REdI Conference – Fall 2017

Overview of FDA's Expanded Access Program

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Poll Question

What is your experience with expanded access?

a) I have submitted an application

b) I understand the process but don't have experience

c) I know the terms but don't know the process

d) I don't know what it is but want to learn!

Learning Objectives

- Why Expanded Access
- What Is Expanded Access
- The Regulatory Foundation
- How Expanded Access Works
- Resources & Contact Information

Why Expanded Access?

1st the ideal…

"Wherever possible, use of an investigational medical product by a patient as part of a *clinical trial* is preferable because clinical trials can generate data that may lead to the approval of products and, consequently, to wider availability."[1] (Emphasis added.)

When enrollment in a clinical trial is not possible and there are no satisfactory alternatives….

…then a patient may be able to receive treatment through *expanded access*.

[1]FDA Expanded Access website: https://www.fda.gov/NewsEvents/PublicHealthFocus/ExpandedAccessCompassionateUse/default.htm

What is Expanded Access?

A regulatory pathway that allows for treatment of a serious or life-threatening disease/condition

with an investigational product

when satisfactory alternatives are not available, the benefit justifies the risk, and treatment does not interfere with trials that could support approval

Keep in mind…

- FDA must determine the expanded access criteria are met
- The manufacturer must be willing to provide the product

The Regulatory Foundation

Final Expanded Access Rule

- Published August 2009, implemented October 2009
- Codified in 21 CFR 312 code of federal regulations

§ 312.310

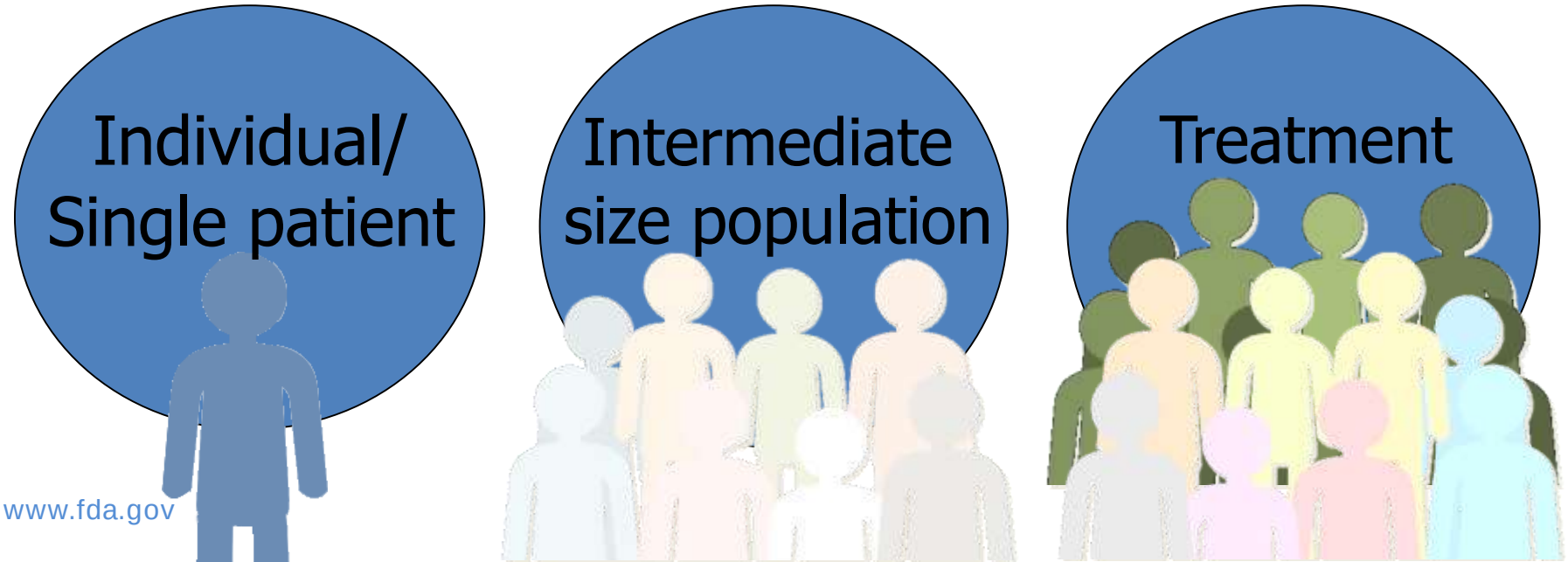
Individual/ Single patient

§ 312.315

Intermediate size population

§ 312.320

Treatment



How Expanded Access Works

What should you consider if you want to submit an expanded access request?

- General elements for all categories
- Specific elements for each category

Criteria- General

§ 312.305 Requirements for all expanded access uses

- Patient(s) must have serious or immediately life-threatening disease/condition and no comparable or satisfactory alternative therapy
- Potential benefit justifies potential risks
- Potential risks are not unreasonable in the context of disease/condition
- Access will not interfere with clinical trials intended to support approval of expanded access use

Safeguards- General

§ 312.305 Requirements for all expanded access uses

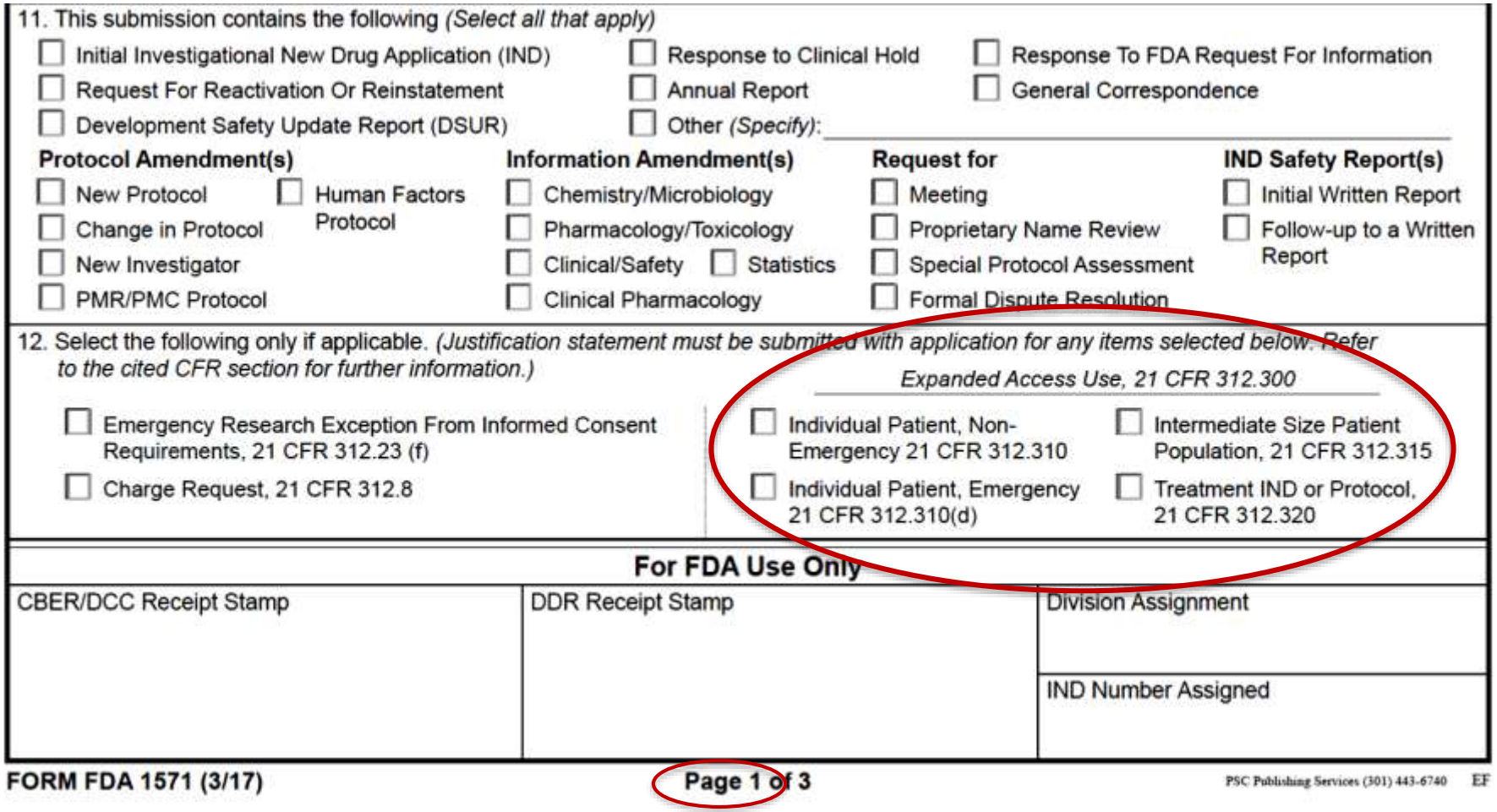
- Must obtain informed consent [21 CFR 50]
- Must obtain IRB review [21 CFR 56]
- Must meet safety reporting and annual reporting requirements [§312.32 and §312.33]
- Must provide Investigator's Brochure if one exists
- Subject to the clinical hold provisions [§312.42]

Submissions- General

§ 312.305 Requirements for all expanded access uses

- Requirements
    a. Cover sheet (e.g. Form FDA 1571)
    b. Rationale for the use
    c. Criteria for patient selection or (for SPI) description of the patient
    d. Method of administration, dose, and duration of treatment
    e. Description of manufacturing facility
    f. CMC information
    g. Pharmacology/toxicology information
    h. Description of the clinical procedures, lab tests, or other monitoring
- Can supply e. – g. requirements by Letter of Authorization
- Must clearly mark “Expanded Access” on the submission cover letter and 1571

FDA Form 1571



11. This submission contains the following *(Select all that apply)*

- ☐ Initial Investigational New Drug Application (IND)
- ☐ Request For Reactivation Or Reinstatement
- ☐ Development Safety Update Report (DSUR)
- ☐ Response to Clinical Hold
- ☐ Annual Report
- ☐ Other *(Specify)*: _____
- ☐ Response To FDA Request For Information
- ☐ General Correspondence

Protocol Amendment(s)

- ☐ New Protocol
- ☐ Change in Protocol
- ☐ New Investigator
- ☐ PMR/PMC Protocol
- ☐ Human Factors Protocol

Information Amendment(s)

- ☐ Chemistry/Microbiology
- ☐ Pharmacology/Toxicology
- ☐ Clinical/Safety
- ☐ Statistics
- ☐ Clinical Pharmacology

Request for

- ☐ Meeting
- ☐ Proprietary Name Review
- ☐ Special Protocol Assessment
- ☐ Formal Dispute Resolution

IND Safety Report(s)

- ☐ Initial Written Report
- ☐ Follow-up to a Written Report

12. Select the following only if applicable. *(Justification statement must be submitted with application for any items selected below. Refer to the cited CFR section for further information.)*

- ☐ Emergency Research Exception From Informed Consent Requirements, 21 CFR 312.23 (f)
- ☐ Charge Request, 21 CFR 312.8

Expanded Access Use, 21 CFR 312.300

- ☐ Individual Patient, Non-Emergency 21 CFR 312.310
- ☐ Individual Patient, Emergency 21 CFR 312.310(d)
- ☐ Intermediate Size Patient Population, 21 CFR 312.315
- ☐ Treatment IND or Protocol, 21 CFR 312.320

For FDA Use Only

CBER/DCC Receipt Stamp	DDR Receipt Stamp	Division Assignment
		IND Number Assigned

FORM FDA 1571 (3/17) **Page 1 of 3** PSC Publishing Services (301) 443-6740 EF

Type of Expanded Access

What type of expanded access request should you submit?

…important factors to consider are:

1) How many patients are you planning to treat?
2) Are you actively seeking marketing approval?

…in addition

there are other unique elements that distinguish each of the 3 types of expanded access categories

Criteria- Single Patient

§ 312.310 Individual patients, including for emergency use

Use when:
Treatment is for a single patient

Requires:

- Physician must determine probable risk from drug does not exceed that from disease, **and**
- FDA must determine patient cannot obtain access under another IND/protocol

Safeguards- Single Patient

§ 312.310 Individual patients, including for emergency use

- Treatment generally limited to one course
- Sponsor must submit written summary at end of treatment
- Special monitoring may be required if use is for extended duration
- FDA may request consolidation of multiple cases into one intermediate-size patient population IND

Submissions- Single Patient

Form FDA 3926

- Finalized in June 2016
- Developed to streamline individual patient expanded access submissions
- For individual investigator use only- may use instead of Forms FDA 1571 and FDA 1572
- IND may simply consist of: Click on picture for link to form→
  - The completed form FDA 3926,
  - A Letter of Authorization (LOA) from the product manufacturer, and
  - The first few pages of the investigator's CV

Emergency Use- Single Patient

§ 312.310 Individual patients, including for emergency use

- Subset of Individual Patient Access
- Emergency use can be authorized over the phone
- Must provide written submission within 15 working days of emergency authorization
- Contact information, including after hours information:

  http://www.fda.gov/NewsEvents/PublicHealthFocus/ExpandedAccessCompassionateUse/ucm429610.htm

Criteria- Intermediate Size

§ 312.315 Intermediate-size patient populations

Use when:

Treatment is for more than one patient, ***and***

Drug not being developed for marketing for the expanded access use, ***or***

Drug is being developed but patient cannot participate in clinical trial ***and*** *the sponsor is not yet actively pursuing marketing*

Requires:

- Sufficient evidence drug is safe at proposed dose & duration to justify size of study, **and**
- Preliminary evidence (clinical or plausible pharmacological) of effect

Safeguards- Intermediate Size

§ 312.315 Intermediate-size patient populations

- FDA performs annual reviews to determine if
  - treatment use should continue?
  - possible to conduct a clinical study of the expanded access use (if not being developed)?
  - access is interfering with clinical development (if being developed)?
  - access under a treatment IND/protocol would be more appropriate?
- Sponsor must monitor for compliance with protocol and regulations

Submissions- Intermediate Size

§ 312.315 Intermediate-size patient populations

- Statement of whether drug is being developed *or* not
- Explanation of why patients cannot be enrolled in clinical study *or* why drug cannot be developed
- Description of patient population

Criteria- Treatment

§ 312.320 Treatment IND or treatment protocol

Use when:

Treatment is for multiple patients, ***and***

Sponsor is actively pursuing marketing approval for the expanded access use

Requires:

- Sufficient evidence of safety and effectiveness (serious condition), **or**
- Reasonable basis for effectiveness without posing significant risk of injury (immediately life-threatening condition)

Safeguards- Treatment

§ 312.320 Treatment IND or treatment protocol

- 30-day post-submission wait before initiating study for both treatment INDs and protocols
- Sponsor must monitor for compliance with protocol and regulations

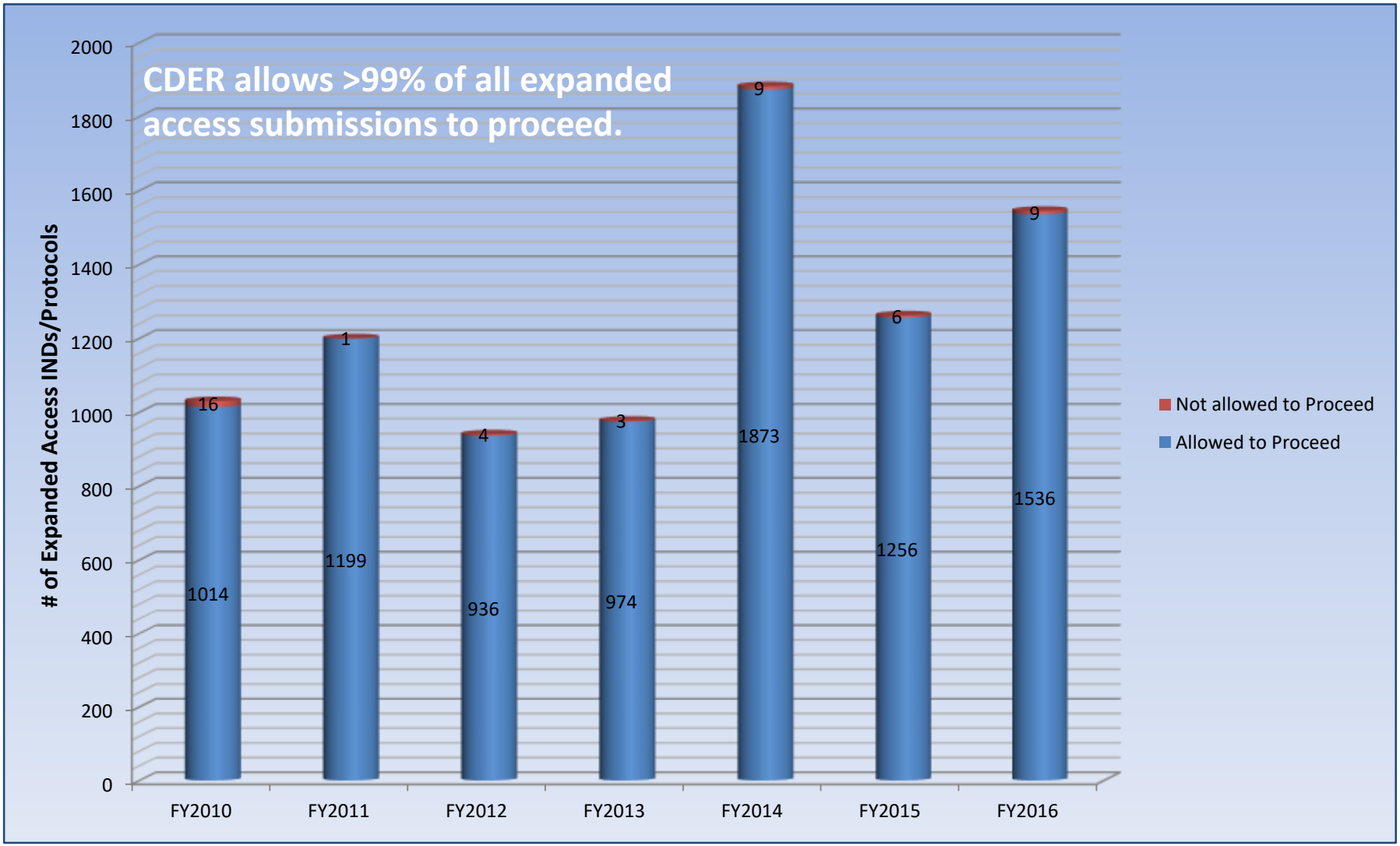
Submissions

Intermediate *vs.* Treatment ?

1. "FDA regulations do not impose specific numerical limitations …"[1] (Emphasis added.)
2. If the drug is ***not*** **being developed for marketing**… **intermediate-size** patient population is appropriate
3. If the sponsor **is actively pursuing marketing**… *regardless of the number of patients to be treated…* **treatment** IND or protocol is appropriate

[1] *Expanded Access to Investigational Drugs for Treatment Use—Questions and Answers*, found on FDA's website at https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm351261.pdf

FDA/CDER Track Record



Raw data available on FDA website at
https://www.fda.gov/NewsEvents/PublicHealthFocus/ExpandedAccessCompassionateUse/ucm443572.htm

Summary

- Why Expanded Access
- What Is Expanded Access
- The Regulatory Foundation
- How Expanded Access Works

Resources

- Federal Register/Vol. 74, No. 155/Thursday, August 13, 2009/Final Rule
- FDA's public website for Expanded Access (Compassionate Use) https://www.fda.gov/NewsEvents/PublicHealthFocus/ExpandedAccessCompassionateUse/default.htm
- Office of Health and Constituent Affairs website on Access http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/AccesstoInvestigationalDrugs/default.htm
- Guidance for Industry*: Expanded Access to Investigational Drugs for Treatment Use: Frequently Asked Questions* http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm351261.pdf
- Guidance for Industry: *Individual Patient Expanded Access Applications: Form FDA 3926* http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM432717.pdf

Contact 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

Please complete the session survey:

surveymonkey.com/r/DRG-D2S06

Personal Contact Information:

Paul.Phillips@FDA.HHS.GOV

301-796-3935

Remember

- The ideal for receiving an investigational product is in a clinical trial, which can lead to approval and broader patient access
- Expanded access is a potential option when no satisfactory alternatives exist
- CDER allows >99% of all expanded access requests to proceed