# Cognitive Dysfunction in MDD: A Regulatory Perspective

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# Historical Perspective

- "Diminished ability to think or concentrate…" is one of the core symptoms of Major Depressive Disorder
- General assumption that, if depression improves, cognition should improve
- Thus, treatment of cognitive dysfunction in MDD considered pseudospecific

# However…

- Recent data suggests this may not be the case.
  - Subjective and objective
  - Associated with illness severity
  - Still present even in “remitters”

# Regulatory Questions

- How should we define cognitive dysfunction in MDD?
- What is the best way to assess it?
- How do we quantify improvement?
- What kind of trial might result in a labeling claim?

# Defining Cognitive Dysfunction

- Subjective, objective, or both?
- What domain is impaired?

- It is important to specifically define the study population, and to provide scientific rationale examining a particular domain.

# Assessment

- FDA has not yet endorsed or rejected any particular cognitive assessment for MDD trials.
- Will likely involve the Study Endpoints and Labeling Development Team

# Quantifying Improvement

- Most important question:

  How do you define a clinically meaningful change?

# Trial Design

- Strong preference for an active comparator
- Monotherapy vs. adjunctive
- Enrichment strategies likely useful
- Discuss design with FDA