Performance Outcome Assessments: Identifying Endpoints that are Meaningful and Measurable

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Patient-Reported Outcome (PRO) Consortium

Formed in 2008 by the Critical Path Institute (C-Path) in cooperation with FDA and the pharma industry

- **Membership**
  - 27 members (pharmaceutical firms)

- **Non-Voting Participants**
  - Representatives of governmental agencies (FDA, NIH)
  - Clinical consultants, patients, academic researchers, and CROs partnering in the development of the PRO measures and other COA tools

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To establish and maintain a collaborative framework with appropriate stakeholders for the **qualification** of patient-reported outcome (PRO) instruments and other clinical outcome assessment (COA) tools that will be publicly available for use in clinical trials **where COA-based endpoints are used to support product labeling claims**
Main categories

- **Sensory function** (e.g., Snellen eye chart)

- **Cognitive function/Cognition** (e.g., ADAS-Cog, Symbol Digit Modalities Test [SDMT])

- **Physical function** (e.g., Timed 25-Foot Walk, Six-minute Walk Test)
Important Considerations when Designing PerfO-based Endpoints

- Identify an aspect of the disease or illness that if relieved, improved, or avoided would be **meaningful** to patients

- Select or develop an assessment tool that measures it in a valid and reliable way (and is feasible within the context of a multinational clinical trial)

- Determine the amount of change on the assessment tool that is **meaningful** to patients and reflects a treatment benefit
Target population: Adults with a clinical diagnosis of mild cognitive impairment (MCI) due to Alzheimer’s disease

MCI due to Alzheimer’s disease (AD) is the symptomatic, predementia stage of AD, during which cognition and daily functioning become impaired, particularly an individual’s ability to engage in day-to-day tasks such as paying bills, communication, preparing meals, or shopping.
**Meaningful aspect of the disease:** Limitations in day-to-day functioning. Limitations in day-to-day function can compromise an individual’s ability to remain functionally independent.

**Type of COA:** Due to progressive cognitive decline, self-report (PRO measure) is not sufficiently valid and reliable; informant-report (ObsRO assessment) is suboptimal due to various factors that can lead to response bias; and clinician-report (ClinRO assessment) is not feasible.
Hence, a performance outcome (PerfO) assessment was deemed appropriate.

Limitations in day-to-day function can be demonstrated by a clinic-based assessment of the performance of tasks (e.g., role play exercises involving handling finances, shopping, communication, or using public transportation) that simulate key real-world activities of day-to-day living.
**COA Qualification Goal:** To obtain FDA qualification of a PerfO assessment tool that measures an individual’s capacity to perform key tasks of daily living (i.e., day-to-day functioning).

**Role in endpoint hierarchy:** Used for deriving co-primary endpoint (with cognition) to establish treatment benefit. To evaluate the efficacy of new treatments targeted for patients with MCI due to AD, it is critical to assess cognition/cognitive function as well as the impact of cognitive changes on a person’s daily life.
Select a PerfO assessment tool: UCSD Performance-based Skills Assessment (UPSA)

- Developed to assess everyday functioning in persons with schizophrenia (Patterson et al. 2001).
- Areas of living skills are assessed through the completion of tasks that require subjects to use props to perform activities that reflect functioning in their daily lives.
- The five areas in the initial version of UPSA are
  - shopping/meal preparation, finances, communication, transportation, and organization and planning.
Determine meaningful change on the assessment tool:

TBD
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- Determine the amount of change on the assessment tool that is meaningful to patients and reflects a treatment benefit.
Thank You

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