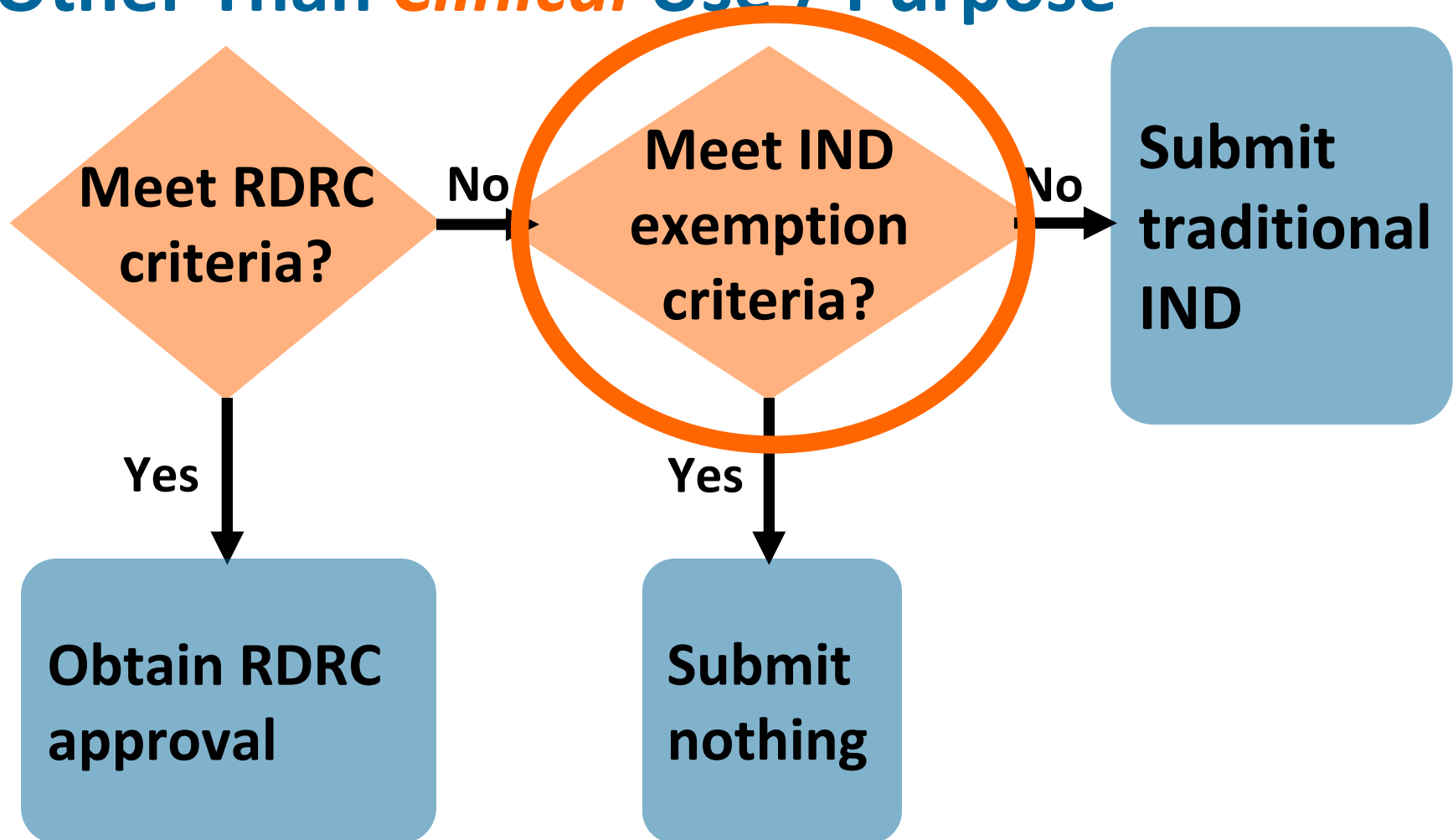
RDRC Info

www.fda.gov

In search box, “RDRC”

The screenshot shows the FDA website's search results for 'RDRC'. The top navigation bar includes the FDA logo, the text 'U.S. Food and Drug Administration Protecting and Promoting Your Health', and a search bar containing 'RDRC' with a 'SEARCH' button. Below the navigation bar are tabs for Home, Food, Drugs, Medical Devices, Vaccines, Blood & Biologics, Animal & Veterinary, Cosmetics, Radiation-Emitting Products, and Tobacco Products. The 'Drugs' section is active, showing a breadcrumb trail: Home > Drugs > Science & Research (Drugs) > Research Areas. A sidebar menu on the left lists 'Science & Research (Drugs)', 'Research Areas', and 'Oncology'. The main content area is titled 'Radioactive Drug Research Committee (RDRC) Program' and contains a list of links: 'What is the RDRC Program?', 'What are the Qualifications and Requirements of RDRC Membership?', 'How Does an RDRC Obtain FDA Approval?', 'What are the Responsibilities of the RDRC?', 'What Information Does the RDRC Review?', 'Federal Regulations (21 CFR 361.1)', 'RDRC Forms and Checklist', 'Guidances for Industry', 'Historical Information for RDRC Program', 'List of active RDRC sites', and 'Contact Us'. Below the list is a section titled 'What is the RDRC Program?' with a paragraph of text: 'The Radioactive Drug Research Committee (RDRC) program began when the Food and Drug Administration published a Federal Register notice on July 25, 1975 classifying all radioactive drugs as either new drugs requiring an Investigational New Drug Application (IND) for investigational use (21 CFR 312) or as generally recognized as safe and effective when administered under the conditions specified in the RDRC regulations (21 CFR 361.1). The RDRC program under [21 CFR 361.1](#) permits **basic research** using radioactive drugs* in

Submission Options for PET Drug Uses Other Than *Clinical* Use / Purpose



IND Exemption Info

www.fda.gov

In search box, “21 CFR 312.2”

The screenshot shows the FDA website's search interface. At the top, the FDA logo and name are displayed. A search bar contains the text "21CFR312.2" and a red "SEARCH" button. Below the search bar is a navigation menu with tabs for Home, Food, Drugs, Medical Devices, Vaccines, Blood & Biologics, Animal & Veterinary, Cosmetics, Radiation-Emitting Products, and Tobacco Products. The search results section shows "Results 1 - 1 of about 1 for 21CFR312.2. Search took 0.04 seconds." A search bar at the bottom of the results section also contains "21CFR312.2" and a "Search" button. An orange arrow points from the text above to the search button in the results section. The search results list a link for "CFR - Code of Federal Regulations Title 21" with a brief description and a URL.

IND Exemption

Sponsor or Sponsor Investigator (SI) determines whether study/trial is exempt

CRITERIA

- **Drug is lawfully marketed**
- **No intent to support new indication, labeling change, or advertising change**
- **No intent to promote/commercialize the drug**
- **No significant risk increase (e.g. dose, route of administration, patient population)**
 - **Compliant with IRB/consent process**

IND Exemption

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

CRITERIA

- Drug is lawfully marketed

Before 12/12/2015

After 12/12/2015

**PET drug used in the
trial is made at a facility
included in NDA/ANDA
submission**

Approved NDA/ANDA

IND Exemption

Before December 12, 2015

CRITERIA

- PET drug used in the trial is made at a facility included in a submitted NDA/ANDA
- No intent to support new indication, labeling change, or advertising change
- No intent to promote/commercialize the drug
- No significant risk increase (e.g. dose, route of administration, patient population)
 - Compliant with IRB/consent process

IND Exemption

After December 12, 2015

CRITERIA

- **PET drug used in the trial is included in an approved NDA/ANDA**
- **No intent to support new indication, labeling change, or advertising change**
- **No intent to promote/commercialize the drug**
- **No significant risk increase (e.g. dose, route of administration, patient population)**
 - **Compliant with IRB/consent process**

Is a drug with a USP monograph exempt from IND?

Answer:

No.



By when should I submit my IND application (if not exempt from IND) ?



Answer:

By June 12, 2012

Anticipated Guidance

Guidance

Investigational New Drug Applications for Positron Emission Tomography (PET) Drugs

[Date]

Clinical/Medical

*See **INDs** in:*

Guidance

**FDA Regulation of PET Drug
Products**

Questions and Answers

**[Date]
Procedural**

If an approved PET drug is used in an investigational therapeutic trial, does there need to be an IND for the PET drug *and* an IND for the therapeutic drug?



Answer:

No. The therapeutic IND should provide documentation that the PET drug is sourced from a facility with an approved NDA or ANDA.

For a PET drug that has not been approved, do I need to submit CMC info to an IND in effect for a therapeutic drug?

Answer:

Before Dec 12, 2015:

No, as long as the PET drug is manufactured at a facility named in an NDA/ANDA submission.

After Dec 12, 2015:

Yes, if the PET drug is not manufactured at a facility named in an approved NDA/ANDA.



Thank you!



Additional questions?

Contact us at: PETDrugs@fda.hhs.gov

