FDA Perspective on Patient Preference Information

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FDA/CERSI PPI Workshop
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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

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Evolution of the Role of the Patient

Traditional Medicine: Provider-led treatment decision-making

Emerging Diseases: Patient advocacy for availability of and access to new treatments

The Internet: Patient empowerment through information

The Future Today: Patient-Provider partnership in treatment decision-making

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Patient Preference

- Patient preferences are defined as qualitative or quantitative assessments of the relative desirability or acceptability to patients of specified alternatives or choices among outcomes or other attributes that differ among alternative health interventions.
- Relevant preferences of care-partners (e.g., parents) and health care professionals may also be considered.

How is PPI different from PRO?

- **Patient-reported outcome (PRO)** is any report of the status of a patient’s health condition that comes directly from the patient, without interpretation of the patient’s response by a clinician or anyone else.
- PRO instruments are designed to measure a patient’s perceptions of health status before, during, and after therapy.
- Patient preference studies measure what specified type of therapy or attributes of a given therapeutic or diagnostic strategy a patient might prefer.

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## PPI Framework 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>
</tr>
</thead>
<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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<tr>
<td>2. Understand what matters most to patients about their disease or treatment</td>
<td>2. Inform performance goal</td>
<td>2. Current treatment options</td>
<td>2. Communicate benefit-risk information to patients</td>
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<tr>
<td></td>
<td></td>
<td>3. Patient perspective on benefit-risk tradeoffs</td>
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Rare pediatric cancer case study          Neurodegenerative case study
Preference Sensitive Decisions for Disease Areas

• PPI may be particularly useful when diseases are “preference sensitive”

• Patient decisions regarding treatment options are preference sensitive when:
  - multiple treatment options exist and there is no option that is clearly superior for all patients;
  - when the evidence supporting one option over others is considerably uncertain or variable; and/or
  - patients’ views about the most important benefits and acceptable risks of a technology vary considerably within a population, or differ from those of healthcare professionals.
Preference Sensitive Decisions for Products

• Is a decision preference sensitive?
• Does the medical product:
  - Have a direct patient interface?
  - Intend to yield significant health and appearance benefits?
  - Intend to directly affect health-related quality of life?
  - Have certain life-saving but high-risk characteristics?
  - Fill an unmet medical need or treat a rare disease or condition?
  - Offer alternative benefits to those already marketed?
  - Represent novel technology?
• Not all decisions are preference sensitive
Recommended Qualities of Patient Preference Studies

Well-designed and conducted patient preference studies can provide valid scientific evidence regarding patients’ risk tolerance and perspective on benefit.

A. All about Patients
   • Patient Centeredness
   • Sample Representativeness
   • Capturing Heterogeneous Patient Preferences
   • Comprehension by Study Participants

B. Good Study Design
   • Established Good Research Practices
   • Effective Benefit-Risk Communication
   • Minimal Cognitive Bias
   • Relevance

C. Good Study Conduct and Analysis
   • Study Conduct
   • Logical Soundness
   • Robustness of Analysis of Results

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# Qualities: All about Patients

## Patient Centeredness
- Patients are the focus of the study
- Should measure the preferences and perspectives of well-informed patients

## Representativeness of the Sample and Generalizability of Results
- Should measure preferences of a representative sample of adequate size so that the study results can be reasonably generalized to the population of interest

## Capturing Heterogeneity of Patients’ Preferences
- Patients’ preferences may be heterogeneous even among those with the same disease or condition
- Should reflect the preferences of patients from the full spectrum of disease for which the device is intended to be used

## Comprehension by Study Participants
- Ensure that study participants fully understand the harm, risk, benefit, uncertainty, and other medical information being communicated to them
Established Good Research Practices by Recognized Professional Organizations

- Quality of a study may be established if it follows guidelines for good research practices established by a recognized professional organization

Effective Communication of Benefit, Harm, Risk, and Uncertainty

- Reduce uncertainty caused by health numeracy
  - Avoid solely verbal descriptions of uncertainty; Use multiple formats simultaneously
  - Pretest the communication format

Minimal Cognitive Bias

- Minimize cognitive biases such as framing, anchoring, simplifying heuristics, or ordering effect

Relevance

- Inclusion and omission of harm, risk, benefit, and uncertainty should be well justified
- Relevance of specific endpoints to potential clinical outcomes should be clearly communicated to properly elicit preference
# Qualities: Study Conduct and Analysis

## Study Conduct
- Compliance of research staff and study participants with the study protocol

## Logical Soundness
- Data should include internal-validity tests of logic and consistency
- Verified for conformity with logic and consistency

## Robustness of Analysis of Results
- Sources of uncertainty
- Sensitivity analysis

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Recommendations for PPI Collection

• Talk to FDA early and often to make sure
  – The study asks a relevant research question and includes the attributes/levels of regulatory interest
  – Ranges of levels cover results observed in clinical study

• Choose an appropriate study design
  – # of interested attribute: Single-attribute (e.g., threshold technique) vs multi-attribute (e.g., DCE, BWS) methods
  – Comparator(s)

• Stratified randomization for balanced subgroups to capture preference heterogeneity

• Encourage data quality assessment plan

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Recommendations for PPI Documentation

• Development of survey instrument
  – Justification for the chosen method
  – Attribution/level generation & selection process

• Pre-test document as critical evidence to show respondents understand questions and can finish the survey

• Specify subgroups prospectively and stratified randomization for balanced subgroups to capture preference heterogeneity

• Encourage data quality assessment plan
General Steps to Measure Preferences

• Different methods, the same questions:
  – Which one would you prefer and how important is it?

• Glossary
  – Attribute: Benefits, risks, and other considerations
  – Levels: Values or categories that attributes may take (e.g., size of benefit, frequency of SAEs, device placement procedures)

• Steps (simplified)
  – Qualitative:
    • Rank outcomes or measure benefit-risk tradeoff preference?
    • Determine attributes of interest (patients, sponsors, clinicians, FDA)
    • Design survey instrument and pretest it with patients
  – Quantitative:
    • Develop experimental design and specify analysis plan
    • Analyze collected data and document study results

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Innovation from Patients for Patients

Collaboration is key to building this field

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Thank You

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FDA/CBER Perspective on Patient Preference Information

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Disclaimer:
‘This is an informal communication and represents my own best judgment. This presentation does not bind or obligate FDA.’
Examples of source of patient input in regulatory setting

| Input from a patient representative or from a patient during open public hearing at advisory committee meeting |
| Patient input such as comments & narrative submitted to FDA by the patient group |
| Patient brought by a sponsor to an FDA-sponsor review meeting |
| Patient-Reported Outcomes (PRO) |
| Patient Preference Information (PPI) |
**Examples of source of patient input in regulatory setting**

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CBER’s Science of Patient Input (SPI) Initiative

- Scientifically valid, qualitative and quantitative methods for capturing patient perspective information such as **PRO & PPI** on the:
  - Benefits and risks of medical products, and
  - Incorporating this information into review and regulatory decision-making
- Supports Agency efforts to more systematically capture and incorporate the patient perspective into our regulatory framework
CBER’s Science of Patient Input (SPI) Initiative

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- Supports Agency efforts to more systematically capture and incorporate the patient perspective into our regulatory framework
- Current focus:
  - Building internal review capacity and expertise
  - Collaborating with our colleagues in other FDA centers & external stakeholders
  - Exploring existing and new ways to effectively integrate PPI into our regulatory framework
  - Tracking our experience to inform continuous improvement of the science
Patient preference is elicited in clinical setting but use in regulatory context is new

<table>
<thead>
<tr>
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<th>Clinical setting</th>
<th>Regulatory setting</th>
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<tr>
<td><strong>Decision context</strong></td>
<td>• Individual</td>
<td>• Representative sample of target population</td>
</tr>
<tr>
<td><strong>Method &amp; scientific rigoristic</strong></td>
<td>• Qualitative</td>
<td>• Qualitative and/or quantitative</td>
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<td>• Rely on clinician knowledge &amp; judgment</td>
<td>• Rigorous method &amp; meet regulatory standard</td>
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<td><strong>Preference-sensitive condition</strong></td>
<td>• Existing therapies (e.g. Symptom management vs curative)</td>
<td>• Experimental therapy (e.g. Therapy X with potential for cure but significant adverse effects)</td>
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<td>• High risk &amp; high efficacy</td>
<td>• High uncertainty &amp; high stakes</td>
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<td><strong>Result</strong></td>
<td>• Qualitative &amp; employ in the context of shared-decision making</td>
<td>• Quantitative &amp; inform benefit-risk analysis</td>
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What resources are available?

Notable Initiative 2012-
• CDER/CBER PFDD meetings
• CDRH/CBER PPI guidance

Example Application 2015-
• FDA CDRH/RTI obesity
• EMA cancer patients study
• Industry SC vs IV rituximab

ICH Format & Structure of B-R
• ISPOR Conjoint Analysis

Incorporating Patient Preferences Into Drug Development and Regulatory Decision Making: Results From a Quantitative Pilot Study With Cancer Patients, Carers, and Regulators

Preference for subcutaneous or intravenous administration of rituximab among patients with untreated CD20+ diffuse large B-cell lymphoma or follicular lymphoma: results from a prospective, randomized, open-label, crossover study (PrefNab)
How to overcome some challenges?

<table>
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<th>Challenges</th>
<th>What we expect from CERSI workshop?</th>
</tr>
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</table>
| Defining benefit and risk attributes for eliciting preference   | • Method of attributes selection  
| for eliciting preference while we know less in pre-market setting| • Scope of PPI at various stage of medical product development  
|                                                                 | • Managing expectation & status of the science                                                |
| Conducting scientifically valid PPI studies                     | • Discussion on how to minimize bias  
|                                                                 | • Choice of valid method  
|                                                                 | • Ideas and collaboration to generate best practice documents                                |
| Generalizing PPI studies                                       | • Discuss preference heterogeneity & sample size  
|                                                                 | • Good survey conduct & sampling practices  
|                                                                 | • Good statistical analysis                                                                  |
| Reviewing PPI submission and incorporating in regulatory        | • Building Capacity  
| decisions                                                        | • Continuous collaboration to advance methods, consensus on definition & scope               |
Thank you!

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