Assessing and Understanding Patient Preferences in Medical Device Development: Webinar to the PCORI Ambassadors

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Today’s Speakers

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Agenda

• Introduction to the Medical Device Innovation Consortium (MDIC)
• MDIC’s Patient Centered Benefit-Risk Project
• FDA/CDRH and Patient Engagement
  − CDRH Strategic Priorities
  − Draft Guidance regarding Patient Preferences
• Patient Engagement in Medical Device Regulation
• Questions
Introduction to MDIC
What is Regulatory Science?

The science of developing new tools, standards, and approaches to assess the safety, efficacy, quality, and performance of FDA-regulated products

- Benefits patients by speeding the rate of important technologies reaching market
- Reduces time and resources needed for device development, assessment, and review. For example:
  - Can lead to quicker, more efficient device approvals
  - Can decrease the size and duration of pre-market clinical trials

**Faster, Safer, More Cost-effective**
MDIC: Public-Private Partnership focused on Regulatory Science

- Members include FDA, Industry, Patient Groups, PCORI, NIH, CMS
- Collaborative Board involving representatives of three core groups
- Working groups organized around specific projects
- Academics and other experts engaged in working groups as needed

- CDRH representatives engaged on the Board and working groups
- NIH and CMS representatives on Board
- Patient advocacy groups
- PCORI

- Large and small companies involvement
- Trade associations

FDA & other Government

Industry

Non-Profits
MDIC Strategies

Create A Forum For Collaboration & Dialogue
- Establish a transparent and flexible governance structure
- Ensure involvement from regulators, manufacturers, and other appropriate stakeholders
- Implement appropriate intellectual property and data sharing policies

Make Strategic Investments In Regulatory Science
- Establish working groups to identify and prioritize key issues
- Develop procedures for requesting and evaluating project proposals and for selecting centers to conduct the research
- Invest in programs aimed at improving the throughput of innovation

Provide Tools To Drive Innovation
- Provide education about the medical device regulatory process and new tools, standards and test methods
- Develop searchable databases and links to relevant reports and methods
- Hold an annual medical device regulatory science symposium
MDIC: Six Major Project Areas

• Clinical Trial Innovation and Reform
• Advancing Clinical Trial Practices
• Computer Modeling and Simulation
• Case for Quality
• Clinical Diagnostic Development and Regulation
• Patient Centered Benefit-Risk Assessment (PCBR)
The science of patient preference assessment and the MDIC Patient Centered Benefit-Risk Initiative
Patient-Centered Benefit-Risk Assessment in Medical Devices

- Landmark 2012 regulatory guidance on benefit-risk determinations regarding medical devices
- Guidance discusses the value of patient’s perspective on benefit-risk
- Guidance does not describe how to collect or use information on patient preferences in the regulatory process
Implications of CDRH Guidance

• Standardization among CDRH staff on benefit-risk assessment, which is the basis for regulatory approval
  – Product approvable if benefit exceeds risk for a patient population
  – Focus on “probable” risks, not theoretical risks

• Benefit-risk assessment should reflect the patient perspective
  – Product approvable if there is a subset of reasonable patients that would accept the risks given the benefits

• Guidance discusses the potential value of patient preference information, but not when or how to collect such information
MDIC Patient Centered Benefit-Risk Framework Report

• Framework for Incorporating Patient Centered Benefit Risk Assessment into Regulatory Submissions: The overarching report of MDIC Patient Centered Benefit-Risk Project
  − Resource for CDRH, MDIC members, and industry on when and how to collect patient preference information for incorporation into the regulatory process
  − Incorporates Catalog of Methods as appendix

• A working document
  − An initial thought piece in an emerging area
  − To be updated as industry, FDA, and patient groups gain experience with collecting/using patient preference information
PCBR Framework Report
Use and Limitations

• PCBR Framework Report is:
  − an initial thought piece in an emerging area of regulatory science
  − intended to help advance the field of assessing patient preferences
  − to be updated as FDA, industry, patient groups, academics and others gain experience with collecting and using patient preference information

• PCBR Framework Report limitations:
  − it does not represent the opinion or policy of FDA
  − it does not include any specific recommendations to the FDA regarding how to collect or use patient preference information in regulatory approval decisions.
  − it is not a substitute for FDA guidance documents or for direct discussions with CDRH staff regarding regulatory submissions
  − it is not intended to be a prescriptive, “how-to” guide nor the definitive document about incorporating patient preference information into the regulatory process
# Framework Report Outline

<table>
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<tr>
<th>Section</th>
<th>Description</th>
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<tr>
<td>I. Introduction</td>
<td>Background on why the project was undertaken and the report’s purpose and scope</td>
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<tr>
<td>II. Definitions and Background Concepts</td>
<td>Define patient preferences, methods, and the concept of preference sensitive decisions in patient care</td>
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<tr>
<td>III. Evaluating the Potential Value of Patient Preference Information in Regulatory Benefit-Risk Assessments</td>
<td>Outlines factors to consider in deciding whether to collect patient preference information as input into the benefit-risk assessment of a particular technology</td>
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<tr>
<td>IV. Potential Use and Value of Preference Information in the Product Lifecycle</td>
<td>Discusses how patient preference information can be collected and used in each phase of the product lifecycle</td>
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<tr>
<td>V. Factors to Consider in Undertaking a Patient Preference Study</td>
<td>Description and summary of methods catalog as well as discussion of factors to consider in designing a patient preference study.</td>
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<tr>
<td>VI. Considerations in using Preference Information in the Regulatory Process</td>
<td>Discusses how patient preference information may be useful in the regulatory process</td>
</tr>
<tr>
<td>VII. Potential Value of Patient Preference Information Beyond the Regulatory Process</td>
<td>Discusses the potential value of patient preference information in reimbursement, marketing, and shared decision making</td>
</tr>
<tr>
<td>VIII. Future Work in the Collection and Use of Patient Preference Information</td>
<td>Outlines opportunities for additional work to improve the ability to collect and incorporate patient preferences into regulatory decisions</td>
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<th>Appendix A</th>
<th><strong>Catalog of Methods</strong></th>
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<td>Appendix B</td>
<td><strong>Glossary of Terms</strong></td>
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Patient preference information can help ensure that the CDRH benefit-risk determination process is patient-centric

Patient preference information can help

− identify benefits and harms most important to patients,
− frame the benefit-risk issues and tradeoffs from the patient perspective,
− identify whether there are subgroups of patients that would choose to use the technology over other alternatives, and
− support quantitative benefit-risk modeling.
Patient preference information is not currently a requirement for FDA PMA or de novo approval

- Such information can be viewed as a means of enhancing regulatory submissions to help assure that benefit-risk determinations are patient-centric
- Patient preference information can be included at the option of the sponsor, perhaps based on a suggestion or request from FDA staff.

Patient preference information does not and is not intended to replace other clinical and safety evidence.

- Patient preference information can be a supplement to clinical and safety data and provide additional data for consideration, but does not eliminate the need for clinical and safety data.
When might a device company want to include patient preference information?

• There is not a “cookbook” or algorithmic approach to when patient preference information may be valuable

• Factors that characterize situations where patient preference information could be useful
  – The perspective of patients as stakeholders: understanding the patient perspective of the condition or use of the device
  – The benefit-risk tradeoffs inherent in a specific technology: including marginal risk-benefit tradeoffs, temporal tradeoffs, substantial differences in benefits and harms from other products
  – Regulatory novelty

- See Section III of the MDIC Framework report (mdic.org/pcbr/framework-pdf/)
When is patient preference information less valuable?

- When the patient is not a major stakeholder or decision-maker
- When the disease state/technology are generally understood by sponsors and FDA staff and there is significant regulatory precedent for approval
- When benefits are high and risks are low
- When the treatment is clearly superior to existing therapies with no tradeoffs in risk
- When the treatment meets an unmet medical need with poor outcomes such that the risk of treatment will not be greater than the risks of the untreated disease

- See Section III of the MDIC Framework report (mdic.org/pcbr/framework-pdf/)
The value of patient preference information as a function of benefit and risk

<table>
<thead>
<tr>
<th>Benefit</th>
<th>Risk</th>
</tr>
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<tbody>
<tr>
<td>High Benefit/Low Risk</td>
<td>High Benefit/High Risk</td>
</tr>
<tr>
<td>Patient preference info less needed if clear benefit and little risk</td>
<td>Patient preference info valuable to show a subset of patients willing to take the high risk for the significant benefit</td>
</tr>
<tr>
<td>Low Benefit/Low Risk</td>
<td>Low Benefit/High Risk</td>
</tr>
<tr>
<td>Patient preference info might be helpful to show that a subset of patients want the limited benefit</td>
<td>Product may only get approved if significant evidence that at least a subset of patients would take the risk for the benefit</td>
</tr>
</tbody>
</table>
Patient Preferences can be useful across the Device Product Lifecycle

Incorporating Patient Preferences into the Medical Device Total Product Lifecycle

Source: FDA Center for Devices and Radiological Health (CDRH)
Appendix A: “Catalog of Methods”: Definition of Patient Preference Methods

Patient preference methods are methods for collecting and analyzing data that allow quantitative assessments of the relative desirability or acceptability to patients of attributes that differ among alternative medical treatment approaches.
# Methods Included in the Catalog

<table>
<thead>
<tr>
<th>Group</th>
<th>Method</th>
</tr>
</thead>
</table>
| Structured-weighting   | • Simple direct weighting  
                        | • Ranking exercises  
                        | • Swing weighting  
                        | • Point allocation  
                        | • Analytic hierarchy process  
                        | • Outranking methods |
| Health-state utility   | • Time tradeoff  
                        | • Standard gamble |
| Stated-preference      | • Direct-assessment questions  
                        | • Threshold technique  
                        | • Conjoint analysis and discrete-choice experiments  
                        | • Best-worst scaling exercises |
| Revealed-preference    | • Patient-preference trials  
                        | • Direct questions in clinical trials |

- Grouping scheme meant only to facilitate discussion of methods
  - Not intended to preclude other grouping schemes
  - Some methods could be assigned to multiple groups
Future Opportunities in Patient Preference assessment

• MDIC project priorities in patient preference research include:
  – Developing resources for sponsors who want to initiate the own patient preference studies
  – Patient Preference Methodology
  – Best practices for Communicating Benefit and Risk

• MDIC wants to support sponsors considering their own patient preference assessment studies
  – Sponsors submitting these studies to the FDA will help advance the science of patient preference assessment
CDRH’s Partner with Patients Strategic Priority

Heather Benz, Ph.D.
External Expertise and Partnerships
Center for Devices and Radiological Health
U.S. Food and Drug Administration
Patients are at the heart of what we do

CDRH Vision: Patients in the U.S. have access to high-quality, safe, and effective medical devices of public health importance first in the world.
Evolution of the Role of Patients

- **Historical:** Paternalistic provider-patient relationships
- **Emerging Diseases:** Patient advocacy for availability of and access to new treatments
- **The Internet:** Patient empowerment through information
- **The Future Today:** Patient preferences informing regulatory decisions
We must interact with patients as partners and work together to advance the development and evaluation of innovative devices, and monitor the performance of marketed devices.
GOALS

• Promote a culture of meaningful patient engagement by facilitating CDRH interaction with patients.

• Increase use and transparency of patient input as evidence in our decision making.
Additional Actions

• Resources permitting, establish in CDRH a Patient-Focused Program

• Convene the Patient Engagement Advisory Committee

• Issue a report summarizing current PRO regulatory usage patterns and gaps

• Develop a framework for patient input to inform clinical study design and conduct

• Develop education and training for CDRH staff and industry
Patient Engagement + Science of Patient Input = Patient-Centric Healthcare
Patient Preference Information – Submission, Review in PMAs, HDE Applications, and De Novo Requests, and Inclusion in Device Labeling

Draft guidance

Patient Preference Information Draft Guidance

- **Patient preference information (PPI):** qualitative or quantitative assessments of the relative desirability or acceptability of attributes that differ among alternative diagnostic or therapeutic strategies
- Outlines CDRH-CBER policy that PPI may be considered along with other evidence
- Outlines ways PPI is useful in regulatory contexts
- Revises device benefit-risk assessment framework
When is patient preference information useful?

• PPI may not be relevant or appropriate for all device types

• Could be useful for those product types and diseases or conditions where usage decisions by patients and health care professionals are “preference-sensitive”

Preference sensitive scenarios may exist for:

• Devices with a direct patient interface
• Devices intended to yield significant health and appearance benefits
• Devices intended to directly affect quality of life
• Certain life-saving but high-risk devices
• Devices developed to fill an unmet medical need or treat a rare disease or condition
• Devices with novel technology
Recommended Qualities of Patient Preference Studies

• Representativeness
• Heterogeneity
• Minimal cognitive bias
• Effective communication
• Robustness of analysis of results
Obesity Case Study

- Explore how to elicit and incorporate patient preferences into regulatory decision making
- Treatments involve difficult benefit-risks tradeoffs
- Broad array of potential devices with diverse benefit-risk profiles
- Used Discrete-choice experiment survey
- Published in Surgical Endoscopy *

A Favorable Benefit-Risk Tradeoff?
Sample: Obese Subjects Willing to Lose Weight

- Jointly developed by CDRH and RTI-Health Solutions
- ~650 subjects with BMI ≥ 30 kg/m²
- Administered via the Internet
- Each subject evaluates choices between 8 pairs of hypothetical weight-loss devices profiles defined by attributes and levels
- Only weight-loss devices are considered
- Subjects assume that insurance covers all costs
Attributes and Levels

- Type of operation (Laparoscopic, Endoscopic, Open)
- Average Weight Loss (0% to 30%)
- Weight loss duration (0 to 5 years)
- Comorbidity improvement (none to 100%)
- Duration of mild-moderate side effects (0 to 5 years)
- Chance of re-hospitalization (0 to 20%)
- Mortality (0 to 5%)
- Dietary restrictions
  - Eat ¼ cup at a time
  - Wait 4 hours between meals
  - Can’t eat sweets or hard to digest foods
<table>
<thead>
<tr>
<th>Attribute</th>
<th>Device A</th>
<th>Device B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of operation</td>
<td>Endoscopic surgery</td>
<td></td>
</tr>
<tr>
<td>Recommended diet restriction</td>
<td>Wait 4 hours between meals</td>
<td></td>
</tr>
<tr>
<td>On average, how much weight is lost</td>
<td>30 lbs.</td>
<td>60 lbs.</td>
</tr>
<tr>
<td>On average, how long the weight loss lasts</td>
<td>Weight loss lasts 5 years</td>
<td>Weight loss lasts 1 year</td>
</tr>
<tr>
<td>Average reduction in dose of prescription drugs for diabetes at the lower weight</td>
<td>Eliminates the need for prescription drug</td>
<td></td>
</tr>
<tr>
<td>On average, how long side effects last</td>
<td>Last 1 month</td>
<td>Last 1 year</td>
</tr>
<tr>
<td></td>
<td>(Remember that side effects will limit your ability to do daily activities several times a month.)</td>
<td></td>
</tr>
<tr>
<td>Chance of a side effect requiring hospitalization</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>Chance of dying from getting the weight loss device</td>
<td>![10%](10 out of 100)</td>
<td>![1%](1 out of 100)</td>
</tr>
<tr>
<td>Which weight-loss device do you think is better for people like you?</td>
<td>![Device A](Device A)</td>
<td>![Device B](Device B)</td>
</tr>
</tbody>
</table>
Most Important Attributes

- **Mortality Risk**, **Weight Loss**, and **Weight-Loss Duration** are the most important.
- Risk of hospitalization for AE is the least important.
## Decision Aid Tool

### Device outcomes and features

<table>
<thead>
<tr>
<th>Feature</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Body Weight loss (TBWL%)</td>
<td>14.3%</td>
</tr>
<tr>
<td>Side effect duration (months)</td>
<td>60</td>
</tr>
<tr>
<td>Chance of side effects requiring hospitalization</td>
<td>5%, surgery</td>
</tr>
<tr>
<td>Recommended diet restrictions</td>
<td>Can't eat sweets</td>
</tr>
<tr>
<td>Expected duration of weight loss (months)</td>
<td>60</td>
</tr>
<tr>
<td>Comorbidities: Reduce treatment dose / chance</td>
<td>No change</td>
</tr>
<tr>
<td>Type of operation</td>
<td>Laparoscopic surgery</td>
</tr>
</tbody>
</table>

### Maximum Acceptable Risk for Selected Group

- Minimum acceptable weight-loss benefit
- Maximum acceptable mortality risk
- Percent judged better than no device

- 0.08% (95% CI 0.03 to 0.21)

### Relative contributions of device attributes

- Average utility of not getting a weight-loss device
- Type of operation
- Comorbidities: Reduce treatment dose / chance
- Expected Duration of weight loss (months)
- Recommended diet restrictions
- Chance of side effects requiring hospitalization
- Side effect duration (months)
- Total Body Weight loss (TBWL%)

Increase or decrease in the maximum level of acceptable risk contributed by each attribute (in %TBWL)
Recent Application at CDRH

• The Maestro System, a vagus nerve stimulator indicated as a weight-loss treatment was approved on January 14, 2015.

• The estimated proportion of patients that would choose Maestro was instrumental to its approval.

• This quantitative method can be adapted for other medical products, e.g., upper limb prostheses.

• This is only one of the methods available. For other methods, refer to the MDIC Catalog of Methods.

http://mdic.org/pcbr/
Patient Engagement
Patient Engagement Activities

• CDRH town hall
• Regulatory review division meetings with patient groups
• Site visits
• Research workshop
Patient Engagement Advisory Committee

• To help assure the needs and experiences of patients are incorporated into our work, the PEAC will:

1. Advise CDRH on ways to include and foster participation of patients where appropriate throughout the total product lifecycle

2. Advise CDRH on patient perspectives about current and new approaches or policies for integrating patient input in regulatory decision-making

3. Serve as a resource to CDRH as a body of experts in patient experience, needs, and the activities of the patient community

• Inaugural Meeting in 2017
Questions
MDIC Framework and FDA CDRH Draft Patient Preference Guidance

www.mdic.org/PCBR