Expanded Access to Investigational Drugs and Biologics

When All Else Fails

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REAGAN - UDALL FOUNDATION FOR THE Food and Drug Administration

What is Expanded Access?

- A process (or pathway) regulated by FDA that allows 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 and cannot participate in a clinical trial. Intent is clearly **treatment.**

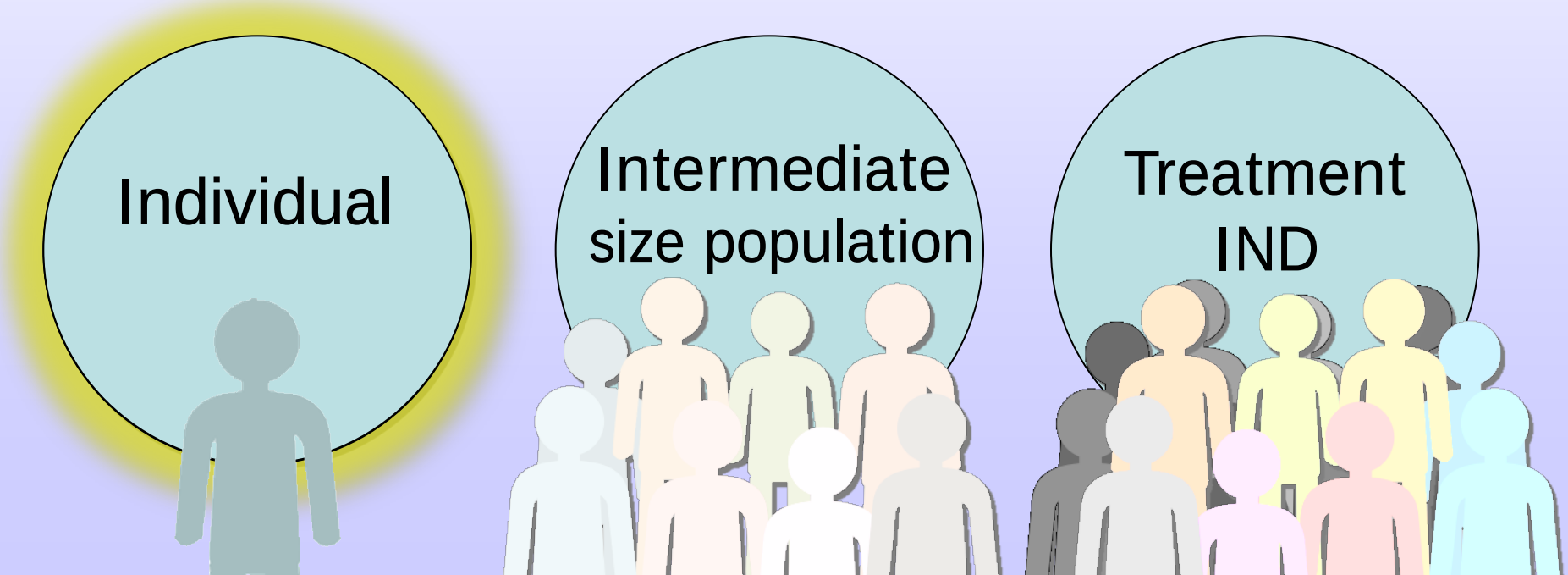
- Contrast with investigational drug in a **clinical trial,** systematic collection of data with the intent to analyze it to learn about the drug.
  The primary intent is **research.**

Expanded Access
21 CFR 312.305

- Patients with 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

Types of Expanded Access INDs

- Three distinct categories of access
- Can be submitted as a new IND or as a protocol to existing IND
- Emergency versus non-emergency Individual



Patient and physician discuss options and consider possible use of investigational agent

Physician or patient need to contact commercial sponsor to request product for treatment use

If the sponsor agrees to provide product, they will provide a Letter of Authorization (LOA) to the physician allowing FDA to cross reference important information on file in the sponsor's original IND

Physician then submits an application (3926) to FDA for review. If allowed to proceed, FDA will provide an IND number allowing the sponsor company to ship the drug to the doctor to treat the patient

Physician certifies treatment will not begin until IRB reviews and signs off on informed consent

Draft Form 3926

DEPARTMENT OF HEALTH AND HUMAN SERVICES
U.S. Food and Drug Administration
Individual Patient Expanded Access
Investigational New Drug Application (IND)
(Title 21, Code of Federal Regulations (CFR) Part 312)

(1) Patient's Initials	Date of Submission *(mm/dd/yyyy)*
☐ Select this box if this form is an initial submission for an individual patient expanded access IND, and complete sections 2 through 6 and sections 8 and 9.	☐ Select this box if this form is a followup submission to an existing individual patient expanded access IND, and complete the fields below, and sections 6 through 9. Investigational Drug Name IND Number

(2) Clinical Information

Indication

Brief Clinical History (Patient's age, gender, weight, allergies, diagnosis, prior therapy, reason for request)

(3) Treatment Information

Investigational New Drug Name and Name of the Entity That Will Supply It (generally the manufacturer)

FDA Review Division, if known

Treatment plan (Provide a brief statement in the space below, including the dose, route of administration, planned duration, and monitoring procedures. Also include modifications to the treatment plan in the event of toxicity)

(4) Letter of Authorization (LOA), if applicable (generally obtained from the manufacturer of the drug):
☐ I have attached the LOA from the manufacturer. *(Attach the LOA; if electronic, use normal PDF functions for file attachments.)*

If there is no LOA, consult the Form Instructions

(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.)*

(6) Physician Name, Address and Contact Information		Email address of Physician
Physician Name *(Sponsor)*		
Address 1 *(Street address, No P.O. boxes)*		
Address 2		Zip Code
City	State	

FORM FDA 3926 (6/24/15)

Telephone Number of Physician	Fax Number of Physician Physician's IND number, if known

(7) Contents of Submission

This submission contains the following materials, which are attached to this form (select all that apply):

☐ 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

(8) 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.

(9) Certification Statements: 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, consistent with Federal requirements, and that an Institutional Review Board (IRB) that complies with the Federal IRB requirements will be responsible for initial and continuing review and approval of this treatment use. 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	Date
For FDA use only. IND Number: _____	Is this an emergency individual patient IND? ____Yes ____No Is this indication for a rare disease (prevalence < 200,000 in the U.S.)* ____Yes ____No

FORM FDA 3926 (6/24/15)

Draft Form 3926

- 1: Patient's initials and date of submission
- 2: Clinical information
- 3: Treatment information
- 4: Letter of Authorization (from manufacturer)*
- 5: Physician's qualification statement
- 6: Physician name, address and contact information
- 7: Request for authorization to use Form 3926
- 8: Certification statements and physician signature
    - When treatment may begin
    - Informed consent and IRB issues
    - Emergency IND procedures

* Attachment

Do adverse event data from EA really have a negative regulatory effect?

- Adverse events not unexpected in these patients, often related to underlying disease
  - FDA reviewers experienced in discerning adverse events relationships
  - Four decades of experience with only rare examples
- Review of >10000 expanded access INDs invoking >1000 commercial INDs revealed only 2 clinical holds (0.2%).
- Expedited AE reporting: no special requirements occurring under expanded access INDs
  - Requirement is to report serious unexpected suspected adverse reactions only, not all adverse events
  - defined to mean “there is evidence to suggest a causal relationship between the drug and adverse event...”

Drugs track record

Expanded Access Submission Received	Reporting Period						
Expanded Access INDs	10/13/2009-10/12/2010***	10/13/2010-10/12/2011***	10/1/2011-9/30/2012	10/1/2012-9/30/2013	10/1/2013-9/30/2014	10/1/2014-9/30/2015	Total
Single Patient Emergency INDs received	516	443	289	315	1069	431	
Single Patient Emergency INDs allowed to proceed	500	442	287	313	1066	428	
Single Patient INDs received	484	652	498	550	696	747	
Single Patient INDs allowed to proceed	484	652	496	550	692	745	
Intermediate Size INDs received	2	0	14	28	52	46	
Intermediate Size INDs allowed to proceed	2	0	14	27	50	45	
Treatment INDs received	0	1	0	0	0	0	
Treatment INDs allowed to proceed	0	1	0	0	0	0	
Expanded Access Protocols							
Single Patient Emergency Protocols received	0	3		2	9	7	
Single Patient Emergency Protocols allowed to proceed	0	3		2	9	7	
Single Patient Protocols received	16	89	121		35	14	
Single Patient Protocols allowed to proceed	16	89	121		35	14	
Intermediate Size Protocols received	5	1	8		9	9	
Intermediate Size Protocols allowed to proceed	5	1	8		9		
Treatment Protocols received	7	11	10	12			
Treatment Protocols allowed to proceed	7	11	10	12			
Totals for Expanded Access							
Total Number of Expanded Access INDs and Protocols received in CDER	1030	1200	940	977		1262	7292
Total Number of Expanded Access INDs and Protocols allowed to proceed	1014	1199	936	974		1256	7253
							Average: 99.5

*** These reporting periods cover a one year cohort starting the day the Final Rule for Expanded Access to Investigational Drugs for Treatment Use and Chargin
Starting with Fiscal Year 2012, the reporting period was changed to a fiscal year to match the reporting period for other IND activity reports.

rugs went into effect.

http://www.fda.gov/NewsEvents/PublicHealthFocus/ExpandedAccessCompassionateUse/default.htm

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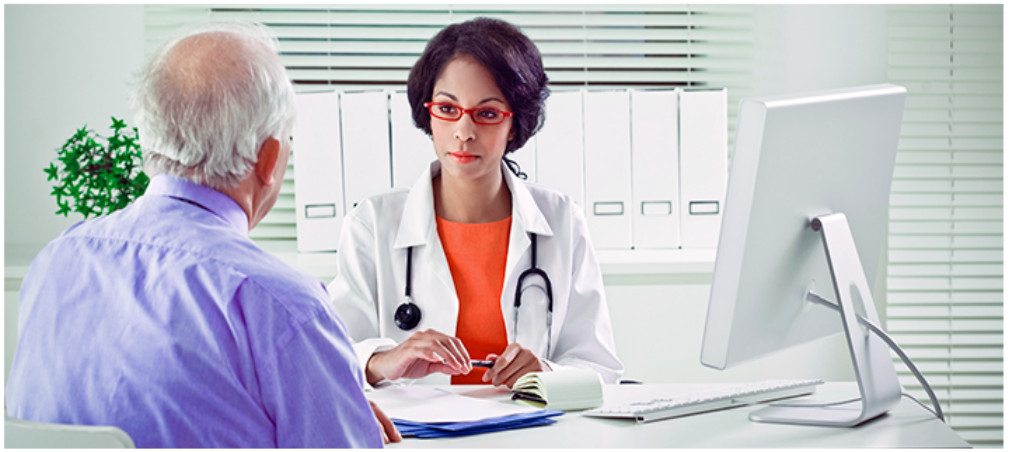
Public Health Focus

Expanded Access (Compassionate Use)

Expanded Access (Compassionate Use)

This section of our website provides information about FDA's current expanded access policies, requirements for enrolling in expanded access programs, and steps you can take to get more information.



Expanded access, sometimes called "compassionate use," is the use outside of a clinical trial of an investigational medical product (i.e., one that has not been approved by FDA). FDA is committed to increasing awareness of and knowledge about its expanded access programs and the procedures for obtaining access to human investigational drugs (including biologics) and medical devices.

Internal Navigation

Office of Health and Constituent Affairs (OC) and Division of Drug Information (CDER)

Take calls from patients, families, and physicians

- Describe regulatory framework for access
  - Explain how process works
  - Describe/interpret criteria for access
  - Explain who is responsible for what in making requests
  - Direct physicians to appropriate review divisions
- Suggest how to approach sponsor/manufacturers
  - Identify contacts in pharmaceutical companies
- Discuss clinical trials as options and how to explore them
  - Assist with clinical trial searches
- Explain role, and help identify IRBs
- Respond to companies about regulatory and policy questions
- Work with 3rd party consultants in the EA arena
- Outreach and education about expanded access

Summary

- There is a well defined process through which a healthcare provider can obtain access to promising investigational products for their individual patients
- Once a completed application is received by FDA, access is granted in over 99% of instances
- Requires knowledge of point of contact within a company and agreement from the company to provide the product outside of clinical trials
- FDA provides direction and assistance to patients, physicians, and others to describe and facilitate access