Advancing the Science of Patient Input in Medical Product R&D: Towards a Research Agenda

Session 2:
Patient Perspectives & Preferences on Benefit-Risk

Kathryn O’Callaghan
CDRH Assistant Director for Strategic Programs
FDA Center for Devices and Radiological Health

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How Patient Preferences Contribute to Regulatory Decisions for Medical Devices

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By: Jeffrey Shuren, M.D., J.D., Anindita Saha and Martin Ho, M.S.

- **Weight loss**
  - Patient-informed trial design
  - PMA approval

- **At home dialysis**
  - Patient risk tolerance
  - Expanded indication for solo at home use

- **Diabetes care**
  - Risk management for pediatric population

- **Ongoing studies**
  - Neurology
  - Oncology
  - Ophthalmics
  - Prosthetics
  - Women’s health
  - Urology
  - Pediatrics
### Begin with the End in Mind: How will this information be used?

#### Framework for Potential Uses of PPI in Medical Product Development

<table>
<thead>
<tr>
<th>Development</th>
<th>Clinical Trial Design</th>
<th>Pre-Market Benefit-Risk Assessment</th>
<th>Post-Market</th>
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<tbody>
<tr>
<td>1. Identify unmet medical need</td>
<td>1. Inform endpoint selection</td>
<td>1. Analysis of condition</td>
<td>1. Inform interpretation of new data affecting benefit-risk assessment</td>
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<td>2. Understand what matters most to patients about their disease or treatment</td>
<td>2. Inform performance goal or effect size</td>
<td>2. Current treatment options</td>
<td>2. Inform studies of new / expanded use populations</td>
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<td>3. Patient perspective on benefit-risk tradeoffs</td>
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<td>4. Population subgroup considerations</td>
<td>3. Communicate benefit-risk information to patients</td>
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Strength of Evidence Needed Depends on Context of Use

- Invention / Discovery
- Early Development
- Clinical Studies
- Regulatory Evaluation
- Clinical Care (Practice Guidelines)
Dec. 2017 CERSI-FDA Workshop:
Advancing Use of PPI as Scientific Evidence for Medical Product Evaluation

WHAT are regulatory PPI studies?
- MDIC PPI Framework
- FDA PPI Guidance
- Demonstrative Case Examples

WHY do a PPI study?
- Framework of PPI Regulatory Uses
- PPI-Reg Scientific Fundamentals

WHEN/HOW to do a PPI study?
- Preference Sensitive Checklist
- Learning Case Studies

WHERE do we go from here?
- Preference Sensitive Studies
- Capacity Building & Sustainability

Adoption

Understanding

Awareness
Recommended Early Focus: Barriers & Potential Strategies

• Limited system capacity to perform rigorous, high quality PPI studies
• Goal is to channel these resources where most valuable
• Where is the sweet spot?
  – “Preference-sensitive” patient decision re: diagnostic / treatment options (no clear single best option for all)
  – Relevance. Patient preferences relate to measures of effectiveness, safety, other attributes relevant to product developers and regulators, AND
  – We understand enough about a) patient perspectives on disease and existing options, and b) characteristics of the proposed new option
Shared Goal
Improve patient health by better understanding patient needs, experiences and preferences

Art of Patient Engagement + Science of Patient Input = Patient-Centric Healthcare

Patient Reported Outcomes (PRO)
- Can be Endpoints in Regulatory studies
- Outcomes to monitor in clinical care
- Interest to patients, providers, payers

Patient Preference Information (PPI)
- Inform endpoints or effect size for Regulatory studies
- Inform subgroup considerations
- Inform studies of new / expanded uses

Shared Goal (FDA)
ADDITIONAL MATERIAL
Patient Input as Evidence*

- Final Guidance*
- Hiring & training staff
- Access to external SMEs
- Expanding collaborative networks

- PPI in IDE Benefit-Risk
- PROs & Outcomes that Matter Most to Patients

*PPI & PRO in Marketing Application Benefit-Risk

- PPI in Compliance Benefit-Risk
- PPI & PRO for new uses
Factors to Consider in Medical Device Benefit – Risk Determinations

- Worksheet with questions to guide evaluation of each factor
- Patient Perspectives are an as important factor:

<table>
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<th>PPI Factors</th>
<th>Questions</th>
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<tr>
<td>Patient-Reported Outcomes</td>
<td>• Do benefit(s) and risk(s) include effects on patients’ health-related quality of life?</td>
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<tr>
<td>Benefit-Risk Considerations</td>
<td>• Which benefits and risks are most important to affected patients?</td>
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<td>• What benefit-risk tradeoffs are acceptable from the patient perspective?</td>
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<td>• Are there clinically-relevant subgroups of patients that would choose a particular benefit-risk profile over other alternatives?</td>
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<td>• Does PPI capture diverse preference across the spectrum of indicated population and thus, generalizable?</td>
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Patient Preference Information (PPI)

• Qualitative PPI may be useful
  – identifying which outcomes, endpoints or other attributes are valued most by patients
  – which factors affect patients’ perspectives on risk and benefit

• Quantitative PPI
  – provide estimates of how much different outcomes, endpoints or other attributes are valued by patients
  – tradeoffs that patients state or demonstrate they are willing to make
Significant Increase in Patient Perspective Studies

- >500% increase submissions with PROs (2009-2015)
- >75% of clinical protocols include PROs (FY17 pivotal study approvals)

Use of PROM in Device Submissions

1Submitted to CDRH as of FY2015
“The FDA’s work requires us to establish objective, consistent criteria on which we base our decisions. But ultimately, the criteria we use to judge benefit and risk turn on the parameters that matter to patients.

“Involving the end-user – the patient – in identifying health priorities and outcomes desired from health interventions is critically important.

“The bottom line is this: When assessing whether valid scientific evidence shows that a device’s probable benefit outweighs its likely risks, the FDA can also consider rigorous, systematically gathered patient preference information as a part of the totality of the evidence from clinical and nonclinical testing.”

- FDA Commissioner Scott Gottlieb, Oct 11, 2017
Thank You

Katie O’Callaghan
kathryn.ocallaghan@fda.hhs.gov