Advancing Use of Patient Preference Information as Scientific Evidence in Medical Product Evaluation
Day 2

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Day 1 Sessions (Yesterday)

- Fundamental concepts and regulatory context of PPI to support medical product development and evaluation
  - Framework for how PPI can be used in regulatory decision making
- Scientific Fundamentals of PPI studies
  - Introducing the science behind patient preference studies
- Discussion of in-depth case studies
  - Two hypothetical case studies re: collecting and using of PPI
  - Case study 1: pediatric cancer/rare disease
  - Case study 2:neurological degenerative disease

Day 2 Sessions (Today)

- CDRH Preference Sensitive Areas for Discussion: Diseases and conditions where patient preference studies could be useful
  - What makes a topic preference sensitive; conditions when decision making might be enhanced by PPI
- Capacity building and sustainability
  - Identifying needs in building capacity for conducting and assessing PPI studies, including best practices

Regulatory Context for Use of PPI to support regulatory decision making

- PPI may be particularly useful in evaluating a device's benefit-risk profile when patient decisions are "preference sensitive."* Patient decisions regarding treatment options are preference sensitive when:
  1. multiple treatment options exist and there is no option that is clearly superior for all patients;
  2. when the evidence supporting one option over others is considerably uncertain or variable; and/or
  3. 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.

* *Patient Preference Information –Voluntary Submission, Review in Premarket Approval Applications, Humanitarian Device Exemption Applications, and De Novo Requests, and Inclusion in Decision Summaries and Device Labeling*; Guidance for Industry et al. 2016

https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM446680.pdf

What is needed to pose specific alternatives or choices to patients?

Patient preference relevant:

- Specific measures of effectiveness (e.g., specific change in symptoms, functioning, or other measures) patient would associate with change in disease state.
- Specific types of associated safety risks, including severity and relative frequency that patient can understand and evaluate
- Other attributes that might matter to the patient and to product developers

Regulatory decision relevance:

- Performance attributes included in studies reflect features of new medical products submitted for regulatory review

Information State ?

For Researchers		Have obtained a good understanding of patient perspective on their disease, and treatment burden and risks	
		No	Yes
Have developed a good understanding of specific benefits offered, burdens associated, and risks posed by proposed intervention(s)	No	PPI study not likely to be the best approach at this stage	PPI study value* a function of how well posited attributes/ endpoints correspond to attributes actually delivered by medical product developed by sponsor
	Yes	PPI study value* a function of how well the known and studied product attributes correspond to what matters most to patients	PPI study positioned to examine patient preferences related to medical product attributes that are identified by and matter most to patients
For Patients	Ideally • Posited benefit attributes of the proposed intervention(s) are familiar and very meaningful • Posited burdens and risks of the proposed intervention(s) are familiar; may already have been experienced by patients		

* For the purpose of informing regulatory evaluation of medical product

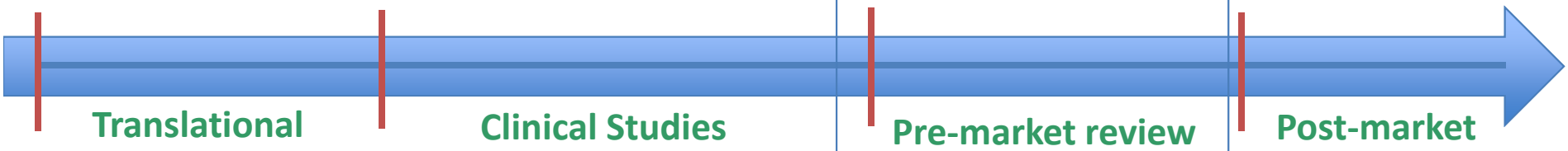
Further integrating patient perspective into medical product development and decision making

What matters most to patients and how can it be measured?

What patient outcomes should we measure? How can trials be more patient-friendly?

How can Clinical Outcome Assessments (COAs) & elicited Patient Preference Information (PPI) be best integrated into FDA benefit risk determination?

How can this data be best communicated? How can patient data be generated in the post-market setting?



Considerations for Use of PPI

- PPI involves preference elicitation tasks.
  - Participants asked to indicate preference ordering or acceptable benefit risk tradeoffs that require judgment and choices that include significant (hypothetical) risks and uncertainty—requires significant cognitive effort

- Human judgment and decision-making under uncertainty employs heuristics that yield biases
  - Perceptions of risk can be greatly skewed by various forms of **availability bias** for example:
    - **Salience**--Studies by Slovic, Fischhoff and Lichtenstein found participants judged accidents to cause as many deaths as disease—although disease was 16 times more likely
    - **It won't happen to me**—people judge their risk of a bad outcome to be much lower than average---especially if it has never happened to them before.
    - **Overconfidence** in judgments (due to inability to think of reasons why you could be wrong, and failure to seek contradictory evidence)
  - **Framing effects**—Study participants exhibited risk-seeking behavior when offered a choice of outcomes characterized as losses and exhibited risk aversion when offered a choice of outcomes characterized as gains
    - **Omission of key information and unstated assumptions** related to probabilities or outcomes will also affect perception of the options.

Other Considerations

- Skill and perspective of investigator conducting the work
  - Experience; Potential for motivational or cognitive bias
- Potential for wide practice variability and study quality
  - Medical literature includes examples where surveyed preference elicitation studies apply methods inappropriately or find substantial heterogeneity in preferences among studied patient populations, or fail to include critical subpopulations (e.g., young children, adolescents)
  - The same can be true for Clinical Outcome Assessment work
- Quality and reliability of study data are critical to delivering value from the investment of scarce resources. FDA guidance will help.
- Approaches could include
  - Share findings: publish; make good work and good data collection tools publicly available for others to use or build on; contribute to establishing standards

Mitigating these and other challenges: Potential strategies and opportunities for further methodological research

Challenge:	**PPI involves preference elicitation tasks. This may involve potentially significant mental effort.**
Potential strategies:	- Review evidence (e.g., pretest results) supporting the instrument to be cognitively feasible including among older, sicker, lower literacy, lower numeracy, other subpopulations - Limit number of attributes and levels, especially attributes with uncertainty - Limit length of survey instruments - Focus on cognitive debriefing, understandability.
Challenge:	**Human judgment (including risk perception) and decision-making under uncertainty employ heuristics that yield biases**
Potential strategies:	- Conduct good qualitative research to understand the way people think about their choices - Use multi-format presentation of probability and other quantitative concepts, including visual/conceptual depictions - Conduct post survey comprehension tests respondent understanding - Conduct tutorial and mini quiz for uncertainty concept before tradeoff questions

Mitigating these and other considerations: Potential strategies and opportunities for further methodological research (cont.)

Challenge:	**Literature on influence of framing effects on risk preference**
Potential Strategies	- Examine recruitment materials to assure they maintain neutrality in choices - Examine PPI study design to assure focus on trade-offs between choices not promotion of one option over others - Focus on pretest which can indicate framing effects - Examine and test for potential framing effect and other potential cognitive biases identified in existing literature during instrument development stage - Describe control and test interventions; their benefits and risks should be as neutral and balanced as possible
Challenge:	**Potential for wide practice variability & study quality**
Potential Strategies:	- Conduct methodological research to refine approaches and clarify best practices - Need to engage with FDA to identify the appropriate research question relevant to decision in hand, and to identify methods that can adequately answer the research question of interest. - Develop and publish materials (research by the FDA or through collaborations) to increase knowledge of best practices - Need to increase capacity and capability in research community, industry and regulatory agency

We look forward to Day 2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