Expanded Access to Investigational Drugs

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Partners in Progress
October 8, 2019

Disclosure Information

- I have no financial relationships to disclose

- I will not be discussing off-label and/or investigational use of drug products in this presentation

Key Points for Today

- Define expanded access
- Explain how patients with cancer can access investigational therapies
- Discuss how FDA intends to broaden access to 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

Access to Treatments

Approved Drugs

Safety and efficacy established

Broadest availability

3rd party reimbursement

Clinical Trials

Provide data to determine safety & effectiveness

Path to approval and broad availability

Expanded Access

For unapproved drugs or approved drugs with restricted availability

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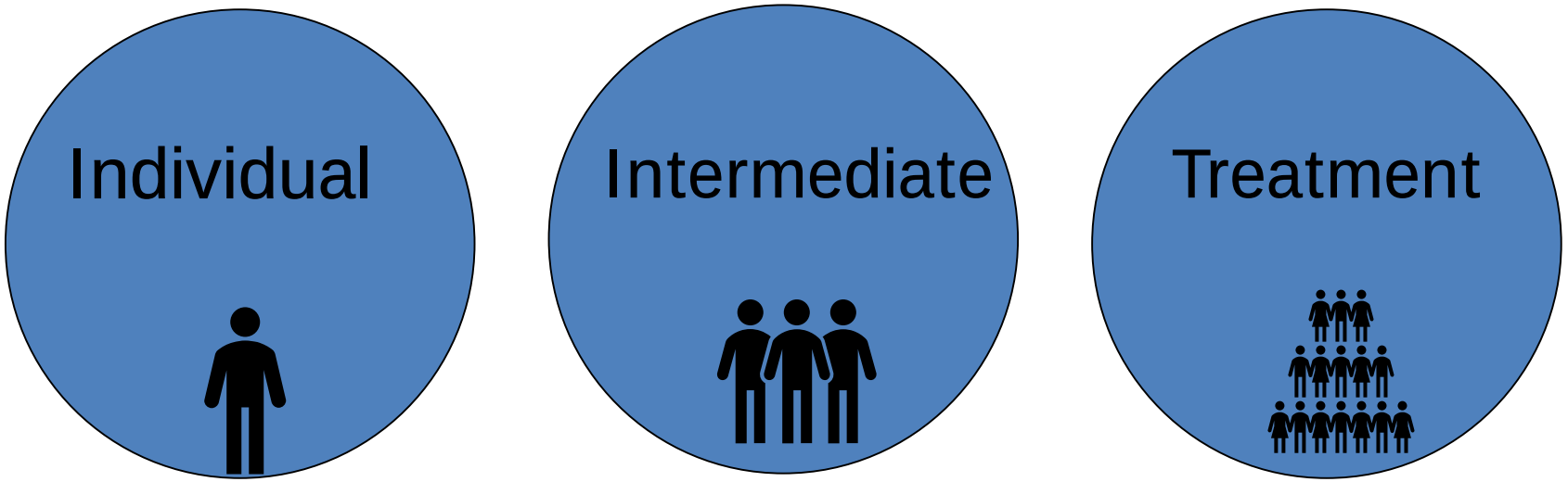
Trial enrollment not possible

Types of FDA Expanded Access Programs (EAPs)

There are three types of EAPs defined in the code of federal regulations:



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 the development of the drug

Examples of Investigational Drug Access Prior to Approval

- Erwinaze (asparaginase *Erwinia chrysanthemi*); 2011
  - for patients with acute lymphoblastic leukemia (ALL) who have developed hypersensitivity to E.coli-derived asparaginase
  - EAP treatment protocol enrolled > 1500 patients

- Voraxaze (glucarpidase); 2012
  - carboxypeptidase enzyme for methotrexate toxicity
  - EAP treatment protocol enrolled > 2500 patients

- Unituxin (dinutuximab); 2015
  - a GD2-binding monoclonal antibody for high-risk neuroblastoma
  - COG EAP treatment protocol enrolled > 800 patients

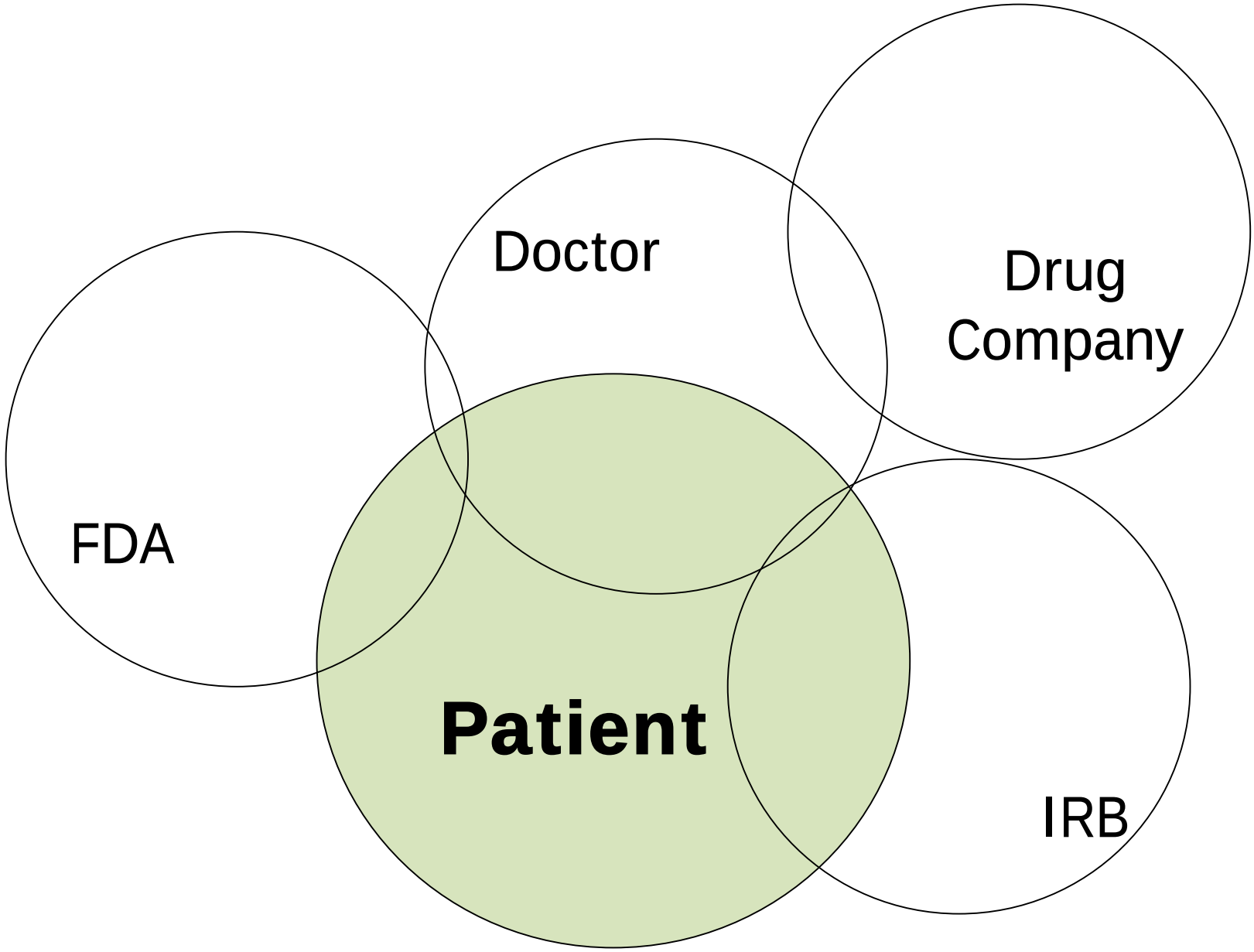
Individual Patient Expanded Access in Oncology

Generally multiply relapsed, refractory patients

Reasons for requesting expanded access may include:

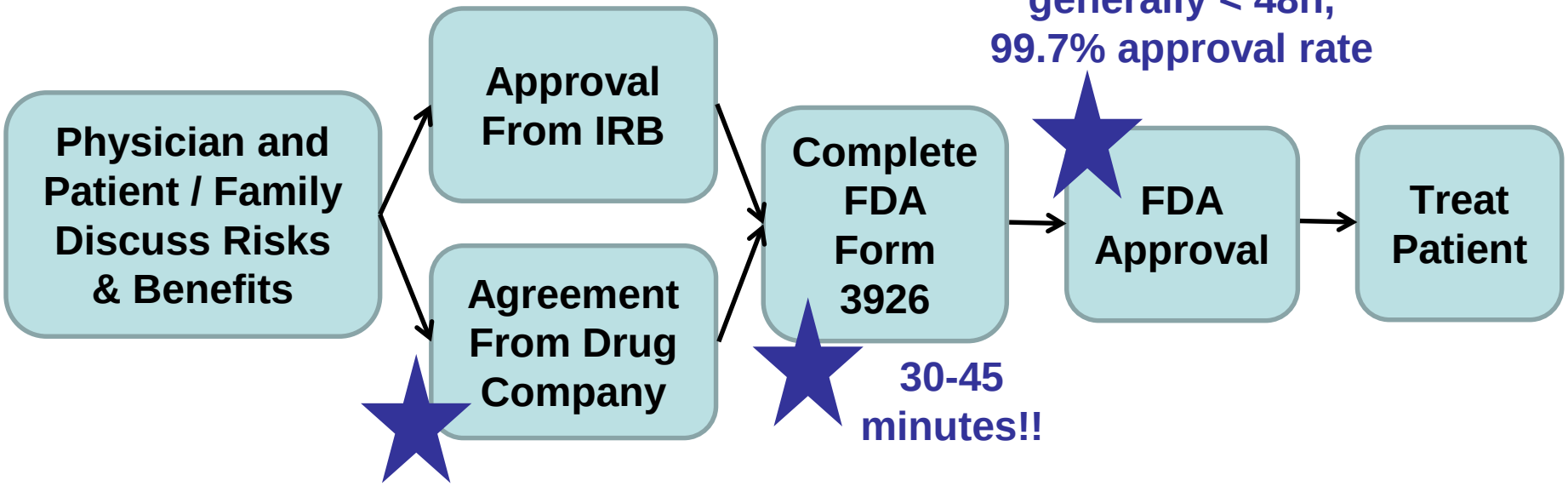
- Promising evidence of activity with a drug being studied
- Previous benefit from a clinical trial
- Clinical trial is closed to accrual
- Drug is not currently being developed

The single patient IND



How to Apply for Expanded Access?

Obtaining a Single Patient IND



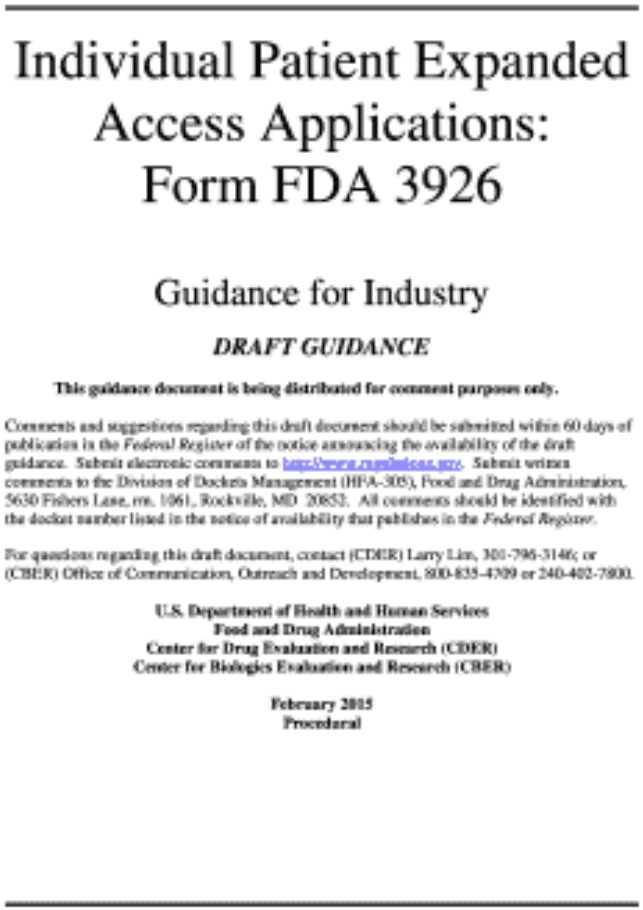
Form 3926 is 2 pages and includes:

- 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

Form 3926



Individual Patient Expanded Access Applications: Form FDA 3926

Guidance for Industry

DRAFT GUIDANCE

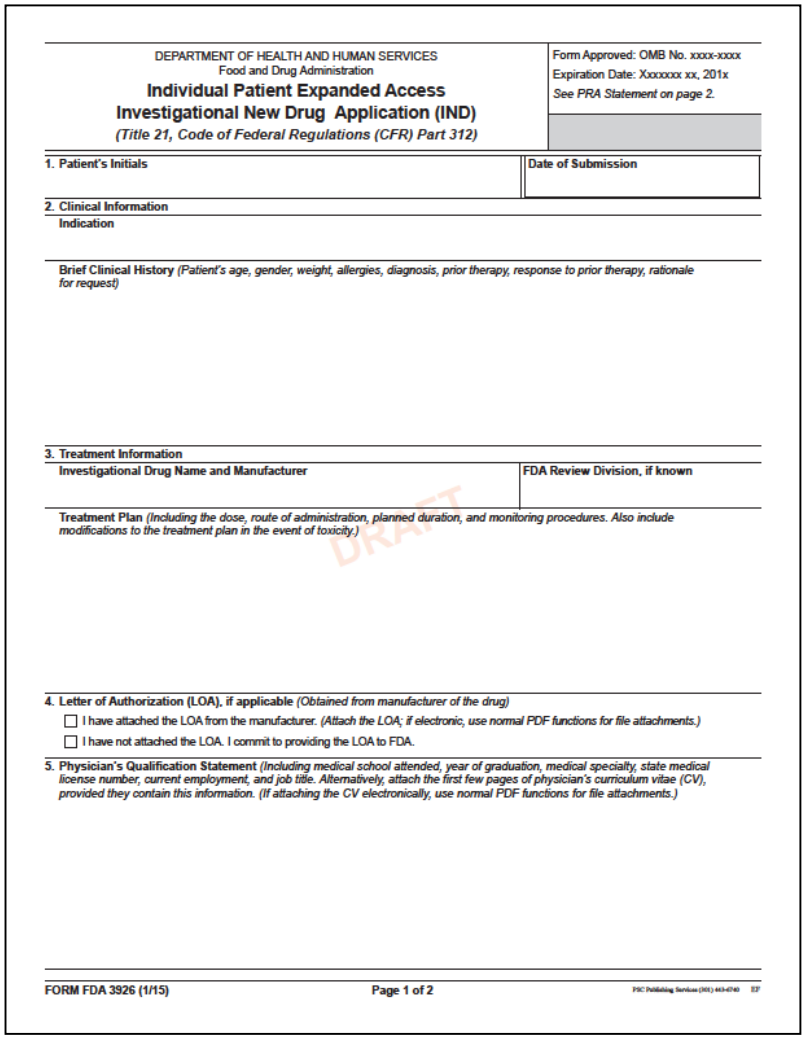
This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Larry Lin, 301-796-3146; or (CBER) Office of Communication, Outreach and Development, 800-835-4709 or 240-402-7800.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

February 2015
Procedural



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. xxxx-xxxx
Expiration Date: Xxxxxxx xx, 201x
See PRA Statement on page 2.

1. Patient's Initials | **Date of Submission**

2. Clinical Information

Indication

Brief Clinical History *(Patient's age, gender, weight, allergies, diagnosis, prior therapy, response to prior therapy, rationale for request)*

3. Treatment Information

Investigational Drug Name and Manufacturer | **FDA Review Division, if known**

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

DRAFT

4. Letter of Authorization (LOA), if applicable *(Obtained from manufacturer of the drug)*

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

☐ I have not attached the LOA. I commit to providing the LOA to FDA.

5. 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.)*

FORM FDA 3926 (1/15) **Page 1 of 2**

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Reasons to Use EAPs With Caution

Risk has not been established for investigational drug

- Confidence in safety more important than consideration of efficacy
- For a patient with an immediate life-threatening condition, evidence burden is low

Potential benefit is often overestimated

- Drug given under EAP with intention to provide benefit
- Anecdotal evidence of even overwhelming efficacy may hold up only in a very small subset of patients, but have toxicities that increase suffering and/or hasten death in everyone else

Adverse effects on clinical trials

- Unrestricted access could slow enrollment to trials; prevent collection of meaningful safety and efficacy data

Benefits and Barriers

BENEFITS:

- Can provide access to patients with serious/life-threatening diseases who have no other alternatives, and may be willing to accept greater risk
- Can provide patients a measure of autonomy over their own health care decision

- Can be a foothold into marketplace for sponsors (especially a treatment IND)
- May offer hope for patients with no other available options

BARRIERS:

- Paperwork/time (New! Form 3926)
- Adverse impact on enrollment to clinical trials
- Manufacturing (drug availability)
- Fear that adverse events on EAPs may disrupt clinical development

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)
  - Age, CNS disease, organ dysfunction
- Separate cohort within a clinical trial with broad eligibility criteria

Right to Try Act

May 30,2018 "Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act"

- Permits/allows eligible patients to have access to eligible investigational drugs
- Criteria:
  - Patient: Life threatening disease, exhausted approved treatments, unable to participate in a trial of the eligible drug, informed consent
  - Drug: Past Phase I, unapproved for any use, active IND, ongoing development (not on clinical hold)

Learn About Other Treatment Options

- Right to Try
- Understanding Investigational Drugs
- Understanding Unapproved Use of Approved Drugs "Off Label"

Right to Try

The Right to Try Act, or the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act, was signed into law May 30, 2018. This law is another way for patients who have been diagnosed with life-threatening diseases or conditions who have tried all approved treatment options and who are unable to participate in a clinical trial to access certain unapproved treatments.

Clinical trials provide information about whether a product is safe to use and can effectively treat or prevent a disease. People may have many reasons for participating in clinical trials. In addition to contributing to medical knowledge, some people participate in clinical trials because there is no treatment for their disease, treatments they tried have not worked, or they are not able to tolerate the current treatments.

For patients with serious or immediately life-threatening diseases, the FDA is committed to facilitating access to investigational medicines while protecting patients and making sure that they are able to make informed decisions. Therefore, for more than three decades, FDA has facilitated

Summary

- Expanded access programs provide access to investigational therapies to patients with life-threatening diseases.
- FDA and key stakeholders intend to broaden access to clinical trials.

Acknowledgments

Ashley Ward
Paul Kluetz
Ann Farrell
Rea Blakey
Gideon Blumenthal
Richard Pazdur

U.S. FOOD & DRUG ADMINISTRATION

PROJECT FACILITATE

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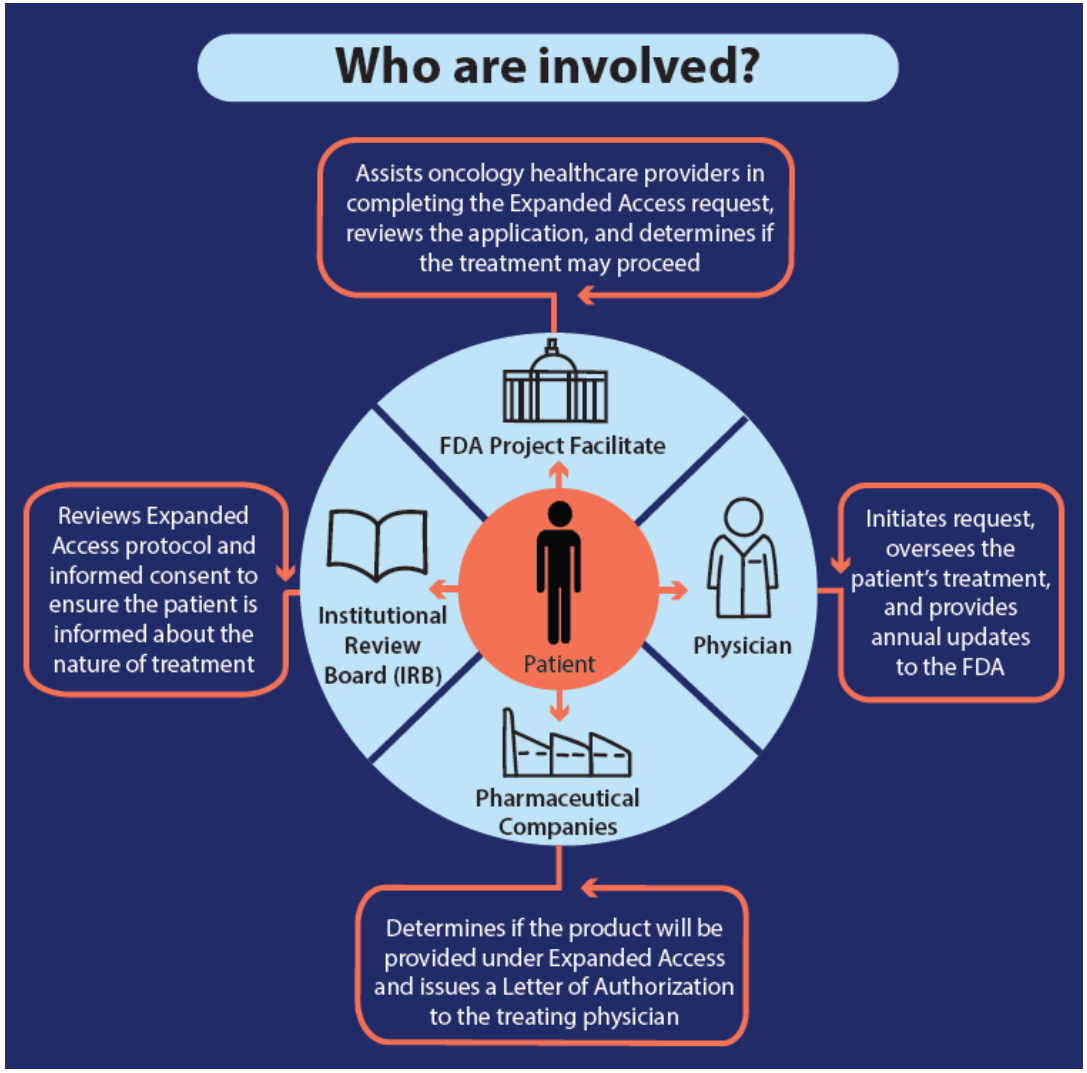
U.S. Food and Drug Administration


Who are involved?
Assists oncology healthcare providers in completing the Expanded Access request, reviews the application, and determines if the treatment may proceed
FDA Project Facilitate
Reviews Expanded Access protocol and informed consent to ensure the patient is informed about the nature of treatment
Institutional Review Board (IRB)
Patient
Physician
Initiates request, oversees the patient's treatment, and provides annual updates to the FDA
Pharmaceutical Companies
Determines if the product will be provided under Expanded Access and issues a Letter of Authorization to the treating physician

PROJECT FACILITATE

Project Facilitate

- Single point of contact for all oncology EA requests
- Step-by-step support in completing EA request:
  - IRB resource options
  - Industry contact
  - Advice on other necessary information (e.g. CV, protocol, patient history) to complete their request
  - Assistance completing form FDA 3926, if needed
- Collection of metrics on if access to drug provided by drug manufacturer, and if not, why?
- Follow up / reminders

Expanded Access Resources

- Patients, Advocacy Groups
  - Reagan Udall Foundation
    - Website: https://reaganudall.org/
    - (202) 849-2075 or admin@reaganudall.org
  - FDA Division of Drug Information (DDI)
    - Website: https://www.fda.gov/news-events/expanded-access/fdas-expanded-access-contact-information
    - (855) 543-DRUG or druginfo@fda.hhs.gov
- Healthcare Professionals
  - Project Facilitate
    - Website: https://www.fda.gov/about-fda/oncology-center-excellence/project-facilitate
    - (240) 402-0004 or ONCProjectFacilitate@fda.hhs.gov


FDA
U.S. FOOD & DRUG
ADMINISTRATION
ONCOLOGY CENTER OF EXCELLENCE
PROJECT FACILITATE
Assisting healthcare providers with requests for access to investigational oncology products
DO YOU NEED HELP SUBMITTING A SINGLE PATIENT IND EXPANDED ACCESS (EA) REQUEST (ALSO KNOWN AS COMPASSIONATE USE) FOR A PATIENT WITH CANCER?
...FDA's Oncology Center of Excellence (OCE) can help:
• Locate IRB resources
• Find an EA contact for a drug/biotech company
• Complete Form FDA 3926
8:00 AM - 4:30 PM Eastern Time (M-F)
Phone: (240) 402-0004
Email: OncProjectFacilitate@fda.hhs.gov
www.fda.gov/oce
Patients: Talk to your healthcare provider to discuss whether expanded access is an appropriate option.

Resources

For questions about FDA's expanded access program, contact the Office of Health and Constituent Affairs' Expanded Access Team at

301-796-8460 or

PatientNetwork@fda.hhs.gov

Patients may call the Division of Drug Information

(855) 543-DRUG (855-543-3784)

FDA Guidance for Industry: *Expanded Access to Investigational Drugs for Treatment Use*, May 2013

http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm351261.pdf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