REdI Conference – Spring 2017

Overview of FDA's Expanded Access Process and What's New

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Learning Objectives

- Summarize the objectives of the FDA's expanded access program
- Identify the types of expanded access requests
- Describe the requirements for requesting expanded access
- Describe the costs physicians may charge patients for single patient expanded access

Poll: Expanded Access

What is your experience with an "expanded access" application?

- I have submitted an expanded access application
- I have worked on an expanded access application
- I am familiar with the expanded access concept
- Huh? What is an expanded access application?

What is Expanded Access?

A process (or pathway) regulated by the Food and Drug Administration (FDA) that allows manufacturers to provide investigational new drugs to patients with serious diseases or conditions who have exhausted approved therapy, and cannot participate in a clinical trial

What is Expanded Access?

- Use of an investigational drug or biologic **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

Treatment Access Early Access

Named Patient Program

Special Access Programme

Compassionate Use

Single Patient IND

Pre-approval access

Pre-launch Access

Expanded Access

Historical Underpinnings

- Facilitating access to investigational therapies reaches back to 1970s
  - Cardiovascular - metoprolol, nifedipine
  - HIV - pentamadine, AZT
  - Oncology (Group C drugs)
- No official regulatory recognition until
- Implicit recognition of other treatment use for individuals

Expanded Access Programs (EAPs): The Option of Last Resort

Approved Drugs

Studied and characterized

Labeled

Broadest Availability

Reimbursement by 3rd party

Clinical Trials

Provide necessary data to determine safety & effectiveness

Most efficient path to market and broad availability

Expanded Access

Represent opportunity when other options exhausted

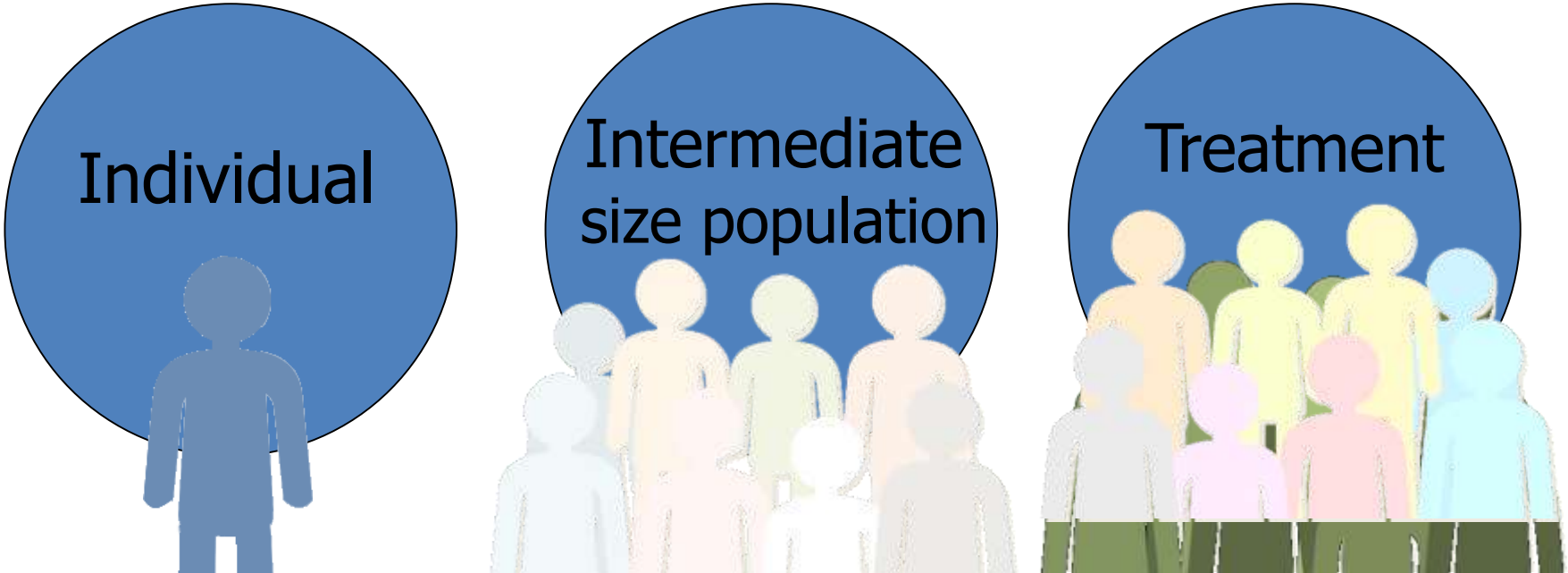
Goal is access to treatment

FDA Published Revised Regulations in 2009

code of federal regulations

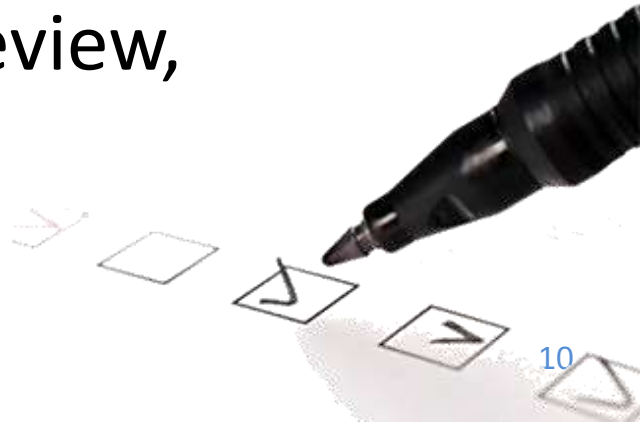
21 CFR 312 / IND Regulations

- Consolidated treatment use into a separate subpart of the IND regulations containing all necessary information in one place
- Describes **<u>three</u> distinct categories** of access



Expanded Access Regulations

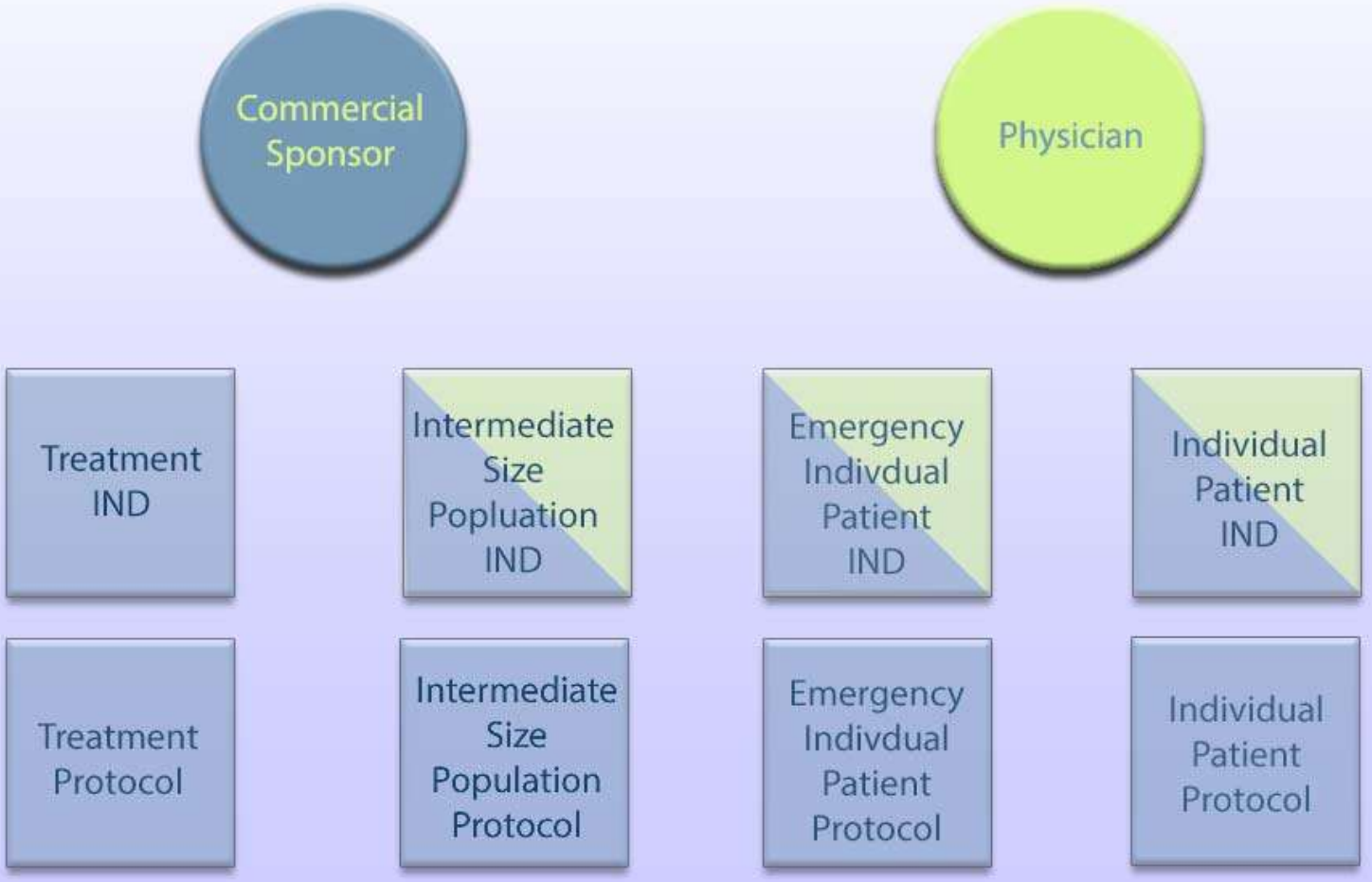
- Describes the **general criteria** applicable to all categories of access, and additional criteria that must be met for each access category
- Describes **requirements for submission**
- Describes the **safeguards** applicable to EAPs (e.g., informed consent, ethics review, reporting requirements)



Requirements shared by all EAPs

- 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

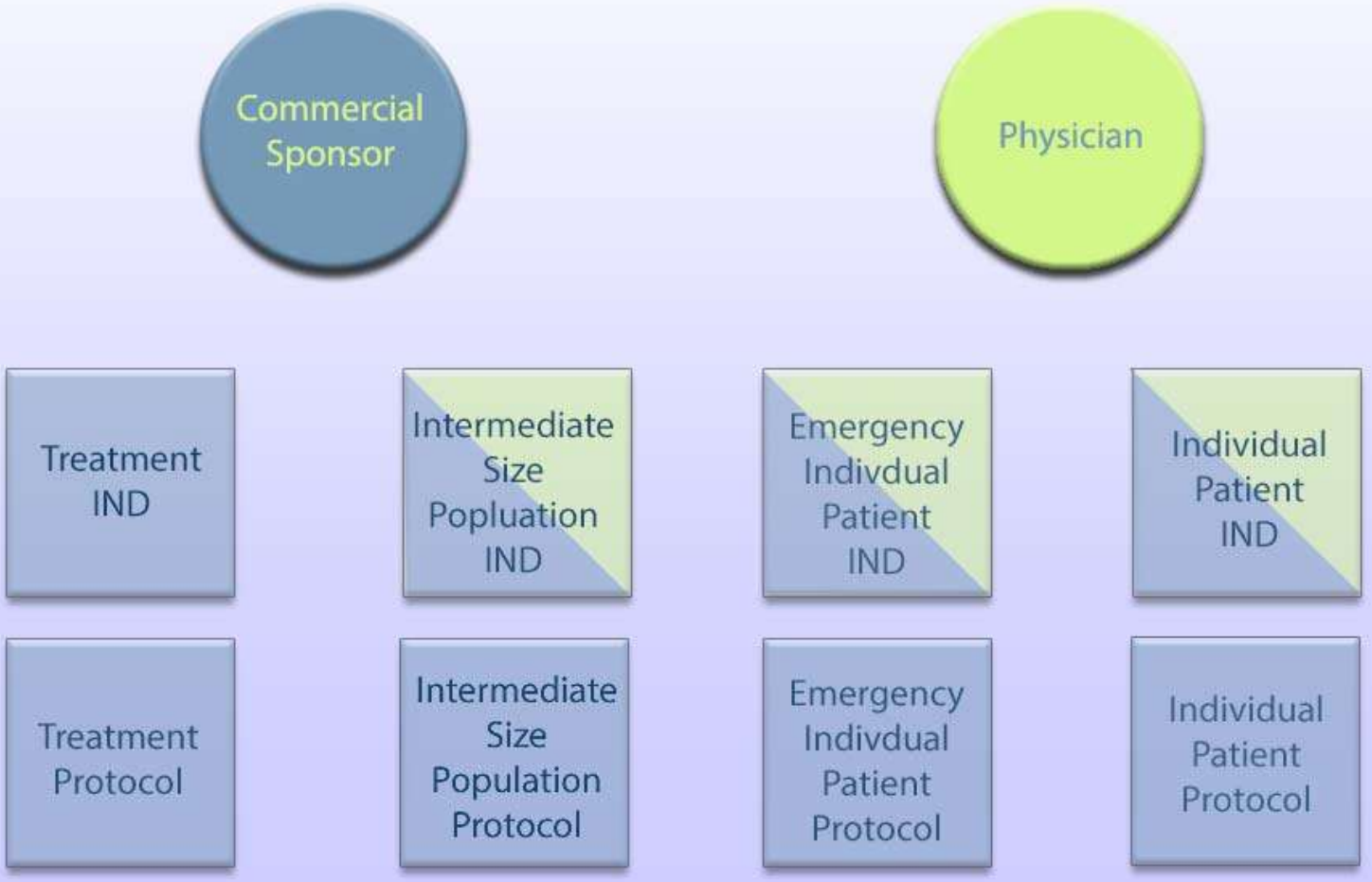
Categories of Expanded Access



Treatment IND

- Drug is being investigated in clinical trial designed to support marketing, or trials are complete
- Company is actively pursuing marketing approval
- Sufficient evidence of safety and effectiveness

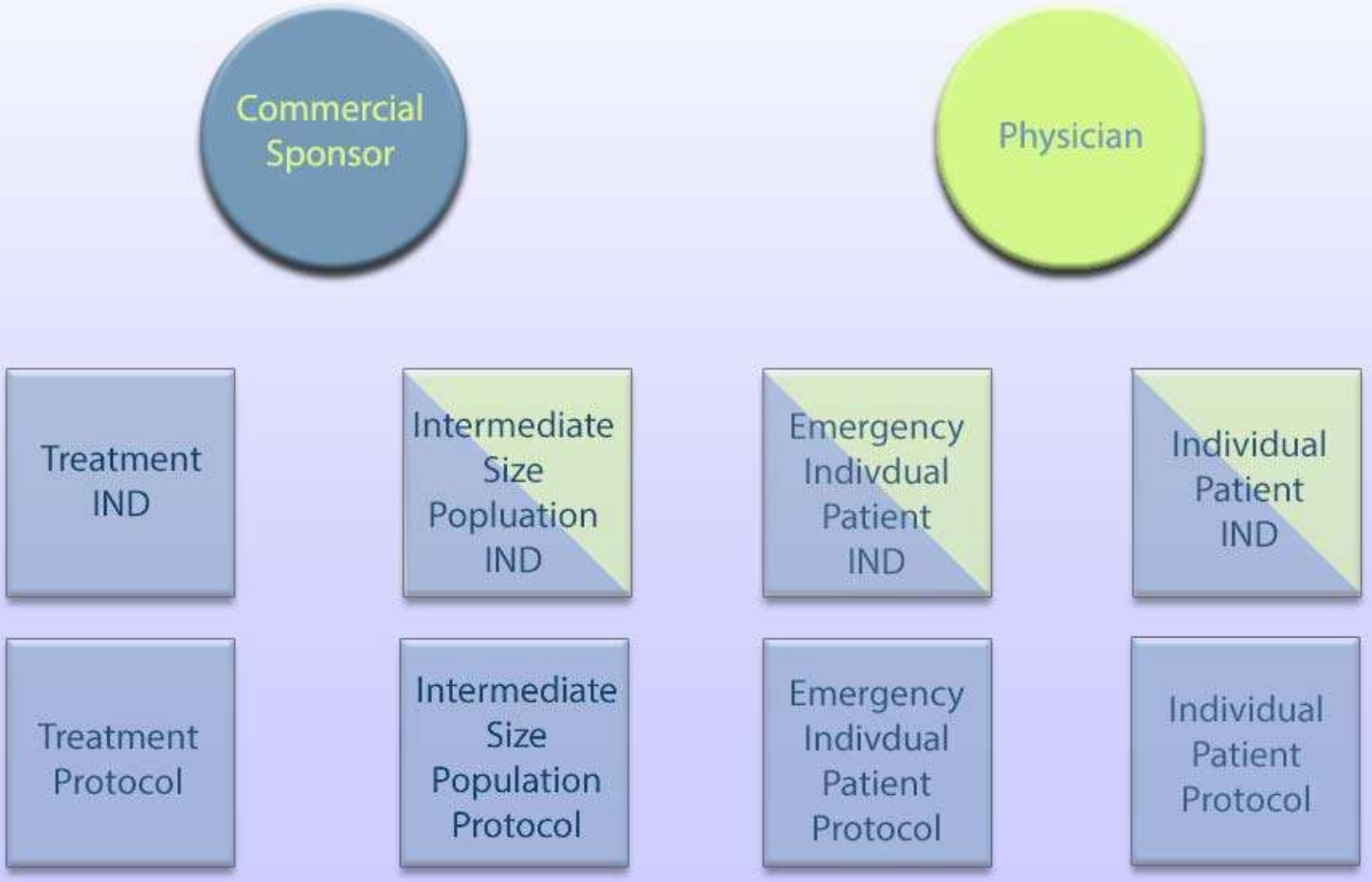
Categories of Expanded Access



Intermediate Size Population

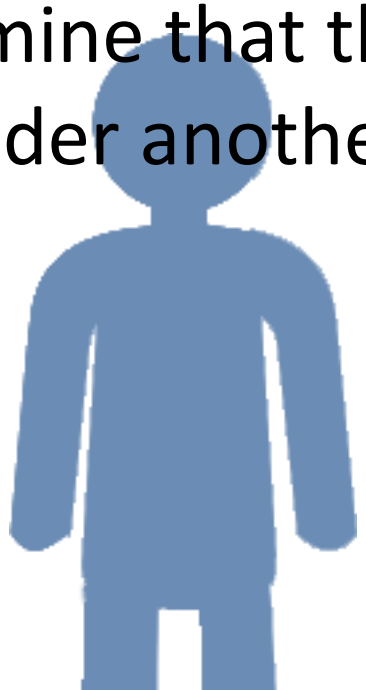
- No fixed numerical requirement
- More than one … generally, less than a lot
- Can be used when a drug is
  - Being developed (e.g., patients not eligible for trial)
  - Not being developed (e.g., rare disease)
  - Approved (e.g., drug withdrawn, drug shortage situation, foreign version of a U.S. approved drug)
- Sponsor can be physician, manufacturer, or 3rd party

Categories of Expanded Access



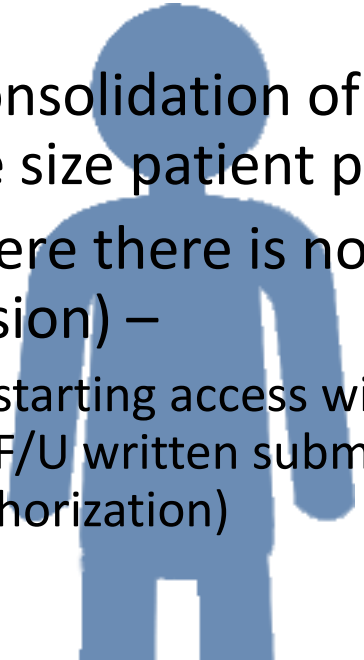
Individual Patient EAPs

- Physician must determine probable risk from drug does not exceed that from disease
- FDA must determine that the patient cannot obtain access under another type of IND



Individual Patient EAPs

- Physician often takes role of sponsor/investigator (responsible for sponsor activities: tracking, reporting, etc.)
- FDA requires written summary report, and may require special monitoring
- FDA may request consolidation of multiple cases into a single, intermediate size patient population IND
- Emergency use (where there is not time to make a written IND submission) –
  - FDA may authorize starting access without submission, with very quick turn-around (F/U written submission required within 15 working days of authorization)



Human Subject Protections Apply to <u>All</u> EAPs

Drugs in EAPs are *investigational drugs*, and they are subject to the following requirements:

- Protection of Human Subjects (informed consent)
- Institutional Review Boards (IRBs)
- Clinical Holds based on safety, and reporting requirements (adverse event reports, annual reports)

Overarching Considerations

- Unknown risks associated with access to investigational products for which there is limited information about safety and effectiveness
  - Some patients may benefit
  - Some patients may experience no effect
  - Some patients may be harmed
- FDA considers:
  - Potential harm to patients
  - Need to exhaust all existing approved treatments
  - Scientific likelihood of an efficacious response
  - Patient functionality

Potential EAP Benefits

- Can provide access to patients with serious/life-threatening diseases who have no other alternatives, and are willing to accept greater risk
- Can provide patients a measure of autonomy over their own health care decision
- The treatment IND can help bridge the gap between the latter stages of product development and approval by making a drug available during that period

How do patients view risk?

Potential overestimation of benefit and/or underestimation of risk

New drugs can have toxicities that cause increased suffering and pain, or the acceleration - or prolonging - of death, with no increase in quality of life

Not always considered by patients or families - Often see risks as abstract

How do IRBs view investigational products and risk?

- Traditionally charged with protecting research subjects from undue risk
- Direct benefit usually not a prerequisite for trials, except in children where additional safeguards are in place
- Efficacy (and safety) of early phase investigational drugs are not proven – and often not known
- Drug might be given in hope of direct benefit to patient

Concerns about Trial Enrollment

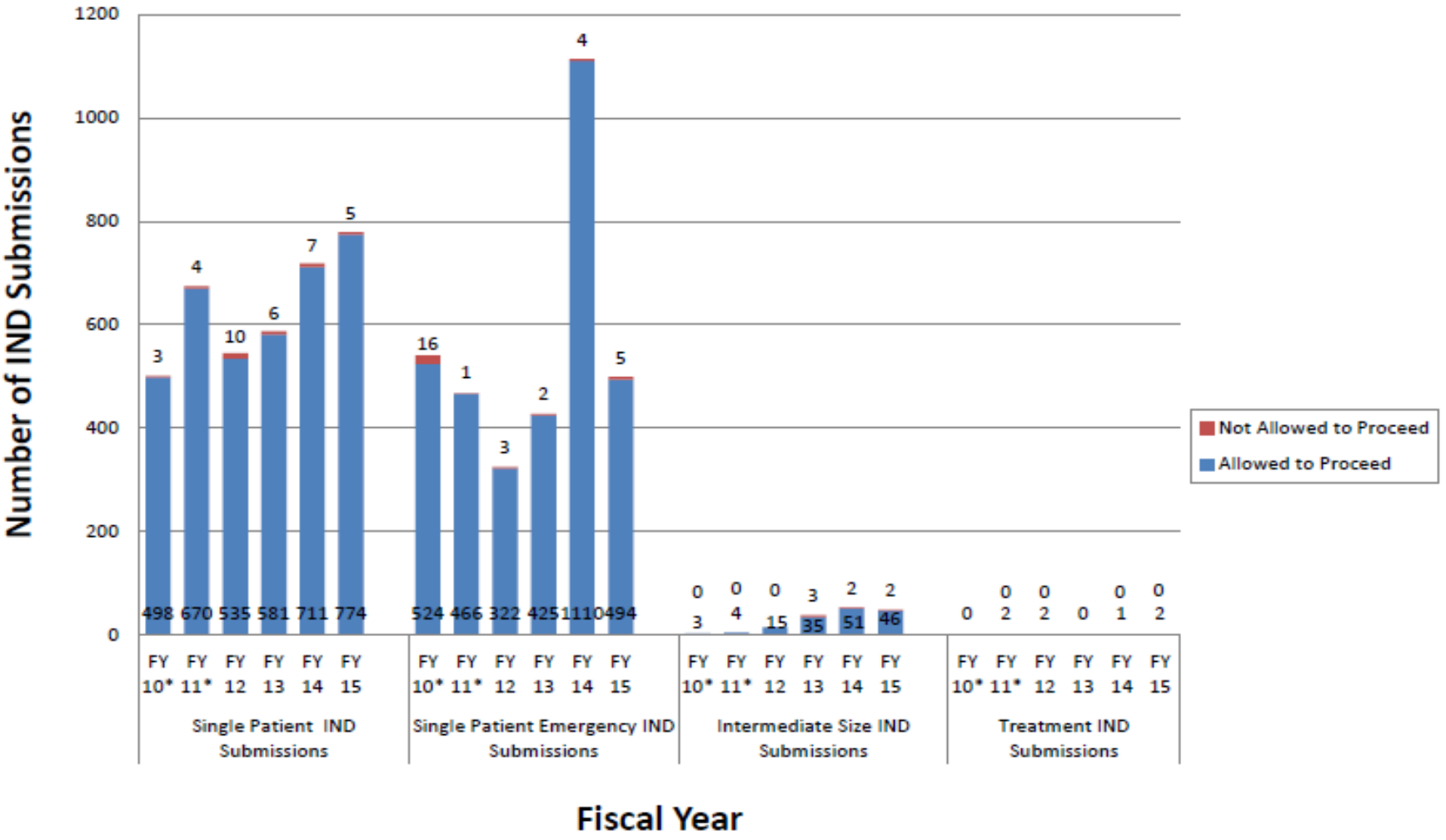
- Early access to investigational therapies could make phase 2 and 3 clinical trials more difficult to perform
- Clinical trial enrollment and conduct is a factor in consideration of treatment access to experimental drugs by manufacturers and FDA

Reasons Company May Deny Expanded Access Requests

Companies may deny a request for a number of reasons:

- Available clinical trials
- Manufacturing capacity is often limited in early phases – diverting drug for expanded access could limit supply for trials
- Concern adverse events would undermine the development program

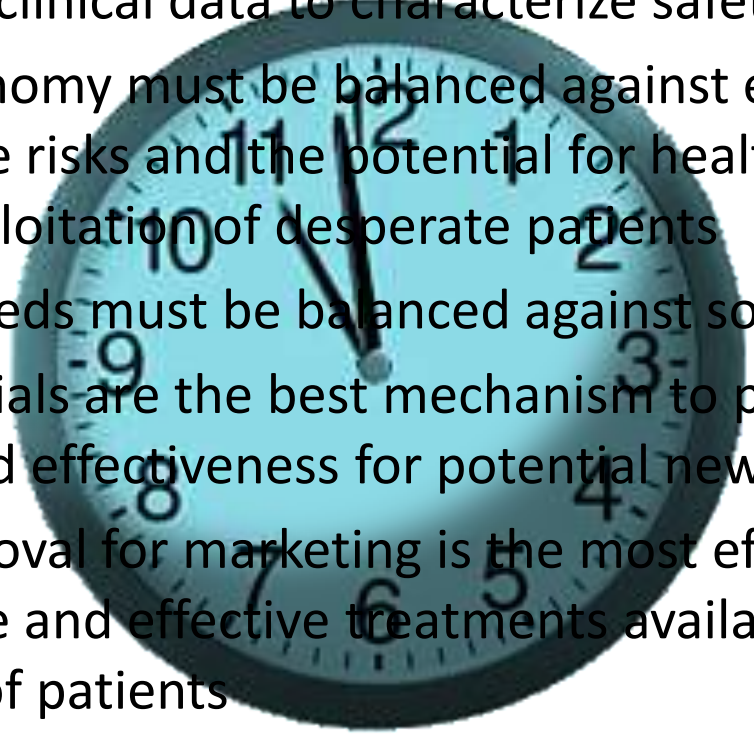
CBER and CDER Expanded Access IND Submissions, FY 2010 - 2015



*For FY 10 and FY 11, the reporting period was October 13 through October 12 of the following year.

Need for Balance

- Treatment access must be balanced against the systematic collection of clinical data to characterize safety and effectiveness
- Patient autonomy must be balanced against exposure to unreasonable risks and the potential for health fraud, and potential exploitation of desperate patients
- Individual needs must be balanced against societal needs
  - Clinical trials are the best mechanism to provide evidence of safety and effectiveness for potential new treatments
  - FDA approval for marketing is the most efficient means to make safe and effective treatments available to the greatest number of patients



EAP-Implementing the process: A community responsibility

- **The Patient:** Consults with their doctor to find and decide about alternative options
- **The Doctor:** Works with manufacturer, files paperwork with FDA, IRB, and is responsible for patient care and reporting
- **The Industry Sponsor:** Provides the investigational product, and permits cross-reference to their original IND information
- **FDA:** Determines eligibility, judges safety data, ensures patient protections
- **IRB:** Reviews consent to assure patient is informed about nature of treatment

Take Aways

- Single FDA mechanism creates a pathway to access
- Single patient application: Can be completed in 45 minutes
- Application decisions are quick – hours to days
- >99% of applications are allowed to proceed
- Patients can't apply for such access
- FDA staff can provide information and assistance
- The purpose is **treatment**, not research, so efficacy data is not needed, but sponsor must:
  - Report serious/unexpected adverse reactions
  - Submit summary report after treatment

Visit: www.fda.gov/expandedaccess

U.S. Food and Drug Administration

SINGLE PATIENT EXPANDED ACCESS:

PHYSICIAN FACT SHEET and APPLICATION CHECKLIST

What is Expanded Access?

Expanded access is the use of an investigational drug outside of clinical trials to diagnose, monitor, or treat patients with serious or life-threatening diseases or conditions for which there are no comparable or satisfactory therapy options available.

When possible, it is preferred that a patient be given an investigational drug as part of a clinical trial rather than through expanded access. This is because clinical trials are designed to generate data that may lead to the product's approval and, consequently, wider availability of the drug. However, patients may be able to receive the investigational product through expanded access when patient enrollment in a clinical trial is not possible (for example, the patient is not eligible for any ongoing clinical trials or there are none available).

Obtaining the investigational drug

To obtain expanded access for your patient, first contact the pharmaceutical company developing the drug. Sometimes, the company will provide the drug to patients according to a pre-established protocol. If not, you should ask the company for approval to obtain its drug. The company does so by issuing a Letter of Authorization (LOA).

Requesting expanded access from the FDA

To request access to an investigational drug for your patient, you must then submit an application to the FDA for expanded access on your patient's behalf. Form FDA 3926 can be used for this application. The expanded access process also includes requesting approval from an Institutional Review Board (IRB), and obtaining informed consent from your patient for the use of the investigational drug. Once the request is authorized by FDA, you will be responsible for managing the patient's medical care.

Ensuring patient safety is a priority; FDA must determine that the potential benefit justifies the potential risks of the use of the investigational drug. Even with safeguards, there may be unknown risks, since there is limited information available about the investigational drug. Your patient may not receive expanded access if the drug company does not provide the drug or if the FDA denies the request. However, FDA has historically granted expanded access to almost all the requests it receives.

If your patient needs the drug on an emergency basis, before a written request can be submitted, FDA can grant the request over the phone and your patient can begin treatment after you receive the medication from the drug company. However, you must still submit an expanded access application to FDA within 15 days and notify an IRB within 5 days of initiation of treatment.

Contact: DrugInfo@fda.hhs.gov or 1-855-543-3784 with any questions.

More Information:

- FDA Information for Physicians: Expanded Access
- FDA Guidance: Expanded Access to Investigational Drugs for Treatment Use -Questions and Answers
- Application for Individual Patient Expanded Access
- FDA's Expanded Access Contact Information, including FDA review divisions

Follow the steps below to request expanded access to an investigational new drug for your patient.

1. Ensure your patient meets the eligibility criteria for expanded access

- They must have a serious or immediately life-threatening disease or condition; there must be no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition; and they generally must be unable to participate in a clinical trial (see clinicaltrials.gov for a list of many clinical trials being conducted around the world).
- You must determine that the probable risk from the investigational drug is not greater than the probable risk from the disease or condition.
- If your practice includes multiple patients who might be good candidates for the investigational product, consider whether an expanded access IND for an intermediate-size population, rather than multiple single patient INDs, would be more efficient.

2. Obtain a letter of authorization (LOA) from the drug manufacturer

- Contact the drug manufacturer/company to request use of the drug outside of the clinical trial setting. FDA may be able to help identify the contact. The manufacturer must decide whether to provide the drug to treat your patient under expanded access.
- If the manufacturer agrees to provide the drug for expanded access, submit a Letter of Authorization from the drug company to the FDA with your IND submission. A template of this letter can be used and is available here.

3. Fill out the "Individual Patient Expanded Access Investigational New Drug Application" form (Form FDA 3926) and submit it to FDA

- Submit the request for your patient. See the guidance Individual Patient Expanded Access Applications: Form FDA 3926 for instructions.
- For emergency requests, you may contact 855-543-3784 and follow the instructions on FDA's Expanded Access Contact Information page. After 4:30 pm EST weekdays and all day on weekends, contact the FDA Emergency Call Center at 866-300-4374.

4. Request Institutional Review Board (IRB) approval

- If you work for an academic medical center, use the IRB procedures in place for your institution. If you are in private practice, seek IRB approval through a local university, hospital or an independent IRB.

5. Discuss the risks of the investigational drug treatment with your patient and obtain informed consent

- Informed consent must be obtained before initiating treatment, unless one of the exceptions in 21 CFR part 50 applies.

6. Await Authorization from FDA and the IRB

- Your patient may begin treatment 30 days after FDA receives the request, unless you receive earlier notification from FDA that the treatment may proceed. Typically FDA responds to these requests in a matter of days (or hours for emergency requests). You must also receive IRB approval before treatment can begin.
- Historically, FDA has approved 99% of expanded access requests. However, this is not a guarantee that yours will be approved.
- Once your request is approved by FDA, notify the drug company and arrange to obtain the drug.
- In certain circumstances, the drug company may be able to charge the patient for the cost of the drug, or it may elect to cover the cost.
- Any additional costs for administering the drug and monitoring its use will depend on the patient's insurance coverage and do not require FDA authorization. FDA has no authority to require that the Centers for Medicare and Medicaid Services (CMS) or any private health insurance company reimburse for investigational drugs for which FDA has authorized charging. It is important that you and your patient consider the cost of the investigational drug and the medical services associated with its use that are not covered by third-party payers such as insurance or Medicare.

7. Begin treatment and monitor the patient

- You are required to adhere to the monitoring procedures described in the treatment plan you outlined in the Form FDA 3926, including adverse event reporting. You may also have to submit a summary of the results of the treatment.

More Information

Visit: www.fda.gov/expandedaccess

- FDA's Office of Health & Constituent Affairs 301-796-4600 or PatientNetwork@fda.hhs.gov
- CDER's Division of Drug Information 855-543-3784 or druginfo@fda.hhs.gov
- CBER at 800-835-4709 or industry.biologics@fda.gov

Questions?

Please complete the session survey:

surveymonkey.com/r/DRG-D1S02

Personal Contact Information:

Kevin.Bugin@FDA.HHS.GOV

301-796-2302

www.fda.gov