No Disease Is Too Rare to Deserve Treatment

Public Policy Working Group

Expanded Access

Max G. Bronstein
Senior Director, Advocacy & Science Policy
EveryLife Foundation for Rare Diseases
Community Congress Overview

- New initiative to bring patient groups and industry together to address urgent policy needs in the rare disease community
- Comprised of 3 working groups: Public Policy, Newborn Screening, Regulatory
- Groups will convene 3-4 meetings/year via webinar and 1 in-person meeting in Washington D.C.
- Each working group will pick a specific issue, identify a policy problem, goal, and action plan to create change
Working Group Structure

Newborn Screening Industry & Patient Co-Chairs & Working Group Members

EveryLife Foundation – Staff Support

Public Policy Industry & Patient Co-Chairs & Working Group Members

Regulatory Science Industry & Patient Co-Chairs & Working Group Members

No Disease Is Too Rare to Deserve Treatment
Thank you sponsors!
Patient Groups

- Dercums Foundation
- Stiff Person Syndrome Action Network
- Sarcoma Foundation of America
- GIST Cancer Awareness Foundation
- American Behcet’s Diseases Association
- BRBN Alliance
- Parent Project Muscular Dystrophy
- Vasculitis Patient-Powered Research Network
- National Fragile X Foundation
- United Leukodystrophy Foundation
- National MPS Society
SAVE THE DATE

In-person Meeting

Wednesday, November 4th

1200 New York Ave, Washington DC

10am-2:30pm
Defining Expanded Access (Compassionate Use)

• Mechanism for providing potential access to experimental therapies, which have not been FDA-approved
• Patients may seek approval for expanded access when facing serious life-threatening disease, often a last resort
• FDA will review requests for individuals and groups
Challenges

• Relatively few companies have well-developed expanded access policies
• FDA almost always approves requests for expanded access but provides little guidance
• Patients have used social media to pressure companies into providing access
A Path Forward?

• Our charge as a working group is to examine possible frameworks for improving expanded access
• Goal of minimizing risks for all stakeholders
• Working together and in-concert with experts and thought leaders, implement the revised framework (publications, events, Hill meetings etc.)
• Email mbronstein@everylifefoundation.org
Expanded Access Perspectives

Fritz Bittenbender
Executive Vice President, Public Affairs
Biotechnology Industry Organization
Principal Goals of Companies

- Listen to patients and work to meet their needs
  - Develop safe and effective therapies and bring them to market
  - Complete clinical studies necessary to secure product approval
  - Secure approval so new products are available to all people who need them
- Carefully work to confront the challenges of using investigational medicines in and out of clinical trials
  - Truly informed consent
  - Control vs. significantly less control
  - Appropriate consideration of data
  - Reduction of incentives to enroll in clinical trials
  - Fairness
Truly informed consent
- Ensuring that the physician and patient understand, both in and outside of a clinical trial, what is known and unknown about the potential benefits and risks for patients
- Ensuring that the physician and patient understand, especially outside of a trial (e.g., individual-patient expanded access), that early data – no matter how exciting they seem – do not guarantee a positive outcome for any given patient

Control vs. significantly less control
- There is frequent oversight of the use of an investigational product in a clinical trial, and strict monitoring. This can provide necessary insights into what’s best for these patients. Such monitoring often is not possible outside a trial (e.g., individual-patient expanded access). This is challenging for patients and companies.
There is concern about how regulators consider and use potentially negative data from use of an investigational product outside a clinical trial (e.g., individual-patient expanded access). Could these data negatively affect completing the development of this product (either slow it or stop it)? Clarification on this point will be helpful.

If clinical trials cannot be enrolled, they cannot be completed, and product development will stop. If patients “opt out” of trials in favor of expanded access, what will the impact be? This is a significant consideration. (One possible rationale: in a clinical trial, enrollees may not receive the investigational drug, but may receive the standard of care or a placebo.)
Companies are concerned about being fair to all patients for whom a new drug may be life-saving or may significantly improve the quality of life. In an expanded access setting, there may be a limit on the number of patients who can receive the investigational product. How is the decision made as to who will, or will not, “qualify”? If there is limited quantity, where is the cut-off that is fair to all? These are questions companies must consider early in their deliberations about creating expanded access programs or granting access to investigational product.
Expedited access to approved products potentially may reduce the desire or need for expanded access. This can be achieved through improving the development process and enhancing the efficiency of regulatory review.

Companies are committed to improving the clinical trials process and other drug development steps so patients will have approved safe and effective drugs as soon as possible. Some suggestions:

- More efficient IRB reviews
- Innovative clinical trial design; “new” statistical approaches
- Use of qualified biomarkers
- Targeted development – trials focused on subpopulations

Companies and FDA are committed to expediting review of new medicines through effective communication and greater efficiency.
Patients’ needs are critical and priority one in expanded access decisions.

Because the needs of all patients are best served by availability of approved product, clinical trials must proceed so medicines can be approved.

Early data often trigger for the desire for expanded access. But such data, which generally are not fully analyzed or understood, can be confusing and provide false hope.

Manufacturing capability is associated with stage of development and product supply may be limited.

Equitable distribution is essential if companies make drugs available before approval and outside of trials.
Some Specific Requirements Regarding Expanded Access

- The treating physician must determine that use of an investigational product is appropriate and that the benefit will justify risk. There must be agreement between a designated company physician and the treating physician that expanded access is the best option for this patient.

- FDA must agree that sufficient evidence exists to support this use of the investigational product at this time (especially evidence about safety).

- The company must make a determination that this will not interfere with the completion of essential clinical trials.
Based on these considerations and others as appropriate, companies make decisions on a case-by-case basis, considering the medical situation of a particular patient and the available data about the investigational product as to whether to make the investigational product available for the given patient.

In some cases, expanded access programs are developed by a company during development, for a group of patients with defined criteria. Such programs are publicly posted on ClinicalTrials.gov.
Some Elements of BIO’s Approach

- Companies’ commitment to make their general policies public and to include in those policies the considerations that guide decisions.
- Companies’ commitment to include in their public policies a point of contact where discussion may occur with a patient’s physician regarding access to an investigational medicine for that patient.
- Develop ways to work with patients and others to help increase understanding of how expanded access can work and how to learn about and access available programs or appropriate alternatives.
- Work with FDA to improve communication and optimize current processes.
- Work with member companies for whom this is unfamiliar territory, and help them navigate.

* BIO Principles
Andrea Sloan CURE Act

Andrea Sloan Compassionate Use Reform & Enhancement (CURE) Act
Compassionate Use - The Basics

• **Compassionate Use** (formally “Expanded Access”) provides a pathway for patients to gain access to investigational drugs - outside of the clinical trial setting - for serious diseases or conditions.

• **Three categories:**
  1. Single patient and emergency
  2. Intermediate size
  3. Treatment

• **General criteria:**
  1. The physician must determine that the probable risk to the person from the investigational drug is not greater than the probable risk from the disease or condition; and
  2. FDA must determine that the patient cannot obtain the drug under another IND or protocol.
Compassionate Use - The Process

• Companies, NOT the FDA, decide if patients get access (at least initially);

• FDA must sign off on the company’s decision;

• An Institutional Review Board (IRB) must review and also approve of the patient’s use; and

• Physicians must report “serious adverse events” to the FDA.
Compassionate Use - The Numbers

Expanded Access Requests Accepted by FDA

2010: 1014
2011: 1198
2012: 936
2013: 974
2014: 1873

Source: www.FDA.gov
www.RegulatoryFocus.org

92% increase in requests in 2014

FDA Action Taken on Compassionate Use Requests (2010-2014)

FDA approves 99% of requests
Compassionate Use - The Problem

• Patients and doctors struggle to navigate the process
  • Hard to identify key decision makers at pharmaceutical companies who receive and process compassionate use requests
  • Procedures, criteria for access and timeframe can vary considerably from company-to-company

• Lack of regulatory certainty for companies
  • Concerns about how the FDA takes into consideration “serious adverse events”
  • Causes many companies to categorically deny access to experimental drugs to patients in need

• Minimal data for policymakers
  • We don’t know the “full universe” of compassionate use requests
  • Prime barriers to access for patients and companies
Compassionate Use Reform & Enhancement
Sec. 2082 and 2083 of the 21st Century Cures Act

1. **Provide critical information:**
   - Ensure companies have public compassionate use policies.
   - Points of contact for patients and doctors.

2. **Remove regulatory uncertainty:**
   - Finalize guidance for industry.
   - Clarify how the FDA uses serious adverse event data.

3. **Analyze current program:**
   - What’s working/not?
   - Barriers?
Thank You

Questions: Andy.Taylor@mail.house.gov
David Farber – King & Spalding

• Partner at King & Spalding, a leading healthcare law practice in the United States
• Represents providers, manufacturers, and others in the health care arena on regulatory, policy, and litigation issues
• Engaged in developing policy solutions for EAP
• Has advised pharma clients on global EAP policies and procedures
• Published on EAP issues: http://healthaffairs.org/blog/2015/05/22/how-state-right-to-try-laws-create-false-expectations/
FDA Authorization of Expanded Access

During the fiscal year ending October 2013, FDA authorized 863 requests or 99% of all cases reviewed (1/3 on emergency basis).

FDA has authorized 99% of requests since October 2009 (on average, 932 requests annually).

99% authorization rate

So what is the problem?
Ebola Raises More Questions

WHO Says ZMapp Is Ethical; Too Bad There’s None Left
Small supplies of the drug bring up a whole host of other ethical dilemmas

By Mary Beth Griggs
SMITHSONIAN.COM
AUGUST 12, 2014

World Health Organization to Ethicists: Should We Use Experimental Ebola Drugs?
Treating two Americans with an untested drug for the deadly disease shifts thinking about ethics of use.
FDA is not the problem, but is also not offering a solution

Should FDA take a more expansive role in the process of navigating requests for Expanded Access?
What’s Next?

- Social media may overtake planning and procedure
- FDA will continue to authorize the vast majority of the Expanded Access requests it receives
- Congress is engaging, forcing policy change
- States, driven by the Goldwater Institute, will continue to enact “Right to Try” laws
Expanded Access: A Business Opportunity?

A Dutch startup has raised 4.5 million Euro to fund a business that navigates expanded access requests (www.mytomorrows.com).

Nonprofits are also trying to establish a space for navigating requests, such as the ALS Emergency Treatment Fund (www.alsetf.org).

We expect others to enter the market in the future.
Status of State “Right to Try” Laws

Source: http://tracking.tenthamendmentcenter.com/issues/right-to-try/#
FDA issued a Proposed Rule on Clinical Trials on November 19, 2014

- If expanded access is authorized, Responsible Party would submit an “Expanded Access Record” with a unique ClinicalTrials.gov Identifier
- Applicable only to expanded access for Intermediate-Size Patient Populations and Large Patient Populations (not for Individual Patients)
- Responsible Party would submit various information, including eligibility criteria, status of drug availability via the program, contact information and the IND number
- Responsible Party would be obligated to update and correct information

What will FDA do in the Final Rule, and will it preempt legislation?
Where Do We Go From Here?

Should patient advocacy and rare disease groups engage, and if so, where?

This is not a simple issue – there is as much opportunity to do harm than to do good

Is social media the best tool for such a nuanced issue? And how does one become a responsible voice in the debate?
A Framework for EAP Solutions

• Social Media attacks are neither ethical, nor effective
• Other healthcare access problems have been solved through innovation and policy engagement
  — NMDPH – Bone Marrow matching and donation
  — UNOS – Organ donation
• The same possibilities are true for expanded access
  — bone marrow matches are no longer a dream
  — And when is the last time someone sued a hospital for failure to get an organ donor
A Framework for a Solution

• All stakeholders lack a central repository for EAP expertise (clinical, ethical, practical, medical, legal)
  — FDA, as a stakeholder, likely cannot fill this gap
• A Trusted Third Party, a so-called “Honest Broker,” is needed to navigate the issues
  — Provides credible and reliable advice to patients
  — Eliminates conflicts for pharma
  — Works with FDA to expand access
  — Brings experience, precedent, expertise and resources to the table
• Can this be privately built, or must it be legislated?
QUESTIONS?
THANK YOU!
Policy Solutions for Early Access Programs

Jess Rabourn, CFA

- ALS Emergency Treatment Fund, Ax-S Pharma
- 5 yrs focus on Expanded Access in the U.S.
- 15 yrs investment / finance background
- Eighteen public speaking engagements on EA
- ALS Drug Development Guidance Project
My Eight Minute Message:

- The problem
- The reasons for this problem
- Policy initiatives to address these issues and make Expanded Access more feasible
The Problem

• Many dying patients and their doctors are blocked from exploring the new medicines that appear to be reasonably safe and that may fundamentally improve the course of disease.

More specifically,

→ We’re not using the Expanded Access channel as often as we could.
The Reasons

1. **Regulatory** Barriers

2. **Economic** Barriers

3. **Political** Barriers

Why drug companies don’t always provide EA, even when medically appropriate.
The Reasons

1. Regulatory Barriers

2. Economic Barriers

3. Political Barriers

Why drug companies don’t always provide EA, even when medically appropriate.
Special exemptions for life-threatening situations

1962 - 1987
Tropical Disease IND
Orphan Drug IND
Open Label IND
Group-C IND
Compassionate IND
Emergency IND
Treatment IND

Treatment IND
Emergency IND & Individual IND

1992 FDA / PHS Statement
Parallel Track

1990/1997
Devices (HDE / T-IDe)

2009 Final Rule
Treatment IND
Intermediate-Size IND
Emergency IND & Individual IND
Feasibility: Drug Company (Sponsor)

**Hard Costs**
- Supply Chain
- Regulatory Prep
- Site Activation, IRB, ICF
- Protocol, IB, Training
- Pharmacovigilance, Safety DB
- Medical Monitoring
- Public Communication
- Insurance / Indemnification
- Coordination

**Elective Costs**
- Cost to Support Sites
- Research (endpoints, EDC, data)
- Patient Assistance Funding

**Hazards**
- uSAE
- E&O / Malpractice
- Budget Shortfall
- Public Perception
  - Favoritism
  - Withholding
  - Promotion
  - Profiteering

**Rewards**
- Engagement / Familiarity
- Safety Data
- Research Outcomes
- Human Mission
Feasibility: Health Care Provider

**Resource Expenditures**
- IRB / ICF Review
- Screening, Enrollment
- Pharmacy / Accountability
- Administering Product (i.v., peg)
- Lab - tox
- Medical Evaluation
- Record Keeping
- Coordination / Training

**Negotiated Costs For:**
- Tax for Institution
- Margin (Overhead)
- Research Endpoints
- Data Collection / CRF entry

**Rewards**
- More options for treating patients
- Familiarity with drug
- Learning outcomes (Responder subgroups)
- Publication / Visibility

**Other Considerations**
- Patient Selection
- Informed Consent / Expectations
- Safety

Rewards

**Negotiated Costs For:**

**Other Considerations**
How much is on the sponsor?

Simplest, “clinical trial” model
(Kyprolis, 2011-2012)

Partnering with HCPs
(Gleevec, 2000-2003)

…with “cost recovery”
(Voraxaze, 2007-2010)

Sponsor pays 100%

- Patient Treatment
- Product Supply
- Program Mgmt
- Research

Sponsor pays minimum

- Product Supply
- Program Mgmt
- Research

- Research
Who pays for patients’ treatment?

1. Absorbed by HCP
2. Medicare Part B
3. Private Health Insurance
4. Patient / Patient Assistance
Sponsor’s Cost Recovery?

1. **Patient / Patient Assistance**
   - Direct Txn between patient and sponsor?
   - Or, bill through clinic? Add on to medical billing.
   - Order management tie-in with A/P, A/R.

2. **Traditional Payers**
   - Very difficult; involve patient advocacy / lobby
My Eight Minute Message:

- The problem

- The reasons for this problem

- Policy initiatives to address these issues and make Expanded Access more feasible
1. **Regulatory / Political:** Every *Guidance* aimed at serious / life threatening diseases should include “best practices” for Expanded Access, to encourage meaningfully-sized, centrally coordinated, EA programs as a part of clinical development.

2. **Economic:** Disease communities should build / promote third-party platforms to collaboratively sponsor EA programs.

3. **Economic:** “Standard of Care” must be redefined in “untreatable”, quick killer diseases. Physician’s prerogative on post-Phase 2 therapeutics should enable full reimbursement from Medicare, private payers.
   a. Billable service charges from HCPs
   b. Tiered supplement for product costs
Questions & Discussion

mbronstein@everylifefoundation.org

Sign-Up for Community Congress at RareCongress.org