

Patient Preference Study Design – Qualitative Steps
First steps for sponsors initiating a patient preference study

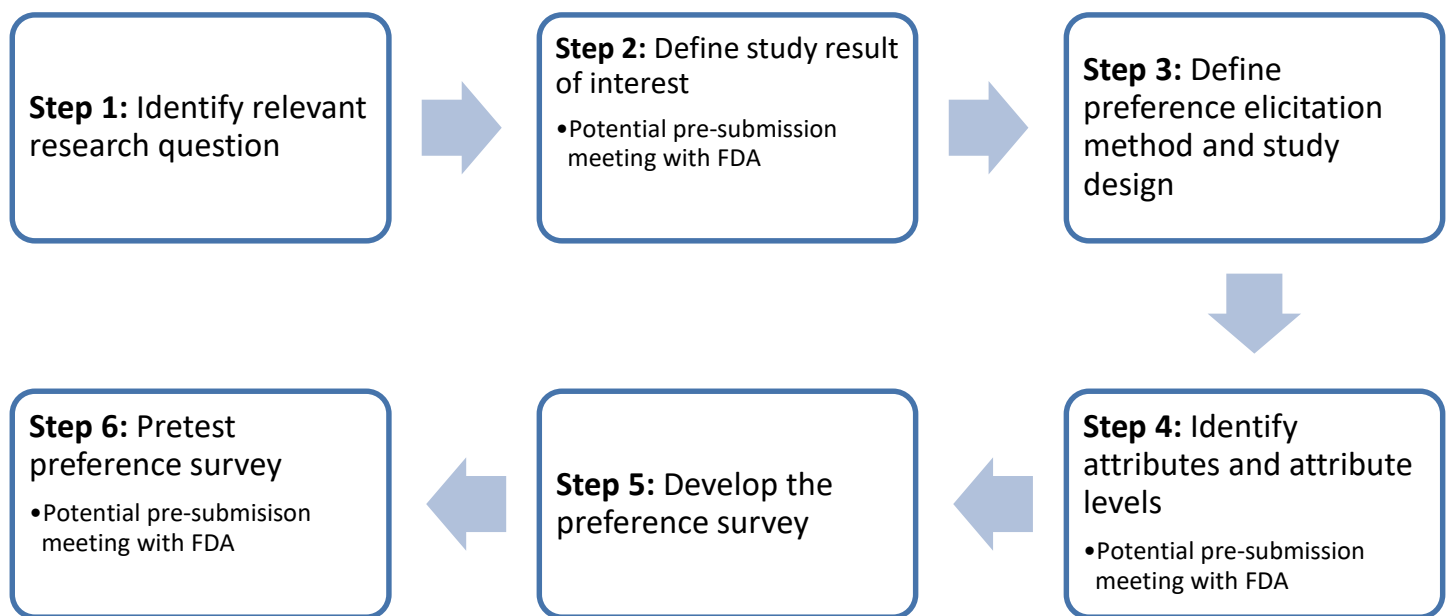
Reference: [FDA guidance on patient preference information](#) and [MDIC Patient-Centered Benefit-Risk Framework](#)

The FDA encourages early interaction, prior to any study design, for sponsors considering a patient preference study.

The MDIC report “A Framework for Incorporating Information on Patient Preferences Regarding Benefit and Risk into Regulatory Assessments of New Medical Technology” and the CDRH Guidance on Patient Preference offer valuable information on the reasons and factors to consider when contemplating the development of a patient preference study to be submitted as part of a regulatory submission. However, the Framework does not outline how to get started. This guide intends to help with those first steps. This guide only includes qualitative steps used to develop the preference survey, and does not include development of the preference study protocol or statistical analysis plan. These activities may occur subsequent to the qualitative steps for survey development, and questions about them could be included in the potential FDA pre-submission meetings outlined below.

Figure 1 presents a summary of the steps discussed in this document for the initiation of a patient preference study. These steps tackle specifically the development of a preference-elicitation instrument to be used to quantify patient preferences.

Figure 1. Summary of qualitative steps for preference survey development



Glossary:

- **Attribute:** Aspects by which desirability or acceptability of medical interventions are evaluated in a preference survey. Attributes include types of benefits and risks associated with medical interventions. Attributes may also include other clinical and nonclinical aspects that can influence desirability or acceptability of medical interventions.
- **Attribute Level:** Values or categories used to characterize the performance of a medical intervention under each attribute.

The following is additional detailed information on the steps outlined in Figure 1.

Step 1: Identify the research goal and relevant research question

A relevant research question should address a preference-sensitive decision that requires information from patients.

Some examples of research goals are the following:

- Label expansion
- Endpoint selection
- Informing the benefit-risk evaluation

Some examples of relevant research questions are the following:

- What benefit-risk tradeoffs are acceptable to patients?
- How does acceptance of benefit-risk tradeoffs vary in the target population?
- Which clinical trial outcomes are most important to patients?
- What would a patient-centered clinical trial endpoint be?
- Are there subgroups with decision-relevant differences in preferences?

Step 2: Define the study result of interest

The patient preference study result should directly address the relevant research question. The result may be used to inform the benefit-risk assessment or clinical trial design. Example results are presented in the table below.

Table 2. Example Study Results

Study Result	Addressed Research Question
Estimates of the minimum benefit required by patients to tolerate a given risk or the maximum risk tolerable to patients in exchange for given benefits	What benefit-risk tradeoffs are acceptable to patients?
Characterization of the distribution of preference estimates across respondents or the statistical significance of differences in preferences for patients in specific subgroups	How do acceptable of benefit-risk tradeoffs vary in the target population?
A ranked list of clinical trial outcomes	Which clinical trial outcomes are most important to patients?
List of current and potential clinical trial endpoints ranked based on the importance that patients ascribe to collecting information on them	What would a patient-centered clinical trial endpoint be?

Potential pre-submission with FDA: Review attributes and levels

Questions for the FDA might include:

- Would addressing this research question with a patient preference study be potentially informative for FDA decision making?
- Are the research question and study result framed appropriately for regulatory purposes?

Step 3: Define the patient preference elicitation method and the study design

The preference-elicitation method and the study design are defined to capture the result of interest. There is a variety of methods available to elicit patient preferences, each with particular assumptions and outputs. Thus, options may be reviewed from published work, e.g., [MDIC PCBR Framework](#) and/or discussed with a patient-preference researcher. For example, a specific aspect of the method that be considered includes:

- **Can the selected method accommodate the decision context of interest?** All preference-elicitation methods use respondents' decisions to infer preferences. The context of those decisions influences the outputs that can be obtained from each method and the interpretation of the results. For example, stated preference

methods elicit preferences from tradeoffs, which may be desirable in benefit-risk evaluations. On the other hand, methods that elicit preferences from tradeoffs may not be appropriate in situations where tradeoffs are not realistic.

Some questions that could be considered when defining the study design are the following:

- Should there be qualitative research or preliminary work done to inform the appropriate use of the preference method?
- What is the study population and how will that affect the feasible sample size?
- How can respondents be recruited to participate in the study?
- Can the preference survey be administered online?
- How long should the preference survey be, given patients' health limitations or issues with the implementation environment (e.g., is the survey administered at home, in a clinic before a medical appointment, or over the phone)?

Patient preference elicitation methods and study design are a topic of considerable discussion and research, so this step may be facilitated by a subject matter expert.

Step 4: Identify attributes and attribute levels

Develop a preliminary list of potential concepts for inclusion in the survey from a review of relevant literature and input from healthcare professionals and medical product developers. Patient-centered benefits may be defined more broadly than clinical outcome measures, and may include concepts such as convenience. If applicable, add to, refine, and prioritize these concepts by engaging with patients and care-partners. A variety of qualitative and quantitative research methods may be leveraged for this step (e.g., “structured-weighting” methods in [MDIC PCBR Framework Catalog](#)).

Select levels that attributes may take, based on existing literature, clinical data, and/or input from experts with a thorough understanding of the medical product. If feasible, the units of the levels should correspond to the ones used to measure these attributes in clinical practice or clinical trials.

Attributes and levels should be meaningful to patients and relevant to the research question and result of interest. If the result is intended to inform benefit-risk assessments, the attribute levels should span the range of possible values relevant to that assessment. Extrapolation of preference values may not be appropriate.

Potential pre-submission with FDA: Review attributes and levels

Questions for the FDA might include:

- What are the benefit-risk profiles of comparator(s) of interest, if appropriate?
- Have all relevant benefits and risks, including those that are relevant for FDA decision making, been included as attributes in the survey?
- Do the selected levels adequately span the range of possible values that may be relevant to FDA decision making (e.g., do the ranges cover the results reported in the pivotal study)?

Step 5: Develop the preference survey

Good research practices and consensus guidelines, when available, should be used in developing the survey instrument. The survey instrument development process should involve patients, to support patient-centeredness of the study. Patients' health literacy and numeracy should be taken into account, there should be mitigation measures for any potential cognitive biases, and the survey should not be too cognitively demanding for the intended population. The survey may include questions that allow a meaningful characterization of the sample (e.g., respondents' disease and treatment experience).

Step 6: Pretest the survey and refine terms and definitions

Following development of a draft survey, pretest the survey with patients to ensure it is understood as intended and that the cognitive burden is acceptable. Include open-ended probing to ensure that no relevant attributes were missed. Ensure educational background, socioeconomic status, geographic location, and any other relevant factors for survey comprehension are considered. Refine the survey design and language based on the pretest.

Potential pre-submission update with FDA: Review updated survey

Questions for the FDA might include:

- Do pretest results support that the instrument is comprehensible and acceptable to the full range of indicated patients?
- Is the survey appropriately designed so that the results may be informative for regulatory decision making or trial design?
- Are there any prospectively specified subgroups that would be informative for regulatory decision making?
- Is the planned patient preference study population adequately representative of and generalizable to the patient population of interest for regulatory decision making?