U.S. FOOD & DRUG ADMINISTRATION

Expanded Access Programs for Drugs and Biologics

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Outline

- Expanded Access Programs (EAP)
- Other initiatives to improve access WITHIN clinical trials

What is Expanded Access (EAP)?

21 CFR 312.300, Subpart I:

Aim is to facilitate the availability of investigational new drugs to patients with serious diseases or conditions when there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the patient's condition

EAP → Treatment

Trial → Research

Expanded Access

- “Compassionate” use
- You have a serious illness and you’ve tried everything else
- You and your doctor think an investigational drug (not FDA approved) might be a good option
- The drug may be studied in clinical trials, but you are not able participate in these trials

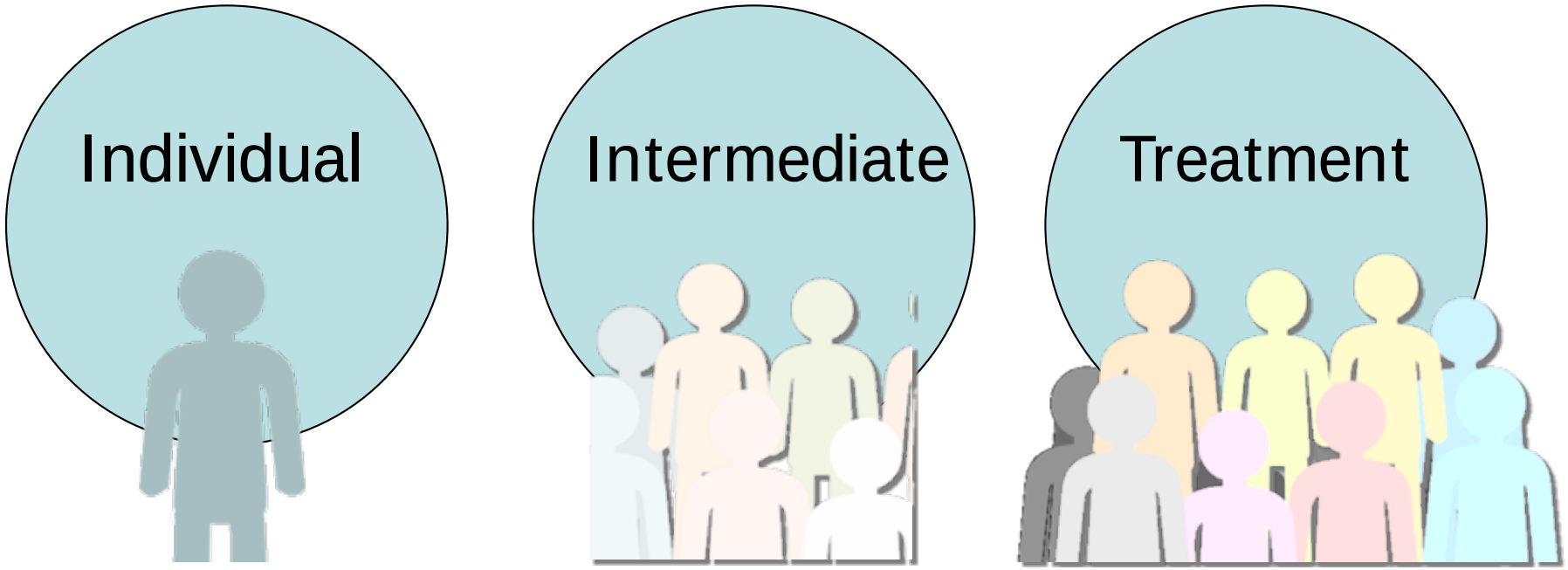
Access to Treatments

Approved Drugs	Clinical Trials	Expanded Access
Safety and efficacy established	Provide data to determine safety & effectiveness	For unapproved drugs or approved drugs with restricted availability
Broadest availability	Path to approval and broad availability	Trial enrollment not possible
3rd party reimbursement		

Slide adapted from Dr. Martha Donoghue

Types of Expanded Access Programs

- 3 types of EAPs are defined in the code of federal regulations (CFR):



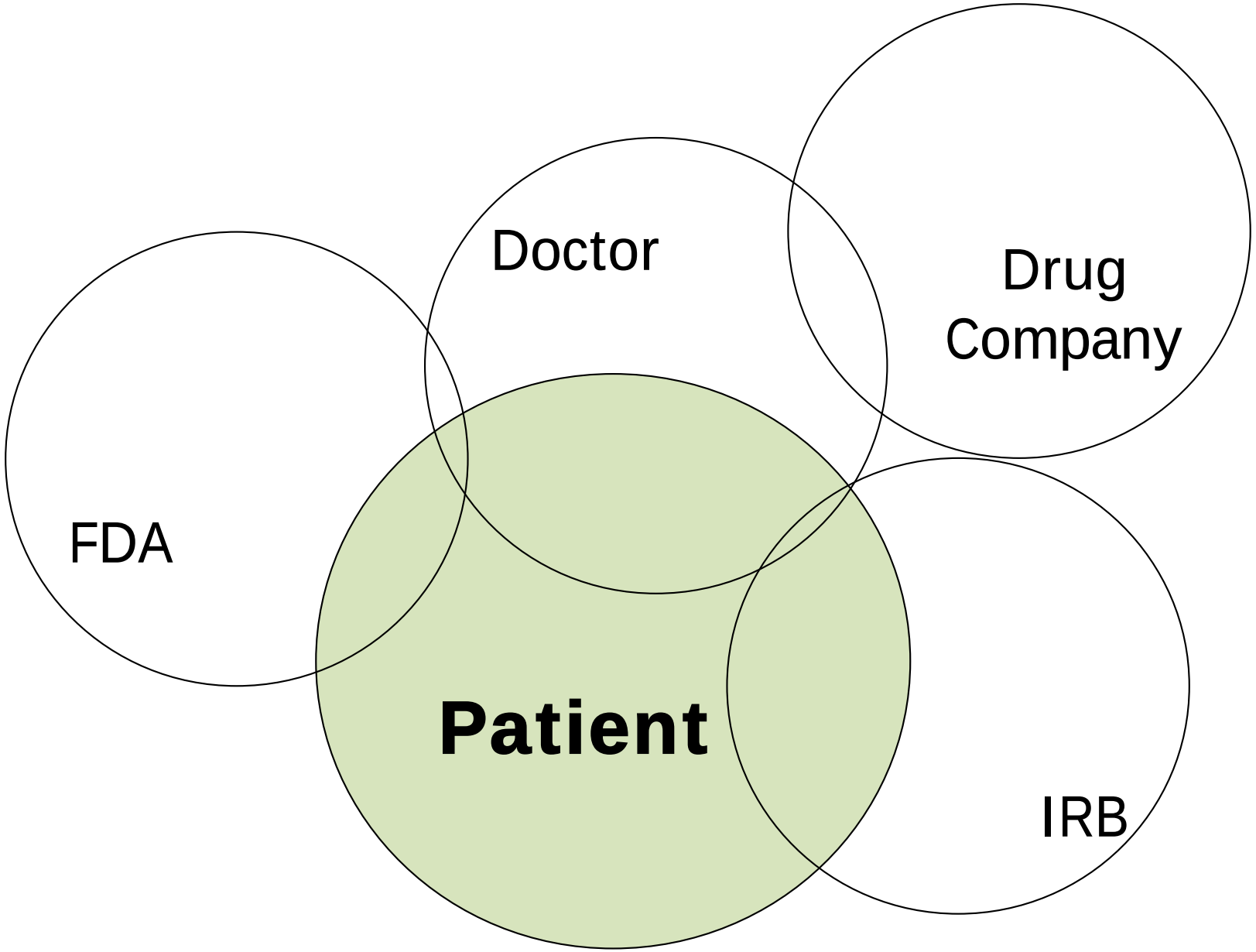
Single Patient IND

- Generally patients with multiply relapsed or refractory cancer

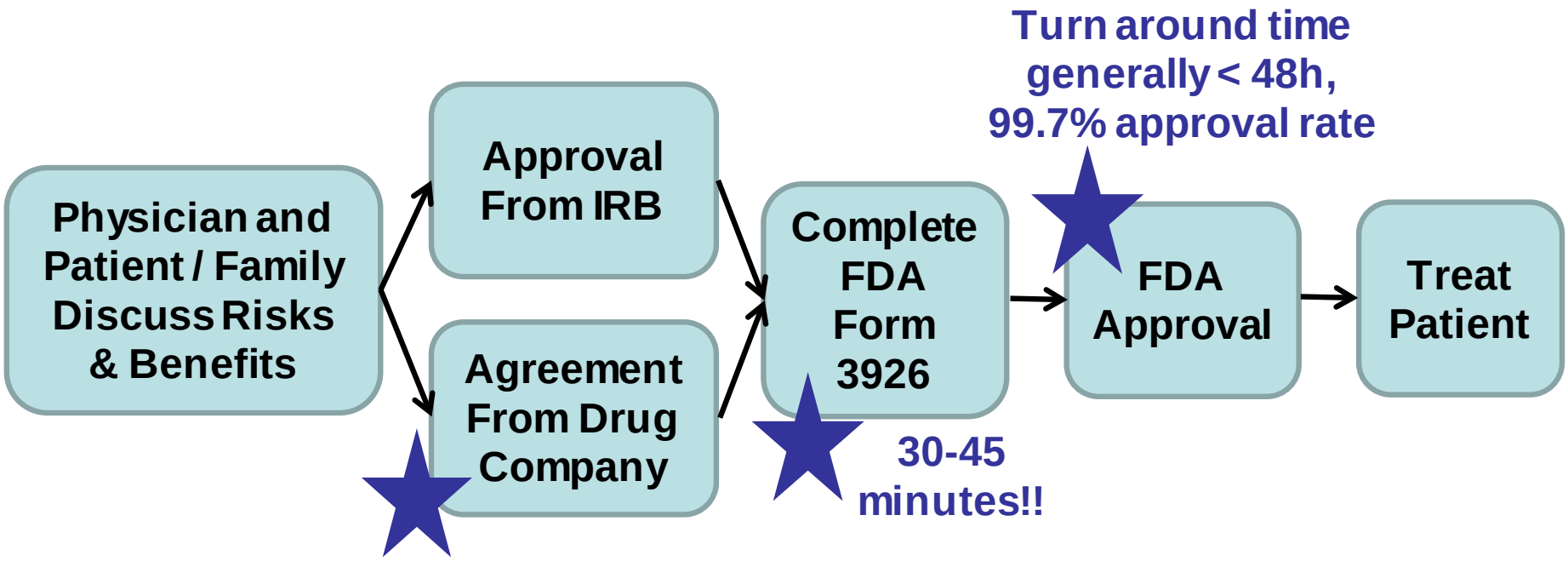
- Reasons for requesting expanded access may include:
  - Promising evidence of activity with a drug in a disease with a similar molecular target or histology
  - Patient received benefit while participating on a previous clinical trial
  - Ineligible for clinical trial but reason to think potential benefit outweighs the risk
  - Clinical trial is closed to accrual
  - Drug is not currently being developed
  - Clinical trial site not accessible to patient (regional)

How to Apply for Expanded Access?

The single patient IND



Obtaining a Single Patient IND



Form 3926 is 2 pages and includes:

- Brief medical history and rationale for trying drug
- Proposed treatment plan with safety and efficacy monitoring

Also submit:

- Letter of authorization from sponsor
- Investigator qualification statement / form 1571

1. Risk has not been established for investigational drug

2. Potential benefit is often overestimated

Pros

- Provides access to potentially lifesaving therapies to patients who have no other alternatives, & may be willing to accept greater risk
- Provides patients a measure of autonomy over their own health care decision
- Bridges gap between drug development and FDA approval
- May provide data to support development
- May offer hope for patients with no other available options

Cons

- Risk has not been established
- May overestimate benefit and underestimate risk
- Drug availability
  - manufacturing
  - fear that adverse events on EAP may disrupt drug development (MYTH!)
- Paperwork! (improved, & ongoing initiatives to overcome)

Could Expanded Access Be Made Obsolete?

- Expanded access programs are in place when no appropriate alternatives exist, but the best access is an approved drug
- To be part of the road to approval, enrollment/treatment on clinical trials is critical

- Considerations for decreasing the need for expanded access in oncology:
  - Expansion of eligibility criteria (broadly)
  - Separate cohort within a clinical trial with broad eligibility criteria
  - Novel trial designs: Master protocols
    - May allow assessment of multiple diseases, treatments, or biomarkers in one protocol
  - Initiatives in pediatrics: FDARA
- The future: novel surrogate endpoints, real-world data mining, personalized medicine

Background: Cancer Drug Development for Children and Adolescents

- Widely leverages adult drug discovery/development

- Impact of legislative initiatives which support pediatric drug development: markedly less obvious in Oncology than in other clinical areas
  - Orphan designation and exemption from the Pediatric Research Equity Act (PREA)

Lag in evolution of cancer drug development paradigm in pediatrics

RACE for Children Act:

- **R**esearch to **A**ccelerate **C**ures and **E**quity for Children Act
  - Incorporated as Title V Sec. 504 of the **FDA Reauthorization Act (FDARA),** enacted August 18, 2017

- **Requires** evaluation of new molecularly targeted drugs and biologics "intended for the treatment of adult cancers *and directed at a **molecular target** substantially relevant to* the growth or progression of *a pediatric cancer*"

- Elimination of **orphan exemption for pediatric studies** for cancer drugs directed at relevant molecular targets

Summary

- Expanded access programs provide access to unapproved, investigational therapies to patients who have no other alternatives
- The single patient IND is the type of expanded access oncologists would most likely encounter
- The single patient IND requires agreement from the patient and doctor, the drug company, the FDA, and the IRB
- Oncology stakeholders are considering options to try and improve access to unapproved drugs

Resources for Single Patient INDs

- https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/ucm107434.htm

Form FDA 3926

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.)*

6. Letter of Authorization (LOA), if applicable *(generally obtained from the manufacturer of the drug)*

☐ I have attached the LOA. *(Attach the LOA; if electronic, use normal PDF functions for file attachments.)*

Note: If there is no LOA, consult the Form Instructions.

7. Physician's Qualification Statement *(Including medical school attended, year of graduation, medical specialty, state medical license number, current employment, and job title. Alternatively, attach the first few pages of physician's curriculum vitae (CV), provided they contain this information. If attaching the CV electronically, use normal PDF functions for file attachments.)*

8. Physician Name, Address, and Contact Information

Physician Name *(Sponsor)*	Email Address of Physician
Address 1 *(Street address, No P.O. boxes)*	
Address 2 *(Apartment, suite, unit, building, floor, etc.)*	Telephone Number of Physician
City / State	Facsimile (FAX) Number of Physician
ZIP Code	Physician's IND number, if known

PSC Publishing Services (301) 443-6740 EF

9. Contents of Submission

This submission contains the following materials, which are attached to this form (select all that apply). If none of the following apply to the follow-up communications, use Form FDA 1571 for your submission.

- ☐ Initial Written IND Safety Report
- ☐ Follow-up to a Written IND Safety Report
- ☐ Annual Report
- ☐ Summary of Expanded Access Use (treatment completed)
- ☐ Change in Treatment Plan
- ☐ General Correspondence
- ☐ Response to FDA Request for Information
- ☐ Response to Clinical Hold

10.a. Request for Authorization to Use Form FDA 3926

☐ I request authorization to submit this Form FDA 3926 to comply with FDA's requirements for an individual patient expanded access IND.

10.b. Request for Authorization to Use Alternative IRB Review Procedures

☐ I request authorization to obtain concurrence by the Institutional Review Board (IRB) chairperson or by a designated IRB member, before the treatment use begins, in order to comply with FDA's requirements for IRB review and approval. This concurrence would be in lieu of review and approval at a convened IRB meeting at which a majority of the members are present.

11. Certification Statement: I will not begin treatment until 30 days after FDA's receipt of a completed application and all required materials unless I receive earlier notification from FDA that treatment may begin. I also agree not to begin or continue clinical investigations covered by the IND if those studies are placed on clinical hold. I also certify that I will obtain informed consent, and that an Institutional Review Board (IRB) will be responsible for initial and continuing review and approval of this treatment use, consistent with applicable FDA requirements. I understand that in the case of an emergency request, treatment may begin without prior IRB approval, provided the IRB is notified of the emergency treatment within 5 working days of treatment. I agree to conduct the investigation in accordance with all other applicable regulatory requirements.

WARNING: A willfully false statement is a criminal offense (U.S.C. Title 18, Sec. 1001).

Signature of Physician

To enable the signature field, please fill out all prior required fields. For a list of required fields which have not yet been filled out, please click here.

Date

For FDA Use Only

Date of FDA Receipt	Is this an emergency individual patient IND?	Is this indication for a rare disease (prevalence < 200,000 in the U.S.)?
IND Number	☐ Yes ☐ No	☐ Yes ☐ No

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 45 minutes per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

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"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

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- Dr. Paul Kluetz
- Dr. Richard Pazdur


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- The FDA has convened an internal group to assess how to effectively and efficiently implement the new law.

- As part of that process, the agency will consider what the FDA needs to do in order to support implementation of the Right to Try Pathway, such as guidance, QAs, or other agency recommendations.

- Ultimately, a burden rests with sponsors developing potentially life-saving or life-extending drugs to consider making these products available, pre-approval, to patients who qualify for access.

- We look forward to providing future updates.

Who to Contact to Request a Single Patient IND!

- General
  - Contact CDER's Division of Drug Information at **855-543-3784 during normal business hours** (8am – 4:30pm EST weekdays), or **866-300-4374 after hours**.

- Office of Hematology and Oncology Products

Division	Phone #
Division of Oncology Products 1	301-796-2330
Division of Oncology Products 2	301-796-2320
Division of Hematology Products	301-796-7550