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Streamlining IRB Procedures for Expanded Access

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Expanded Access Goes by Many Names

Treatment Access

Named Patient Program

Special Access Programme

Compassionate Use

Single Patient IND

Pre-approval access

Pre-launch Access

What is Expanded Access?

- Use of an investigational drug or biologic, outside of a clinical trial, **to treat a patient** with a serious disease or condition who does not have comparable or satisfactory alternative therapies to treat the disease or condition.
  - Intent is clearly **treatment**

- Contrast with investigational drug in a **clinical trial** where the primary intent is **research**
  - systematic collection of data with the intent to analyze it to learn about the drug

Why Expanded Access?

- Not all patients can wait for approved drugs
  - No effective therapy for condition
  - Exhausted approved options
  - Intolerant of approved products
  - Ineligible or otherwise unable to participate in trials
- Expanded access allows access to unapproved/investigational drugs that might potentially provide benefit, when company is willing to provide, and ethical protections are in place (IRB/informed consent)

Requirements shared by all EAPs

21 CFR 312.305

- Serious or immediately life threatening illness or condition
- No comparable or satisfactory alternative therapy
- Potential benefit justifies the potential risks of the treatment, and those risks are not unreasonable in the context of the disease or condition being treated
- Providing drug will not interfere with or compromise development for the expanded access use

Expanded Access Program

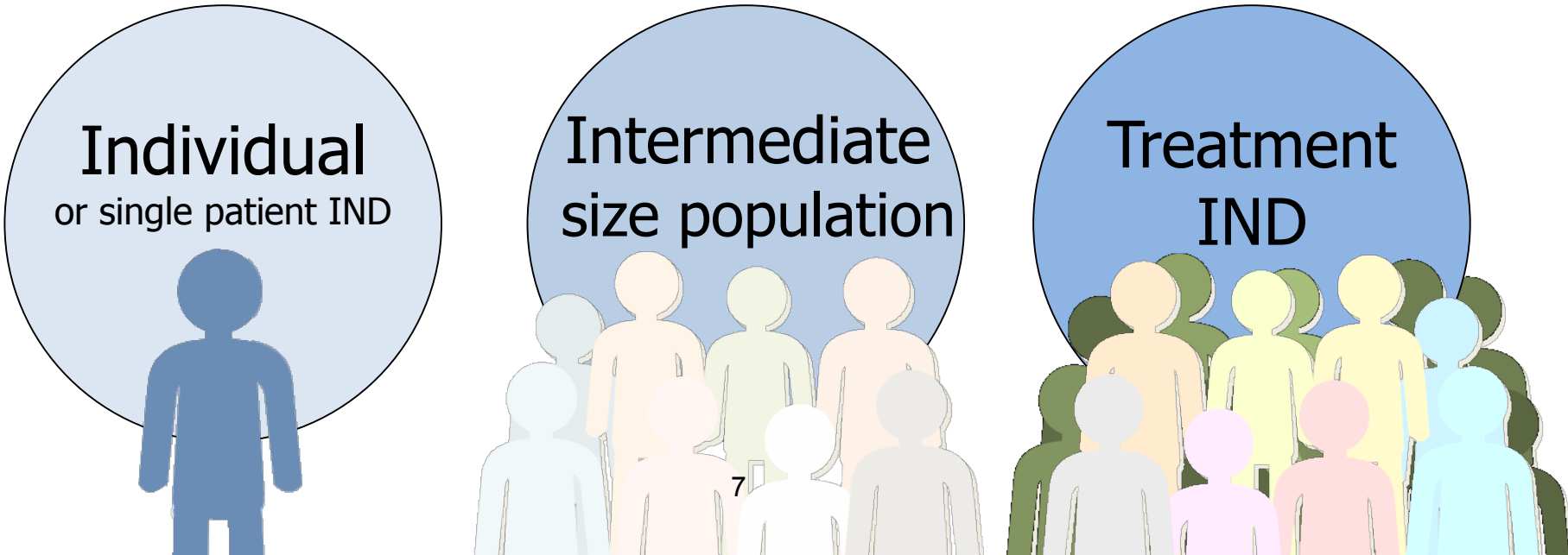
- FDA approves treatment uses under its expanded access regulations when:
  - The patient and a licensed physician are both willing to participate;
  - The patient's physician determines that there is no comparable or satisfactory therapy available to diagnose, monitor, or treat the patient's disease or condition;
  - That the probable risk to the patient from the investigational product is not greater than the probable risk from the disease or condition;
  - FDA determines that there is sufficient evidence of the safety and effectiveness of the investigational product to support its use in the particular circumstance;
  - FDA determines that providing the investigational product will not interfere with the initiation, conduct, or completion of clinical investigations to support marketing approval;
  - The sponsor submits a clinical protocol (a document that describes the treatment plan for the patient) that is consistent with FDA's statute and applicable regulations for investigational new drugs applications (INDs) or investigational device exemptions (IDEs), describing the use of the investigational product; and
  - The patient is unable to obtain the investigational drug under another IND or to participate in a clinical trial.

- Note: regulations differs for expanded access uses for investigational medical devices and investigational new drugs and biologics.

Two Categories of Access Based on Urgency

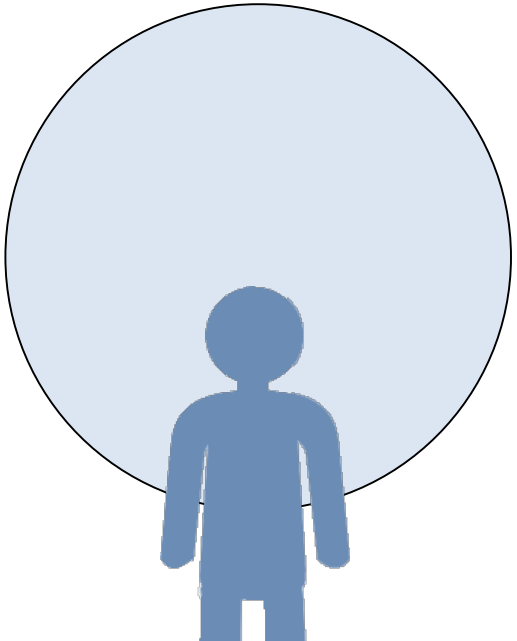
- Emergency
- Non-emergency

Three Tiers of Access Based on Size of Group



This webinar addresses

- Single patient
- Non-emergency
- Uses involving investigational drugs

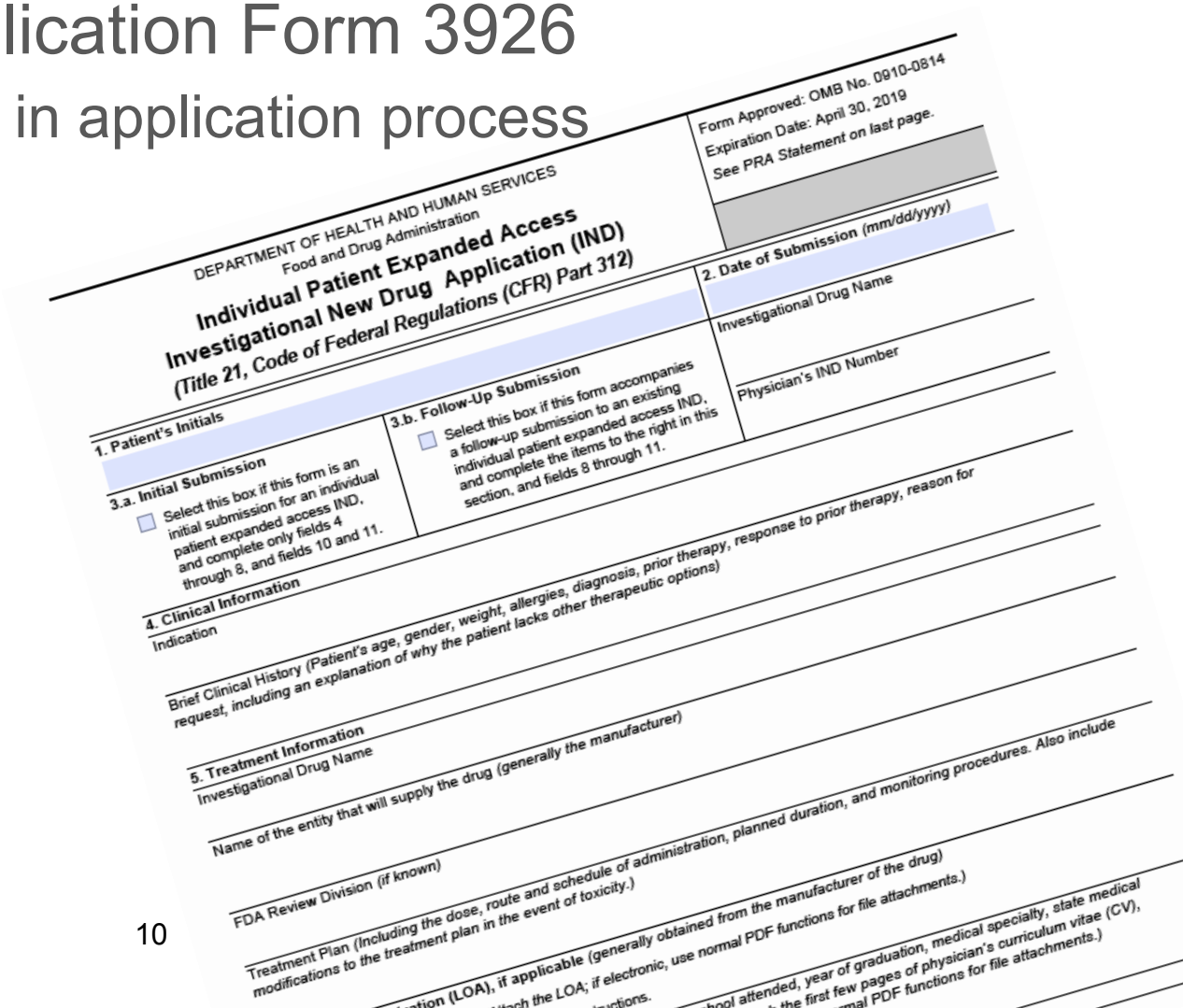


Increasing Attention on Expanded Access

- Media attention
- Right to Try laws
  - 34 states have laws
  - National bills pending in the House and Senate
- Attention on FDA
  - Guidance released in June 2016
  - Form 3926
  - About 1,200 requests per year, FDA approves over 99%
- Development of Reagan-Udall Foundation for FDA Navigator for physicians and patients

FDA streamlining request process for Single Patient INDs

- Simplified application Form 3926
  replaces 1571 in application process



DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Individual Patient Expanded Access
Investigational New Drug Application (IND)
(Title 21, Code of Federal Regulations (CFR) Part 312)

Form Approved: OMB No. 0910-0814
Expiration Date: April 30, 2019
See PRA Statement on last page.

1. Patient's Initials

2. Date of Submission (mm/dd/yyyy)

3.a. Initial Submission
☐ Select this box if this form is an initial submission for an individual patient expanded access IND, and complete only fields 4 through 8, and fields 10 and 11.

3.b. Follow-Up Submission
☐ Select this box if this form accompanies a follow-up submission to an existing individual patient expanded access IND, and complete the items to the right in this section, and fields 8 through 11.

Investigational Drug Name

Physician's IND Number

4. Clinical Information
Indication

Brief Clinical History (Patient's age, gender, weight, allergies, diagnosis, prior therapy, response to prior therapy, reason for request, including an explanation of why the patient lacks other therapeutic options)

5. Treatment Information
Investigational Drug Name

Name of the entity that will supply the drug (generally the manufacturer)

FDA Review Division (if known)

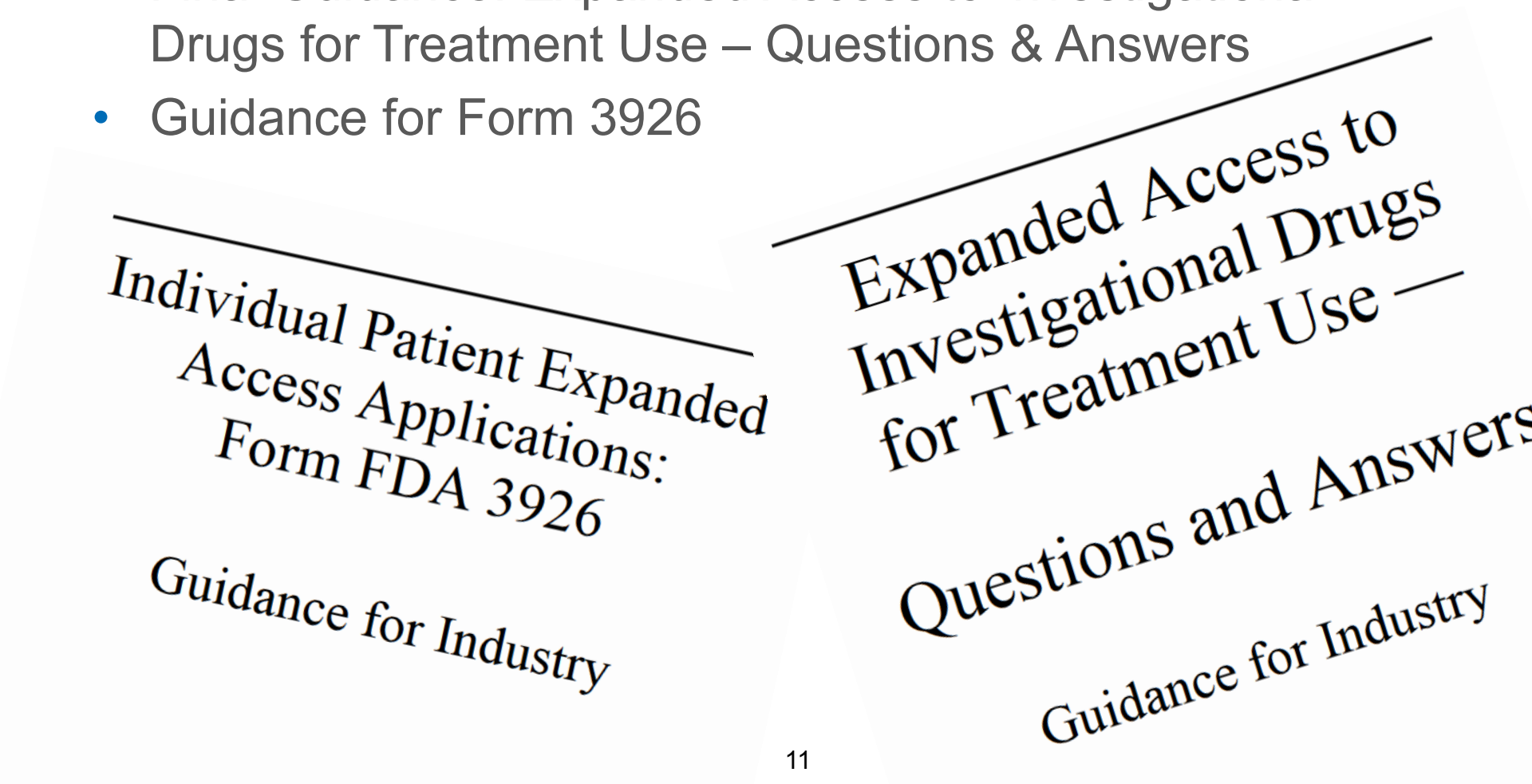
Treatment Plan (Including the dose, route and schedule of administration, planned duration, and monitoring procedures. Also include modifications to the treatment plan in the event of toxicity.)

tion (LOA), if applicable (generally obtained from the manufacturer of the drug)
ach the LOA; if electronic, use normal PDF functions for file attachments.)

hool attended, year of graduation, medical specialty, state medical
the first few pages of physician's curriculum vitae (CV),
mal PDF functions for file attachments.)

FDA streamlining request process for Single Patient INDs

- Final Guidance: Expanded Access to Investigational Drugs for Treatment Use – Questions & Answers
- Guidance for Form 3926



FDA streamlining request process for single patient INDs

- Comprehensive website explaining expanded access

IRBs

- To date, little attention focused on IRBs

- Complaints about IRBs include:
  - Many treating physicians don't have access to, or know how to access IRBs
  - Long time to review an expanded access request delays access
  - Some IRBs refuse to review an expanded access request
  - Don't know how to review the request
  - Cost

What can IRBs do to help streamline the process of review

- Awareness about request
- Application and submission
- Quick turn-around for review
- Assist IRB members in interpreting review criteria
- Monitoring/tracking the treatment use

Awareness about request

- IRBs report that they are not given advance notice about the expanded access request
  - Encourage physicians to work with the IRB as soon as they start the expanded access application with the sponsor

IRB application and submission

- Revise IRB application procedures so that the treating physician may submit as the application:
  - FDA Form 3926
  - Investigator Brochure or another source of information to determine potential risks and benefits
  - Draft consent document
  - Confidentiality and privacy – how to handle
- IRB electronic systems – document upload

Quick turn-around time

- Non-emergency expanded access requests are time sensitive
- Have a system so that application is identified as expanded access when submission occurs
- Send to a convened IRB meeting as soon as possible (Note: Non-emergency expanded access requests involving INDs must be reviewed by a convened IRB; an expedited review procedure is not permitted)
- Meeting can be convened to review application

Review criteria

- Provide recommendations or similar guidance to your IRB members about how to review single patient expanded access requests.
- To determine whether the criteria for approval (21 CFR 56) and the single patient expanded access regulations (21 CFR 312.305 and 312.310) are met.
- Suggestions:
  - Confirm the medical evaluation of the patient's condition based on the information provided by the treating physician (for example, using the information on Form 3926 and the IND number).

Review criteria – con't

- Ensure that informed consent or appropriate permissions will be obtained and documented. Given the compassionate nature of the request and FDA's involvement, consent documents should meet the requirements listed in 21 CFR 50.25, using plain language that is specifically aimed at "patients" who expect direct benefit, as opposed to "subjects" who may not expect benefit.
- Receive documentation that FDA has made its determinations regarding safety and effectiveness and has given clearance for the use. Such documentation is the IND number and any comments from FDA.
- Review the physician's treatment plan (or sponsor-provided treatment protocol) to determine that it makes adequate provision for ensuring the safety of the patient including adequate monitoring (timing and type of tests/exams, etc.) and appropriate plans for collecting and reporting the data.

Review criteria – con't

- Confirm that HIPAA requirements will be followed to ensure confidentiality of the medical record.
- Confirm that the treating physician will follow standard medical practice to protect the privacy interests of the patient.
- When the patient is likely to be vulnerable to coercion or undue influence additional safeguards are included in the treatment plan to protect the rights and welfare of the patient. When the patient is a child, confirm the provisions of 21 CFR 50.52 are met.

Monitoring and tracking treatment use

- Continuing review is required if the treatment use exceeds one year or a second treatment use is requested for the patient.
- Changes to treatment use and adverse events must be reported to the IRB (as well as FDA).
- Summary report to FDA and sponsor are required at the end of the treatment use. IRB should consider asking for a copy of this report to close out the treatment use when it ends.

Qs & As

Contact Information

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