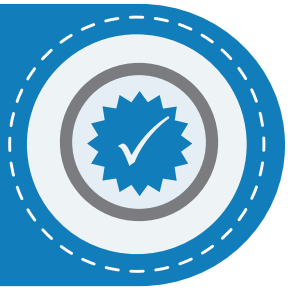
U.S. FOOD & DRUG ADMINISTRATION

Patient-Focused Drug Development: Selecting, Developing, or Modifying Fit-for-Purpose Clinical Outcome Assessments

Draft Guidance

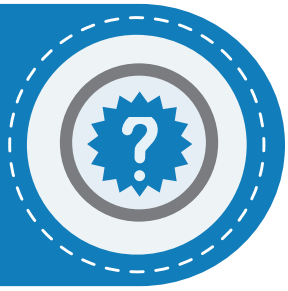
What is recommended in the guidance?

This guidance provides recommended approaches for selecting, modifying, developing, and validating measurements in clinical trials that evaluate outcomes important to patients.



Why is this guidance important?

This guidance helps ensure that clinical outcome assessments (COAs) used during medical product development measure what matters to patients; are clear about what was measured; appropriately evaluate the effectiveness, tolerability, and safety of treatments; and avoid misleading claims.



Clinical Outcome Assessment Key Points

A COA IS A MEASURE THAT DESCRIBES HOW A PATIENT FEELS, FUNCTIONS, OR SURVIVES. THERE ARE FOUR TYPES OF COAS:

- Patient-reported outcome (PRO) measures
- Observer-reported outcome (ObsRO) measures
- Clinician-reported outcome (ClinRO) measures
- Performance outcome (PerfO) measures

A CONCEPT OF INTEREST AND THE CONTEXT OF USE SHOULD BE EXPLICITLY DEFINED

- Concept of Interest is the aspect of an individual's experience or clinical, biological, physical, or functional state that the COA is intended to capture (reflect).
- Context of Use should clearly specify the way COA scores will be used as the basis for an endpoint, including the interpretation of the endpoint results in a medical product development program.

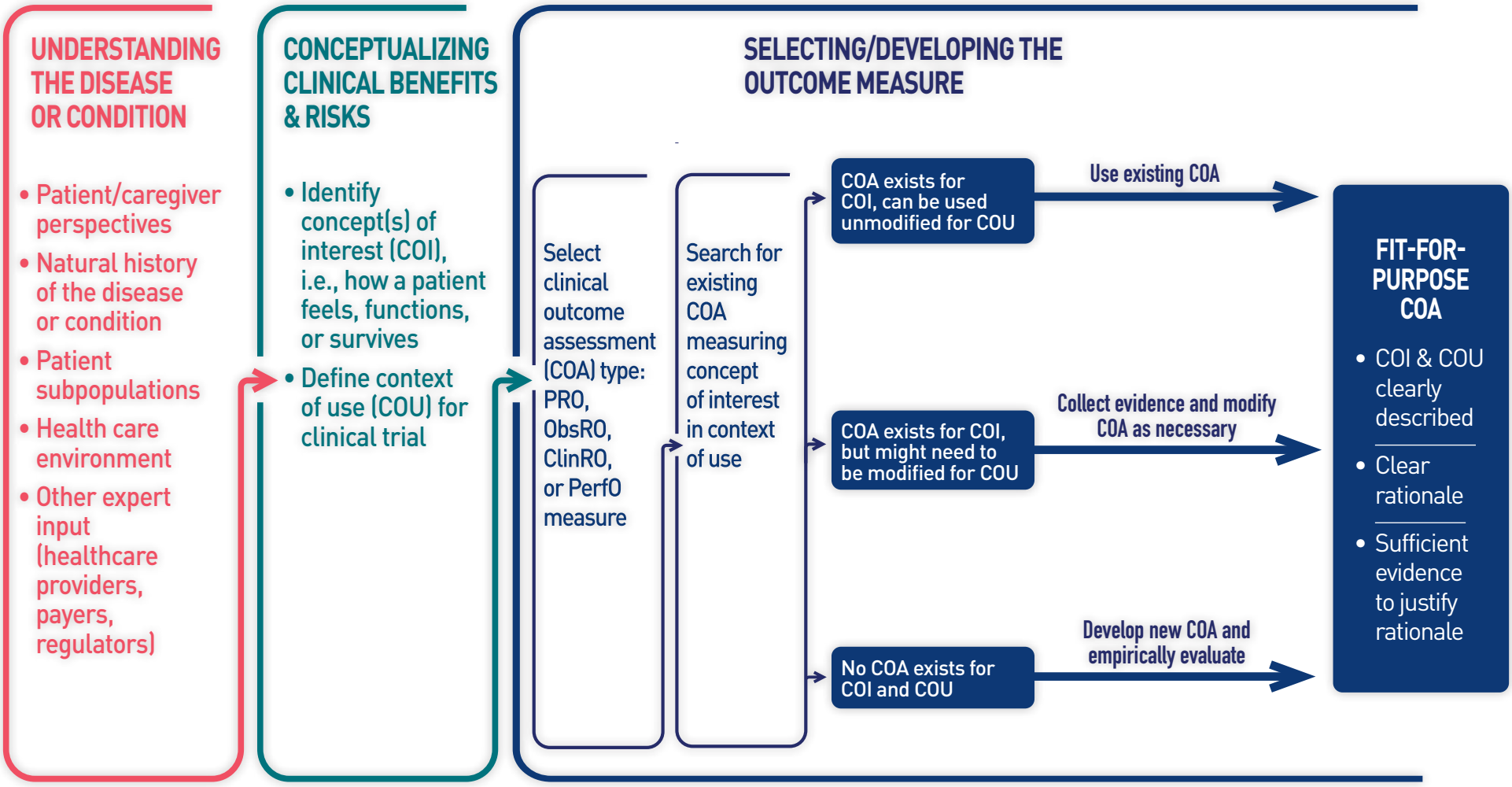
COA SHOULD BE FIT FOR PURPOSE

A COA is considered fit for purpose when "the level of validation associated with a medical product development tool is sufficient to support its context of use" (BEST (Biomarkers, Endpoints and Other Tools) Resource, 2016).

Guidance Snapshots are a communication tool and are not a substitute for the guidance document.
To learn more about Patient-Focused Drug Development, read the guidance:
http://www.fda.gov/regulatory-information/search-fda-guidance-documents/patient-focused-drug-development-selecting-developing-or-modifying-fit-purpose-clinical-outcome

Roadmap for Developing a Fit-For-Purpose, Patient-Focused COA

This is a general roadmap for developing fit-for-purpose, patient-focused COAs in clinical trials. Sponsors and COA developers are not required to use this approach, and it may not fit every development program. FDA recommends sponsors seek FDA input as early as possible and throughout medical product development to ensure COAs are fit-for-purpose for the intended context of use.



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Eight Evidence-Based Considerations for Supporting a COA as Fit-for-Purpose

Evidence collected in support of the use of a COA should support the rationale that explains how and why the specific COA is expected or intended to work. This table lists eight considerations that should be included in the rationale and supporting evidence or justification section of submissions to FDA. It is important for FDA to understand each part of a sponsor's rationale and the evidence being offered in support of each part. The considerations listed below are likely but not necessarily needed in the rationale for a specific COA, concept of interest, and context of use. Each rationale can be tailored to the specific situation.

A The reason for the choice of type of COA (i.e., PRO, ObsRO, ClinRO, or PerfO) selected to assess the concept of interest is clear.

B All important aspects of the concept of interest are covered by the chosen COA.

C Respondents understand the instructions and items/tasks of the measure as intended by the measure developer.

D Scores of the COA are not be overly influenced by processes/concepts that are not part of the concept of interest.

E The method of scoring responses to the COA is appropriate for assessing the concept of interest.

F Scores from the COA correspond to the specific health experience(s) the patient has related to the concept of interest.

G Scores are sufficiently sensitive to reflect clinically meaningful changes within patients over time in the concept of interest within the context of use.

H Differences in COA scores are interpreted and communicated clearly in terms of the expected impact on patients' experiences.

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What is the difference between a COA, a COA score, and an endpoint?

This guidance differentiates a COA, from a COA score, and an endpoint in the following ways:

COA

A COA is a measure that describes or reflects how a patient feels, functions, or survives and includes any instructions, administration materials, content, formatting, and scoring rules.

COA SCORE

A COA score refers to any numeric or rated values generated by a COA through a standardized process. A COA might produce more than one type of **score**, especially if the COA is designed to measure more than one concept.

ENDPOINT

An endpoint is a precisely defined variable intended to reflect an outcome of interest that is statistically analyzed to address a particular research question (e.g., mean COA Score at 12 weeks post-randomization).

Medical Product Timeline – When to Apply the Guidance Recommendations?

During clinical development: When a sponsor is developing or significantly modifying a COA, FDA encourages sponsors to request a meeting with FDA to discuss plans early in the development process. Earlier trials represent an opportune time to evaluate measurement properties of COAs, and sponsors are encouraged to include prospectively planned analyses to inform subsequent trials. If this is not a feasible option, FDA recommends conducting a standalone observational study prior to the initiation of a registration trial(s) to aid in the development of a fit-for-purpose COA measure(s).

Guidance Recap Podcast – Hear Highlights Straight from FDA Staff

Speakers: David Reasner, PhD, Director of the Division of Clinical Outcome and Laura Lee Johnson, PhD, Director for the Division of Biometrics III.

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Share your thoughts on the revised draft guidance:

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https://www.fda.gov/regulatory-information/search-fda-guidance-documents/patient-focused-drug-development-selecting-developing-or-modifying-fit-purpose-clinical-outcome.gov

To see additional Guidance Snapshots, check out the pilot program:
https://www.fda.gov/drugs/guidances-drugs/guidance-snapshot-pilot