Reorienting the Research Environment: Advocating for the Value of the Patient’s Voice
Presenters

Marc Boutin, JD
Chief Executive Officer
National Health Council

Pat Furlong
Founding President and Chief Executive Officer
Parent Project Muscular Dystrophy

Ron Bartek
President and Co-Founder
Friedreich’s Ataxia Research Alliance (FARA)
Learning Objectives

At the end of this session, participants will be able to:

• Understand and incorporate the role of patient groups in PCOR

• Describe local, national, and international examples of how PCOR has become an important aspect of clinical outcomes research and drug development

• Cite examples of practical methods to advocate for the inclusion of the patient’s voice in research and to lead PCOR initiatives big and small
Session Overview

1. The Many Roles of Patient and Patient Advocacy Organizations in PCOR
   - Marc Boutin, National Health Council

2. Case Examples
   - Pat Furlong, Parent Project Muscular Dystrophy
   - Ron Bartek, Freidreich’s Ataxia Research Alliance

3. Questions and Discussion
Back to Basics: HIV/AIDS Advocacy as a Model for Catalyzing Change
Reorienting the Research Environment: Getting to Patient-Driven Research and Care

Researchers are in the “driver’s” seat. They turn to the public to collaborate consultant but on the researcher’s terms.

Public is encouraged to provide diverse and in-depth views, perceptions, preferences, experiential knowledge, and ideas.

Public is empowered to become active partners in an ongoing collaboration.

Public drives the research, researchers participate on its own terms.

What Can You Do?

Examples

• Policy and Advocacy
• Research Funder
• Research Partner
• Citizen Researcher
The Arc of Public Engagement

Problem
The Arc of Public Engagement

Problem

Solution
The Arc of Public Engagement

Problem

Solution

Saliency
Prescription Drug User Fee Act (PDUFA)
Evolution of PDUFA

- **1993** PDUFA I: Backlog reduction
  - Reducing review times
- **1998** PDUFA II: FDAMA
  - Reducing review times
- **2003** PDUFA III: BTP
- **2008** PDUFA IV: FDAAA
  - Unintended consequences
  - Process for engagement
- **2013** PDUFA V: FDASIA
  - Benefit/Risk framework
  - Biomarkers/PROs
  - PFDD
  - Rare diseases
- **2018** PDUFA VI: Patient engagement throughout the development lifecycle

**Timeline**

- Initial patient group engagement
- Shift to consumer engagement
- Patient groups re-engage
Public Policymaking Process in the U.S.

Interest Group Preferences, Demographics, Technological Inputs

Policy Formulation Phase

Development of Legislation

Policy Implementation Phase
Rulemaking → Application

Policy Modification Phase – Feedback

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PDUFA V Strategy

Policy Formulation Phase

Goals
Organizational Considerations
Tactics
Constituencies
Targets
PDUFA V Asks

• Develop an objective, qualitative benefit-risk framework that includes robust patient input

• Expand the use of biomarkers, patient reported outcomes in clinical trials, and companion diagnostics

• Increase resources for Rare Disease Program

• FDA is holding at least 20 public meetings over the course of PDUFA V, each focused on a specific disease area. The Voice of the Patient reports will summarize each of these public meetings.
Public Policymaking Process in the U.S.

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  Rulemaking → Application

Policy Modification Phase – Feedback

National Health Council Patient Stratification Tool

The Patient Stratification Tool consists of three sections:

Section I: Identification of Subpopulations
Section II: Description of Disease Diagnosis and Impact
Section III: Description of Treatment and Management Options

Those applying the tool should be mindful of potential variances between patient and caregiver needs and preferences, as well as ensure that information from hard-to-reach populations is captured.
Public Policymaking Process in the U.S.

Dialogue / Advancing Meaningful Patient Engagement in Drug Research, Development & Approval

- Build consensus around a common vision
- Provide all stakeholders with a viable path forward
Create Regulatory Guardrails

**PRIMARY ACTIONS**
- Formalize regulatory asks for negotiation in PDUFA
- Prioritize development of guidances
- Enhance FDA division alignment on the use of tools for evaluating patient information

**SUPPORTIVE ACTIONS**
- Align stakeholder advocacy strategies
- Increase transparency
- Create more opportunities to collect feedback
Promote a Culture Shift

**PRIMARY ACTIONS**
- Generate buy-in
- Create accountability for collecting/integrating patient perspectives
- Create public-private partnership

**SUPPORTIVE ACTIONS**
- Develop/implement tools and metrics
- Train/educate researchers
- Help patient groups solicit/fund patient-centered studies
Facilitate Open Communication

PRIMARY ACTIONS

• Make information comprehensible
• Document impact of patient perspective studies
• Make publicly available experiences, advice, best practices, lessons learned, and other resources

SUPPORTIVE ACTIONS

• Create a feedback system
• Utilize open-source production model whenever possible
• Create partnerships to encourage information sharing
Public Policymaking Process in the U.S.

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PDUFA VI Asks

• Adopt FDA guidance to integrate patient voice into drug development and approval

• Increase resources for qualifying biomarkers and patient-reported outcomes

• Pilot adaptive clinical designs

• Minimize barriers to FDA hiring

• Clarify oversight of combination products that have cross-center jurisdiction
Case Example:
Parent Project Muscular Dystrophy
An (Evolving) Example of Stakeholder Influence

Parent Project Muscular Dystrophy (PPMD)

• Began following the Food and Drug Administration Safety and Innovation Act (FDASIA) and Prescription Drug User Fee Act (PDUFA V) - 2012
  – Committed FDA to Patient-Focused Drug Development Program
  – Aims to inform FDA’s benefit/risk assessments and systematically obtain patient perspective on disease impact and treatment benefits
• Anticipating that Duchenne/Becker would not be chosen...

(http://www.fda.gov/forindustry/userfees/prescriptiondruguserfee/ucm326192.htm)
Food and Drug Administration Safety and Innovation Act (FDASIA)

Opportunity through legislation:

PDUFA (FDASIA) Food and Drug Administration Safety and Innovation Act (2012)

Pieces we advocated for were included:

• Accelerated approval provision
• “Breakthrough Therapy designation” provision
• Patient Focused Drug Development initiative
Putting Patients First

Recommendations to speed responsible access to new therapies for Duchenne muscular dystrophy and other rare, serious and life-threatening neurologic disorders

Benefit-Risk Assessments in Rare Disorders

THE CASE FOR THERAPEUTIC DEVELOPMENT IN DUCHENNE MUSCULAR DYSTROPHY AS THE PROTOTYPE FOR NEW APPROACHES
PPMD Initiated Benefit Risk Study

Benefit Risk Study seen as potential model within Patient Focused Drug Development

– Converting patient voice into acceptable data
– Survey results presented to FDA and other stakeholders
– Conclusion that caregivers are willing to accept considerable risk for stopping or slowing progression
– “Tell your story” tool
– 170 personal stories from Families to the FDA
PPMD Realized the Importance of Measuring Preferences

• The FDA:
  • Wants to improve their benefit-risk framework
  • Is mandated to better understand the patient experience and preferences
  • Is interested in testimony but... deals in data
Beyond Testimony: PPMD’s “Share Your Story”

• “I understand the need for caution and care, but I also know that our children are dying. Parents should be able to decide the risk/benefit of a drug that has gone through and passed preliminary testing. I would rather my son die trying and fighting than waiting and wondering and wishing....I am one parent willing to take an educated risk!”
“PATIENTS ARE WAITING…”
Messages from Duchenne Muscular Dystrophy Families to the FDA

To collect meaningful information from a broad group of people and caregivers managing Duchenne muscular dystrophy (Duchenne) and to advance the development of new treatments, Parent Project Muscular Dystrophy (PPMD) launched its Benefit/Risk in Duchenne Therapies program in late 2013. The goal is to inform the FDA and other government agencies, as well as biopharmaceutical companies about the priorities and risk tolerance of the Duchenne community.

Duchenne families often feel as if the FDA is an untouchable and unreachable group of professionals tasked with making critical decisions on potential drugs. In order to bridge that gap, PPMD’s Benefit/Risk Program includes:

1. A sponsor-free initiative focused on patient-generated data that produced data on treatment preferences and risk tolerance using stated-preference methods, and
2. “Share Your Story,” an open-ended survey that allowed parents and patients to speak directly to the FDA.

Objectives and Methods:

The program objective is to share stories from the community with the FDA and other stakeholders to help them better understand the perspectives of Duchenne families. Using an online, open-ended survey implemented on the Parent Project Muscular Dystrophy website, we asked families, “If you had a chance to talk to the FDA, what would you want them to know?” No further prompts were given to participants. The responses were publicly available, so participants could read previous entries before posting their own comments.

Data is vitally important to inform the FDA’s benefit-risk assessments. But nothing can replace the impact of sharing family stories of their experiences living with Duchenne muscular dystrophy.

Results:

168 people participated in Share Your Story — a mix of individuals with Duchenne, parents of individuals with Duchenne, brothers and sisters, and grandparents. Quotes and stories are included from families who choose to remain anonymous while sharing them with the FDA and others.

Major Themes:

Participants had several key messages that they listed as the most important things they wanted to communicate to FDA leaders:

1. **URGENT NEED**
   - Reported by 79% of participants
   - "The large majority of participants described an urgent need based on sincere worry about our children. Under those terms, many participants expressed a compelling, immediate need for access to clinical trials and new treatment options.
   - "All of us as parents know what the outcome is. We don’t try anything. Keep you or hasten death and treatments through the Duchenne pathway. ‘Time is something our boys do not have’".
   - "Because CMTSharenets like life span of those affected, I would encourage the FDA to consider being more aggressive with the approval of certain drugs where the benefits include quality of life and life span. Some families welcome the risks that may come with treatments, feeling that doing something is better than just waiting for their child to deteriorate and die."

2. **INCREASED FLEXIBILITY**
   - Reported by 62% of participants
   - "We hear each kicks of the clock very loudly in our hearts, worried that science will take too long to develop a treatment that will slow or eliminate the progression. Our bigger worry is that science will develop it and the FDA will take too long to approve it."

3. **URGENT NEED**
   - Reported by 39% of participants
   - "To meet the urgent need for new treatment options, more than half of the participants urged the FDA, sponsors, and other stakeholders to come together and facilitate a faster, more flexible drug development and approval process. This major theme includes requests to harmonize efforts between U.S. and other regulatory bodies to allow..."
FDA Engagement

• Meetings with Division of Neurology
• Duchenne Policy Forum (December 2013)
  – 19 FDA officials in attendance
  – Harmonize with efforts happening in EU (meeting and guidance)
  – Agreement with agency that the Duchenne community would create draft guidance on Duchenne for consideration

Setting the stage for the draft guidance
June 25, 2014

Guidance Document Submission
Division of Dockets Management [HFA-305]
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

LEADING THE FIGHT TO END DUCHENNE

Topic Areas Addressed:

- Benefit Risk
- Clinical Trial Design
- Biomarkers
- Natural History
- Imperatives
- Diagnostics

Our submission is prefaced by the Duchenne Imperatives, which begins with a few case studies, summarizes the document’s key points, and explains the Duchenne community’s key imperatives — what we hope will be the take-home messages from the community for the sponsors, the academic community, and for the FDA, and to serve to frame the importance of the development of guidance for the community. We understand that the FDA may choose not to formally adopt this preface, though it is hoped that such information will inform FDA’s deliberations regarding adoption of the formal draft guidance, which follows.

PPMD submitted draft Guidance to FDA June 2014

FDA published draft Guidance for Industry for Duchenne June 2015

Guidance for Industry Duchenne Muscular Dystrophy Developing Drugs for Treatment of Duchenne

Timeline:

- PPMD submitted draft Guidance to FDA
- FDA published draft Guidance for Industry for Duchenne
Current PPMD Stated Preference Projects

• Phase II of PPMD’s benefit/risk research
  • Exploring meaningful benefit
  • Understanding risk tolerance
Demands and Benefits to a Disorder Community

• Highly collaborative process
• Outcomes inform advocacy
• A large number of people can participate, even those who cannot/do not want to testify
• Resource and time intensive
• You may not get the results you “want”
• Requires larger sample sizes; more generalizable than testimony
The Vital Role of Patient/Advocacy Organizations

Collaborating with experts in stated preference research to:

• Set the research agenda
• Develop a meaningful study
• Weigh in on interpreting the results
• Disseminate to sponsors and regulators (and your community)
Case Example:
Clinical Trials Transformation Initiative-Patient Group and Clinical Trials Project
Clinical Trials Transformation Initiative (CTTI): Patient Group and Clinical Trials Project

• CTTI Mission:
  – Identify and promote practices to increase the quality and efficiency of clinical trials

• CTTI Patient Groups and Clinical Trials Project:
  – No definition, metrics or evidence-based best practices existed for patient group involvement at any phase of clinical trial continuum.
  – Working group, lit review, survey, interviews, expert meeting; recommendations prepared to address issue
Clinical Trials Transformation Initiative (CTTI): Patient Group and Clinical Trials Project

- Objective – Improve clinical trials enterprise by enhancing patient engagement across full R&D continuum:
  - Define consensus, evidence-based principles for Patient-Group (PG) engagement reflecting perspectives of patients, industry and academia as well as government partners (e.g., NIH, FDA)
  - Increase clarity as to **how, when and by whom** patients and PGs should be engaged
  - Develop metrics by which effective patient engagement might be measured
PG Engagement Across the Research & Development Continuum
From Bench to Bedside and Back

**Pre-Discovery**
- Input re interest of research question to patient community
- Providing data on unmet need & therapeutic burden
- Fundraising and direct funding for research to identify target molecules
- Facilitating collaboration with NIH
- Characterizing the disease & relevant mechanisms of action

**Pre-Clinical**
- Fundraising & direct funding for research, trial operations support
- Assistance in selecting & recruiting optimum clinical sites
- Clinical infrastructure support
- Helping educate/motivate patient community & recruit for trials
- Providing patient feedback on participant experience
- Serving on Data & Safety Monitoring Board
- Input for any trial adaptations or modifications
- Accompanying sponsor to milestone meetings, e.g., after phase 2 & 3

**Phase 1/2/3**
- Fundraising and direct funding for research
- Providing translational tools (assays, cell & animal models, bio-samples, biomarkers, etc.)
- Helping define study’s eligibility criteria
- Natural history database & patient registry support
- Input on meaningful clinical endpoints
- Assistance re informed consent form
- Working with FDA re benefit-risk and draft guidance
- Accompanying sponsor to Pre-IND FDA mtg to advocate for study

**FDA review & approval**
- Providing public testimony at the FDA Advisory Committee & other FDA hearings
- Preparing submission for newborn screening when appropriate

**PAS/Outcomes**
- Serving on post-market surveillance initiatives
- Helping return study results to participants
- Co-presenting results
- Publications/communications re results
- Feedback on how patient community views results
- Natural history database & registry support
- Working with payers re reimbursement

*Adapted from Parkinson’s Disease Foundation materials for CTTI’s Patient Groups & Clinical Trials Project*
Clinical Trials Transformation Initiative (CTTI): Patient Group and Clinical Trials Project

• Assessing the PG - recommendations provide tools, e.g.:
  – To what extent is it able to engage as in previous figure?
  – Does it engage collaboratively with industry, academia, government (NIH, FDA, Congress), other PGs?
  – Are its leadership, vision, mission, goals & areas of focus sound?
  – Are its operational programs well structured, performing well and demonstrating good, measurable impact?
  – Are its budget and fundraising programs adequate to its needs or showing signs of becoming so?
  – Are its communications systems effective in engaging, educating and motivating its patient community, medical, scientific, industry and government partners?
Through active, continuous engagement in the development program, PGs can demonstrate a unique value to their industry partners.

This value has the effect of:

- De-risking early-stage development with funding and public-private partnerships for basic, translational, and early clinical research
- Reducing uncertainty in the regulatory process by working closely with the regulators throughout the entire R&D process
Active, continuous engagement in the development program – cont.

Helping to develop more effective, efficient trials with a greater chance of success through:

- better questions and study design
- efficient recruitment and improved retention
- fewer protocol amendments
- procedures that are better-suited to the patient
- clinical endpoints that are well-grounded in the natural history of the disease
- potential benefits that are most important to the patient
BARRIERS TO COLLABORATION CONFIRMED IN INTERVIEWS

- Mismatched expectations between trial teams & PGs
- Providing PGs w/ only a token seat at the table, not making them full partners in the trials process
- Internal resistance, lack of buy-in
- Perceived difficulty of overcoming legal barriers to industry/patient collaboration
- Excluding PGs from early stages of trial planning & design
- Lack of best practices for engagement & lack of infrastructure to support patient outreach operations
- Lack of demonstrated value
- Lack of funding
- Unsure of how to identify/engage w/ PGs
- Lack of sophistication of PGs
CTTI PGCT Project Conclusions

- Partnerships with PGs around clinical trials are occurring with greater frequency;
- Several modifiable barriers to successful relationships have been revealed;
- Evidence on engagement with PGs around clinical trials was previously anecdotal. Now we have emerging quantitative and qualitative evidence on the best practices and shared benefit to partnerships captured in CTTI’s recommendations;
- Read the full set of recommendations at http://www.ctti-clinicaltrials.org/what-we-do/investigational-plan/patient-groups
- Stay tuned for publications from CTTI’s work on value and impact of patient group engagement in the clinical trial enterprise.
Questions?
Session Resources

- Value of the Patients’ Voice: PATIENTS Program--Stories from Patients
  [http://www.patients.umaryland.edu/whatwedo/patientsvoice/](http://www.patients.umaryland.edu/whatwedo/patientsvoice/)

- National Health Council—Information Collection tool to help patient advocacy orgs capture and organize patients concerns about treatment options

- Genetic Alliance; Best Practices for Joining and Participating on Advisory Committees.

- Rare Disease Legislative Advocates: Advocacy Tools and Resources for Rare Diseases

- Background on FDA and Patient-Focused Drug Development (US Food and Drug Administration webinar)