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*Thank you for your patience while we
register all of today's participants.*

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Patient Preference Information – Voluntary Submission, Review in PMAs, HDE Applications, and De Novo Requests and Inclusion in Decision Summaries and Device Labeling: Final Guidance

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Agenda

- Provide context and overview of Patient Preference Information Final Guidance
- Describe key updates to the Benefit-Risk worksheet in the “Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approval and De Novo Classifications” Guidance
- Q&A

History of the Patient Preference Initiative and Guidance Development

CONTEXT AND SCOPE

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

Patient preferences informing regulatory decisions

Factors to Consider for Benefit – Risk Determinations Medical Device Premarket Approval and De Novo Classifications

Patient perspective on risk and perspective on benefit:

*“if risks are identifiable and definable, **risk tolerance will vary among patients**, and this will affect individual patient decisions as to whether the risks are acceptable in exchange for a probable benefit. ... FDA recognizes that patient perspectives on benefits and risks **may reveal reasonable patients who are willing to tolerate a very high level of risk to achieve a probable benefit**, especially if that benefit results in an improvement in quality of life.”*

CDRH Strategic Priority 2016 – 2017

Partner with Patients



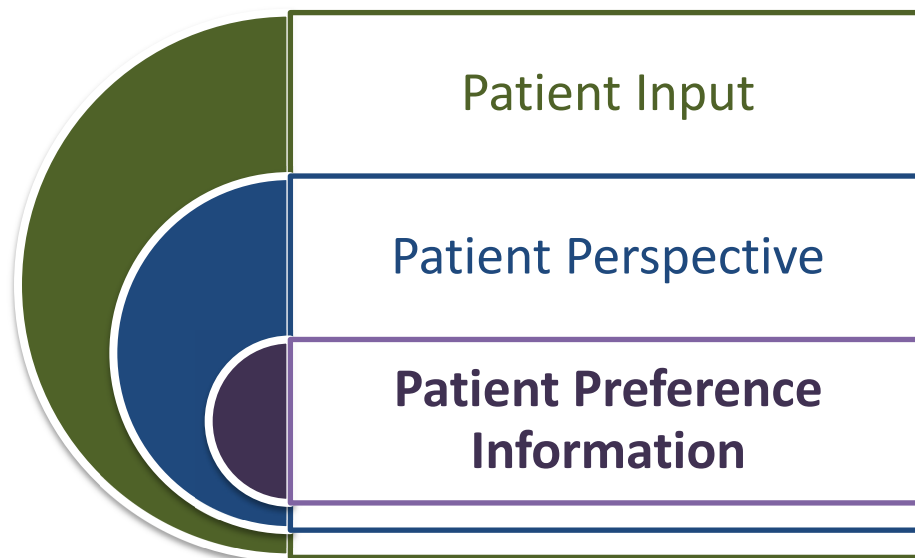
We interact with patients as partners and work together to advance the development and evaluation of innovative devices, and monitor the performance of marketed devices.

1. Promote a culture of meaningful patient engagement by facilitating CDRH interaction with patients.
2. Increase use and transparency of patient input as evidence in our decision-making.

Patient Input



- Patient input includes a range of information and perspectives
 - Anecdotal comments in correspondence to the FDA
 - Testimony at Advisory Committee Panel meetings
 - Patient opinions expressed publicly including through social media
 - Patient responses to qualitative *ad hoc* surveys
 - Quantitative measurements of patient-reported outcomes



Patient Perspectives

- Patient perspectives refer to a type of patient input
- Information relating to patients' experiences with a disease or condition and its management
- May be useful for:
 - better understanding the disease or condition and its impact on patients
 - identifying outcomes most important to patients
 - understanding benefit-risk tradeoffs for treatment



Patient Input

Patient Perspectives



What is Patient Preference Information (PPI)?

- For the purpose of this guidance, Patient Preference Information (PPI) is 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



What PPI Can Provide and How It Can Be Used

- PPI data can provide valuable information about:
 - Which benefits and risks are most important to affected patients
 - What benefit-risk tradeoffs are acceptable from the patient perspective
 - How do these patients think about these tradeoffs
 - Are there clinically-relevant subgroups of patients that would accept a particular benefit-risk profile and/or choose one treatment option over other alternatives
- Potential Uses of PPI:
 - Inform endpoints or effect size for regulatory studies
 - Inform subgroup considerations
 - Labeling changes / expanded indications
- Other potential uses outside regulatory context, such as shared medical decision-making.

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
- In contrast, patient preference studies measure what specified type of therapy or attributes of a given therapeutic or diagnostic strategy a patient might prefer



Highlights Objectives, Scope, and Guidance Sections

GUIDANCE OVERVIEW



Objectives

1. To encourage submission of PPI, if available, by sponsors or other stakeholders to FDA and to aid in FDA decision-making;
2. To outline recommended qualities of patient preference studies, which may result in valid scientific evidence;
3. To provide recommendations for collecting and submitting PPI to FDA; and,
4. To discuss FDA's inclusion of PPI in its decision summaries and provide recommendations for the inclusion of such information in device labeling.

Scope

- Explains concepts that sponsors and other stakeholders should consider when choosing to collect PPI, which may inform FDA's benefit-risk determinations in the premarket review of PMAs, HDE applications, and *de novo* requests.
- Discusses FDA's inclusion of PPI in its decision summaries and provides recommendations for the inclusion of such information in device labeling for certain devices.



PPI Submission to FDA is Voluntary



- PPI may not be relevant or appropriate for all device types.
- May be useful for sponsors to collect and submit such information where usage decisions by patients and health care professionals are preference-sensitive.
- Devices that could benefit from PPI include those with the following characteristics:
 - A direct patient interface,
 - Intended to yield significant health and appearance benefits,
 - Intended to directly affect health-related quality of life,
 - Certain life-saving but high-risk devices,
 - Developed to fill an unmet medical need or treat a rare disease or condition,
 - Offer alternative benefits to those already marketed; and,
 - A novel technology.

PPI as Valid Scientific Evidence

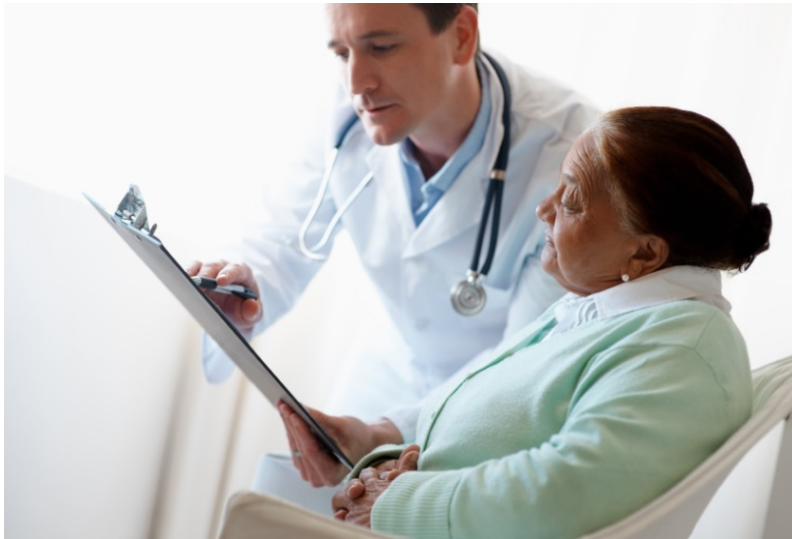
- FDA may consider submitted PPI along with other evidence from clinical and nonclinical testing when making benefit-risk determinations.
- This guidance does not change any review standards for safety or effectiveness.
- It provides recommendations relating to the voluntary collection of PPI that may be submitted for consideration as valid scientific evidence as part of FDA's benefit-risk assessment.



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. This may inform FDA’s evaluation of a device’s benefit-risk profile during the PMA, HDE application, and *de novo* request review processes.

- 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



Recommended Study Qualities: All about Patients

Patient Centeredness

- Patients are the focus of the study
- Studies should measure the preferences and perspectives of well-informed patients

Representativeness of the Sample and Generalizability of Results

- Studies should measure the 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' benefit-risk tradeoff preferences may be heterogeneous even among those with the same disease or condition
- Studies 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

Recommended Study Qualities: Good Study Design

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
- Example 1: Avoid solely verbal descriptions of uncertainty; Use multiple formats simultaneously
- Example 2: 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
- Useful to ensure some consistency among the benefits, harms, risks and other attributes
- Relevance of specific endpoints to potential clinical outcomes should be clearly communicated to patients to properly elicit preference

Recommended Study 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

Regulatory Considerations



- For studies submitted with other premarket review data, applicable regulations including IDE regulations in 21 CFR Part 812 must be followed.
- For studies done independent from a device clinical study, FDA generally considers the studies to be nonsignificant risk.
- Conditions of Approval
 - FDA may impose conditions of approval in certain PMA approvals, including where the Agency takes PPI into account to mitigate risk and facilitate use in patients for whom benefits are expected to outweigh risks.
 - FDA may require collection of postmarket evidence through a postmarket approval surveillance study for PMAs.

Submission of PPI to FDA

FDA encourages sponsors and other stakeholders to have early interactions with the relevant FDA review division if considering collecting and submitting PPI.

- Request an informational pre-submission meeting to discuss plans for designing or submitting a patient preference study
- Request participation from Martin.Ho@fda.hhs.gov and Anindita.Saha@fda.hhs.gov



Inclusion of PPI in Decision Summaries and Device Labeling



- When FDA considers patient preference studies in its consideration of a premarket submission, such studies generally are included in the **decision summary**
- Inclusion of PPI in FDA's public decision summaries can be helpful to health care professionals and patients in making health care decisions involving difficult benefit-risk tradeoffs or novel treatments
- PPI that is reviewed by FDA and supports FDA's approval or marketing authorization should also be described in the device labeling
 - It is important for the device product labeling to contain sufficient information about the benefits and risks of the treatment and diagnostic options under consideration (*Please see FDA Guidance: Labeling – Regulatory Requirements for Medical Devices (FDA 89-4203)*).

Examples and Resources

- CDRH Patient Preference Obesity Study
 - M. Ho, M. Gonzalez, H. Lerner, C. Neuland, J. Whang, M. McMurry-Heath, A. Hauber, and T. Irony. "Incorporating patient-preference evidence into regulatory decision making." *Surgical endoscopy*.29(10): 2984-2993
- Guidance for Industry and Food and Drug Administration Staff : Factors to Consider for Benefit – Risk Determinations in Medical Device Premarket Approval and De Novo Classifications
- Guidance on Medical Device Patient Labeling
- MDIC Patient-Centered Benefit Risk Project: A Framework for Incorporating Information on Patient Preferences Regarding Benefit and Risk into Regulatory Assessments of New Medical Technology (<http://mdic.org/pcbr>)



Summary of changes to the Benefit-Risk Guidance

UPDATING THE BENEFIT-RISK WORKSHEET

Changes to the Benefit-Risk Worksheet



- Updated the PMA and de novo Benefit-Risk Guidance for consistency with the terminology and concepts in the PPI Guidance
 - Section 4: Factors FDA Considers in Making Benefit-Risk Determinations
 - 4.3: Additional Factors in the Assessment of the Probable Benefits and Risks of Devices
- Addition of PPI in the worksheet that FDA staff uses to guide benefit-risk determinations of PMA and de novo requests
 - Patient perspective on risk and perspective on benefit
- PPI guidance and the Benefit-Risk guidance have a 60 day implementation period from the date of publication

Final Considerations



- Voluntary submission of PPI may be informative during benefit-risk determination.
- PPI may also be informative earlier in device development (e.g., to inform clinical study parameters such as endpoint selection and effect size).
- FDA encourages early interactions with FDA review staff if planning to design a PPI study or to submit PPI.
- Contact Martin.Ho@fda.hhs.gov and Anindita.Saha@fda.hhs.gov



Thank You



Questions?

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Slide Presentation, Transcript and Webinar Recording
will be available at:

<http://www.fda.gov/training/cdrhlearn>

Under Heading: How to Study and Market Your
Device; Sub-heading: Cross-Cutting Premarket Policy

