Patient-Centeredness and Engagement in Clinical Research: Opportunities for Industry

February 5, 2014

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Our speakers

Freda Lewis-Hall, MD, DFAPA
Chief Medical Officer, Pfizer Inc.
PCORI Board Member

Janet Woodcock, MD
Director, Center for Drug Evaluation and Research, FDA

Our speakers

Anne Beal, MD, MPH
Deputy Executive Officer and Chief Officer for Engagement, PCORI

Susan Sheridan, MBA, MIM
Director of Patient Engagement, PCORI
Our objectives for today

1. Share how PCORI, industry, FDA, patients and other healthcare stakeholders are advancing the cause of “patient-centeredness” and engagement in clinical research;

2. Discuss how increased patient engagement will lead to changes in clinical trial processes;

3. Begin to understand how these paradigm changes will impact the pharmaceutical industry’s efforts in clinical research.

We Are at an Inflection Point

<table>
<thead>
<tr>
<th>Where Are We Today?</th>
<th>At an inflection point on patient engagement in the drug/device/diagnostics development process</th>
</tr>
</thead>
<tbody>
<tr>
<td>What Do We Have Now?</td>
<td>A heightened sensitivity to transform all aspects of healthcare to focus more acutely on the unmet needs of the patient</td>
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<tr>
<td>What Do We Need?</td>
<td>A clear framework to engage patients and incorporate their feedback into development and approval processes</td>
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Agenda: FDA's Recent Activities

- Patient-focused drug development meetings
- Patient reported outcomes
Patient-Focused Drug Development under PDUFA V

- FDA’s drug benefit-risk assessment considers severity of disease condition and degree of unmet medical need—clinical context

- Patient-Focused Drug Development is part of FDA commitments under PDUFA V
  - Convene at least 20 meetings on specific diseases
  - Patient perspective helps inform our understanding of the context for the assessment of benefit-risk and decision making for new drugs
  - Input can inform FDA analysis both during and outside of review

Which 20 Disease Areas? Criteria Used for Nomination

- Disease areas that are chronic, symptomatic, and affect functioning and activities of daily living
- Disease areas for which important aspects of that disease are not formally captured in clinical trials
- Disease areas for which there are currently no therapies or very few therapies, or the available therapies do not directly affect how a patient feels, functions, or survives
- Disease areas that reflect a range of severity
- Disease areas that have a severe impact on identifiable sub-populations (such as children or the elderly)
- Disease areas that represent a broad range in terms of size of the affected population
Identifying Disease Areas for the Patient-Focused Meetings

- In September 2012, FDA announced a preliminary set of diseases as potential meeting candidates
  - Public input on these nominations was collected through an online docket and at a public meeting held in October 2012
  - Over 4,500 comments were submitted, which addressed over 90 disease areas
  - FDA carefully considered these public comments and the perspectives of our drug review divisions at FDA

- FDA selected a set of 16 diseases selected to be the focus of meetings for fiscal years 2013-2015
  - This set was published in the Federal Register in April 2013
  - Another public process will be initiated in 2015 to determine the set for fiscal years 2016-2017

What Questions to Ask?

**Disease symptoms and daily impacts that matter most to patients (draft questions)**

1. Of all the symptoms that you experience because of your condition, which 1-3 symptoms have the most significant impact?
2. Are there specific activities that are important to you but that you cannot do at all or as fully as you would like because of your condition?
3. How has your condition and its symptoms changed over time?
4. What worries you most about your condition?
Questions for Patients regarding current approaches to treatment

1. What are you currently doing to help treat your condition or its symptoms?
2. How well does your current treatment regimen treat the most significant symptoms of your disease?
3. What are the most significant downsides to your current treatments, and how do they affect your daily life?
4. Assuming there is no complete cure for your condition, what specific things would you look for in an ideal treatment?

Patient-Focused Drug Development Meetings Held in FY 2013

- Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) - April 25, 2013
- Human immunodeficiency virus (HIV) - June 14, 2013
- Lung cancer - June 28, 2013
- Narcolepsy - September 24, 2013
Disease areas to be the focus of meetings for FY 2014-2015

FY 2014 – 2015

- Alpha-1 antitrypsin deficiency
- Breast cancer
- Chronic Chagas disease
- Female sexual dysfunction
- Fibromyalgia (December 10, 2013)
- Hemophilia A, Hemophilia B, von Willebrand disease, and other heritable bleeding disorders
- Idiopathic pulmonary fibrosis
- Irritable bowel syndrome, gastroparesis, and gastroesophageal reflux disease with persistent regurgitation symptoms on proton-pump inhibitors
- Neurological manifestations of inborn errors of metabolism
- Parkinson’s disease and Huntington’s disease
- Pulmonary arterial hypertension
- Sickle cell disease (February 7, 2014)

Product of Patient-Focused Meetings

- Each meeting will result in a meeting report that will be posted on the FDA website
  - The patient perspectives captured in these reports will provide helpful insights for FDA reviewers
- The Voice of the Patient: A Series of Reports from FDA’s Patient-Focused Drug Development Initiative
  - [http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm368342.htm](http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm368342.htm)
  - [The Voice of the Patient Report: Chronic Fatigue Syndrome and Myalgic Encephalomyelitis (PDF - 267KB)](http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm368342.htm)
• Describe a process NOT evidentiary standards

• Qualification process described for Biomarkers, Animal Models, and Clinical Outcome Assessments (COA)


First Clinical Outcome Assessment Qualified 1/14

• EXACT
  – A PRO for the measurement of symptoms of acute bacterial exacerbation of chronic bronchitis in patients with chronic obstructive pulmonary disease
COA Qualification Projects Status Report by Stage (January 24, 2014)

<table>
<thead>
<tr>
<th>COA DDT Stage</th>
<th>Number in Stage</th>
</tr>
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<tbody>
<tr>
<td>Initiation Stage</td>
<td>20</td>
</tr>
<tr>
<td>Initiation – DDT # assigned</td>
<td>11</td>
</tr>
<tr>
<td>Initiation – Letter of Intent (LOI) received</td>
<td>5</td>
</tr>
<tr>
<td>Initiation – revised LOI requested</td>
<td>4</td>
</tr>
<tr>
<td>Consultation and Advice Stage (C&amp;A)</td>
<td>26</td>
</tr>
<tr>
<td>C&amp;A – Initial Briefing Package requested</td>
<td>9</td>
</tr>
<tr>
<td>C&amp;A – Active</td>
<td>17</td>
</tr>
<tr>
<td>Review Stage</td>
<td>3</td>
</tr>
</tbody>
</table>

49 COA qualification projects including: 35 PROs, 4 ClinROs, 3 PerfOs, 1 containing multiple elements including, PRO, ClinRO, ObsRO components, and 6 TBD (appropriate reporter will be based on additional research)

Ongoing COA Qualification Efforts

- Qualification projects actively underway for a wide variety of conditions, including but not limited to:
  - Multiple sclerosis
  - Cancer fatigue
  - Mild cognitive impairment
  - Irritable bowel syndrome
  - Asthma
  - Cystic fibrosis
  - Depression
  - Non-small cell lung cancer
  - Functional dyspepsia
  - Community-acquired bacterial pneumonia
  - Acute bacterial skin and skin structure infections
  - Ulcerative colitis
  - Crohn’s disease
  - Esophagitis
Ongoing COA Qualification

- CDER partnering with multiple consortia, patient groups, academics, researchers, and others on COA qualification projects, including:
  - FNIH Biomarkers Consortium
  - Critical Path Institute PRO-Consortium (includes 7 distinct working groups: Functional Dyspepsia, Irritable Bowel Syndrome, Non-Small Cell Lung Cancer, Rheumatoid Arthritis, Depression, Cognition)
  - Critical Path Institute Coalition against Major Diseases (CAMD) Consortium
  - Critical Path Institute Multiple Sclerosis Outcomes Assessments Consortium (MSOAC)
  - PROOF-C Cancer Fatigue Consortium
- CDER is collaborating with NIH to explore potential qualification of selected PROMIS measures
- CDER continues to encourage instrument development and qualification, particularly for pediatric populations, rare diseases, and other areas of unmet need

Summary

- FDA is actively engaged in incorporating the patient’s voice into drug development
- We are holding a series of disease-specific, patient focused meetings under PDUFA 5
- We also are involved in qualifying many PROs
- These will be utilized in our structured benefit-risk assessments
Patient-Centeredness and Engagement in Clinical Research: Opportunities for Industry

Anne C. Beal, MD, MPH
Deputy Executive Director and Chief Officer for Engagement

DIA/PCORI Webinar
February 5, 2014

PCORI

An independent non-profit funder of clinical comparative effectiveness research.

Authorized by Congress as part of the 2010 Patient Protection and Affordable Care Act (ACA).
Why PCORI?

- Research has not answered many questions patients face
- People want to know which treatment is right for them
- Patients need information they can understand and use

Our Mission

PCORI helps people make informed health care decisions, and improves health care delivery and outcomes, by producing and promoting high integrity, evidence-based information that comes from research guided by patients, caregivers and the broader health care community.
Our Growing Research Portfolio (as of January 2014)

Total number of research projects awarded: 279

Total funds awarded: $464.2 million

Number of states where we are funding research:
39 states (plus the District of Columbia and Quebec, Canada)

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What PCORI-Funded Researchers Are Studying

<table>
<thead>
<tr>
<th>Conditions Studied</th>
<th>Populations Studied</th>
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<tbody>
<tr>
<td>(Broad Funding Cycles I – III)</td>
<td>(Broad Funding Cycles I – III)</td>
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<tr>
<td>Studies Funded</td>
<td>Studies Funded</td>
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<tr>
<td></td>
<td>Racial/Ethnic Minorities</td>
</tr>
<tr>
<td>Mental Disorders</td>
<td>31</td>
</tr>
<tr>
<td>Cardiovascular Diseases</td>
<td>31</td>
</tr>
<tr>
<td>Cancer</td>
<td>24</td>
</tr>
<tr>
<td>Endocrine System Diseases</td>
<td>10</td>
</tr>
<tr>
<td>Nervous System Diseases</td>
<td>16</td>
</tr>
<tr>
<td>Musculoskeletal Diseases</td>
<td>7</td>
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How We Engage Patients and Others in PCORI’s Work

"Research Done Differently"
Patient engagement as a path to rigorous research

Tell us what PCORI should study
Help determine what we fund
Engagement
Tell us how we are doing
Help us share research findings
Tell us what PCORI should study

Help Determine What We Fund

Advisory Panels & Working Groups

PCORI Reviewers
Patient-Centeredness vs. Patient Engagement

- **Patient-Centeredness** is a component of what PCOR is looking for in research applications.
  - Does the project aim to answer questions or examine outcomes that matter to patients within the context of patient preferences?
  - Research questions and outcomes should reflect what is important to patients and caregivers.

- **Patient engagement** is about having patients as partners in research as opposed to merely subjects.
  - Active engagement between scientists, patients, and stakeholders.
  - Community, patient, and caregiver involvement already in existence or a well-thought out plan.

Dissemination & Implementation

Blueprint for the PCORI Dissemination and Implementation Action Plan:

- D&I roundtable and webinar (July, 2013)
- RFP issued to develop D&I plan (Feb, 2014)
- September 2014 workshop of experts and stakeholders in implementation science and quality improvement.
The Case for Addressing the Implementation Gap

Optimal Healthcare Delivery

PCORI's Blueprint for Dissemination and Implementation Targets the Gap

Implementation Gap to Improve Practice

New Investments in Knowledge

Current Knowledge and Practice

Research + Practice

Facilitating Patient Partnership in Research

Engagement Awards

Pipeline to Proposals
Purpose of Engagement Awards

Projects designed to provide “wrap-around” support and enhance impact of our major research awards

- NOT meant to be research, but meant to:
  - Support knowledge of PCORI’s work, and inform about our program efforts
  - Training and development of “non-usual suspects” and others
  - Disseminate the results of our research to promote implementation into practice

- Smaller awards, up to $250,000 total, and less than two years in length

- Other objectives:
  - Engage new groups who have not previously been involved with PCORI
  - Develop new mechanisms for disseminating research findings
  - Promote research done differently by supporting the engagement and partnering

Pipeline to Proposals

The chart below summarizes the three tiers of the Pipeline to Proposal Awards Program.

<table>
<thead>
<tr>
<th>Summary of Funding Tiers</th>
<th>Start Date</th>
<th>Funding Level</th>
<th>Purpose of Funding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tier I</td>
<td>December 2013</td>
<td>Up to $15,000 per award for 9 months</td>
<td>Building the community and capacity necessary to later develop a patient-centered comparative effectiveness research (CER) project addressing the issue of interest to the audience.</td>
</tr>
<tr>
<td>Tier II</td>
<td>Early 2014</td>
<td>Up to $50,000 per award for 12 months</td>
<td>Maturation of research partnerships with the goal of increasing PCORI or other CER project funding. The funds are to be used to strengthen the partnerships and further develop the infrastructure and governance structure laid out during Tier I and to lay groundwork for the ultimate drafting of a patient-centered CER proposal.</td>
</tr>
<tr>
<td>Tier III</td>
<td>Early 2014</td>
<td>Up to $50,000 per award for 12 months</td>
<td>Proposal development, targeting advanced potential research partnerships (those who are “almost there”) that could benefit from working with seasoned partners to draft a strong patient engagement plan and a rigorous science proposal.</td>
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</table>
What is Patient Engagement in Research?

Find Us Online

www.pcori.org

Check out our webinar on the Engagement Awards on February 13, 2014
Meaningful Patient Engagement in Clinical Research

Sue Sheridan, MIM, MBA
Director of Patient Engagement

Getting to know the Patient and Family Engagement Rubric
Why develop a rubric?
- The rubric is a response to frequent questions from the patient and research communities asking what we mean by “engagement in research.”

What is the rubric?
- The rubric is a framework that provides a variety of options for incorporating engagement, where relevant, into the research process.

How will the rubric be used?
- The rubric will be used as a guide for applicants, merit reviewers, awardees and Engagement Officers.

Elements of the Rubric
- Planning the Study
- Conducting the Study
- Disseminating the Study Results
- PCOR Engagement Principles
Elements of the Rubric

Planning the Study

Conducting the Study

Disseminating the Study Results

PCOR Engagement Principles

Rubric: Planning the Study

Formulating Research Questions and Study Design

Patient partners participate in:

- Identifying the topic and developing the research question to be studied.
- Creating the intervention to be studied (if applicable) and identifying comparators.
- In identifying the goals or outcomes of the interventions to be studied.
- Defining essential characteristics of study participants.
- Other study design and preparation.
Elements of the Rubric

- Planning the Study
- Conducting the Study
- Disseminating the Study Results
- PCOR Engagement Principles

Rubric: Conducting the Study

Participating in and monitoring the conduct of the project

Patient partners participate in and monitor the conduct of the research project.

- Provide letters of support from patient partners that clearly describe the role of the patient partners in conducting and monitoring the study.
- Clearly articulate in the application the roles of the patient partners in each component of the study, (e.g., helping to draft survey tools and focus group questions, reviewing participant materials for readability, etc.), including the dissemination and implementation assessment.

The research team, including patient partners, participates in all potential evaluation activities of patient engagement.

- Include in your application a plan for “check-ins” with patient partners to monitor their perceptions of the extent to which a) they are meaningfully involved in the study and b) their participation is contributing to the study.
- Also include a plan for “check-ins” with the other research team members to monitor their perceptions of the extent to which a) patient partners are meaningfully involved in the study and b) their participation is contributing to the study.
### Rubric: Conducting the Study

#### Participating in and monitoring the conduct of the project

<table>
<thead>
<tr>
<th>Patient partners participate in the recruitment and data collection from the study participants, when appropriate.</th>
</tr>
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<tr>
<td>The research team, including patient partners, participates in all potential evaluation activities of patient engagement.</td>
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### Rubric: Conducting the Study

#### Participating in and monitoring the conduct of the project

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- Also include a plan for “check-ins” with the other research team members to monitor their perceptions of the extent to which a) patient partners are meaningfully involved in the study and b) their participation is contributing to the study.
Rubric: Disseminating the Study Results

Helping to plan the dissemination of the study’s results.

Patient partners are involved in plans for disseminating the study’s findings to patient, stakeholder, and research audiences so that the findings are communicated in understandable, usable ways.

- Provide letters of support from patient partners that clearly describe the role of the patient partners in planning the dissemination of the study’s results.
- In the application, clearly identify the role of patient partners in planning the dissemination of the study’s findings.
Elements of the Rubric

Planning the Study

Conducting the Study

Disseminating the Study Results

PCOR Engagement Principles

Rubric: PCOR Engagement Principles

**Reciprocal Relationships**

The roles and decision-making authority of all research partners, including patient partners, are clearly stated.
Rubric: PCOR Engagement Principles

Co-learning

The application includes plans to ensure that the patient partners will understand the research process and the researchers will understand patient centeredness and patient engagement.

Examples:
- Training and educational opportunities are provided such as patient advocacy organizations, patient/survivor, and clinician/caregiver for the researchers providing the intervention (e.g., training in better communication with patients, led by patient instructors).
- Compensation for patient partners is included in the research budget, as well as reasonable and thoughtful time commitment requests.
- When the patient partners represent unique populations, the research team proposes to accommodate their cultural diversity and/or disability.

Partnership

Time and contributions of patient partners are valued and demonstrated in fair financial compensation, as well as reasonable and thoughtful time commitment requests.

When the patient partners represent unique populations, the research team proposes to accommodate their cultural diversity and/or disability.
Rubric: PCOR Engagement Principles

<table>
<thead>
<tr>
<th>PCOR Engagement Principles</th>
<th>Trust, Transparency, Honesty</th>
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<tr>
<td><strong>Trust, Transparency, Honesty</strong></td>
<td>Trust, Transparency, Honesty</td>
</tr>
<tr>
<td>▪ Major decisions are made inclusively and information is shared readily with all research partners,</td>
<td></td>
</tr>
<tr>
<td>▪ Patient partners and research partners express commitment to open and honest communication with one another.</td>
<td></td>
</tr>
<tr>
<td>▪ The study team commits to communicate the study’s findings back to the study community in a meaningful and usable way.</td>
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Elements of the Rubric

- Planning the Study
- Conducting the Study
- Disseminating the Study Results
- PCOR Engagement Principles
Have Questions?

We welcome your questions and comments at getinvolved@pcori.org

Find Us Online

www.pcori.org
An Industry Perspective

Freda Lewis-Hall, MD, DFAPA

Where Are We Today?

Companies Are:

- Devoting new resources and staff roles to integrating patient engagement into product development lifecycle
- Seeking alignment with regulators and patients/patient advocates on the definitions of patient engagement and its fundamental activities
- Partnering with patient advocacy groups to develop new treatments for rare diseases where patients/groups collaborate in research
  - Sanofi/Michael J. Fox Foundation – Pfizer/Cystic Fibrosis Foundation
What Actions by FDA will Help Industry be More Patient-centered?

1. A clearly articulated and transparent **pathway** to incorporate the patient's voice consistently, including a clear pathway/guidance for:
   - Innovators to incorporate the patient's view into the development plan,
   - Regulators to incorporate results into product review and labeling
   - Clinicians and patients to incorporate new info into joint decision-making

2. Regulatory **consensus** on both accepted methods for patient engagement and specific guidance on how to use gathered information in product development plans

3. Uniform **standards** accepted by all FDA divisions and other regulators -- and within those standards, flexibility to accommodate differences in patient populations, culture, geography, and diseases

What Actions by PCORI will Help Industry be More Patient-centered?

1. A more holistic viewpoint on how to bring greater value to the healthcare system through patient engagement;

2. The methods and tools to fully engage patients across the research spectrum, (“the leads to get to those needs”);

3. Examples of patient engagement models – resulting in substrate we can pick up and carry forward.
How Can Industry Help Itself Become More Patient-centered?

- Identify existing gaps in processes
- Explore innovative models of patient engagement
- Increase focus on external collaborations to drive engagement

So What Is Our Plan of Action?