# Regulatory View on Use of Reward Processing in Patient Segmentation and as a Marker for Treatment Response

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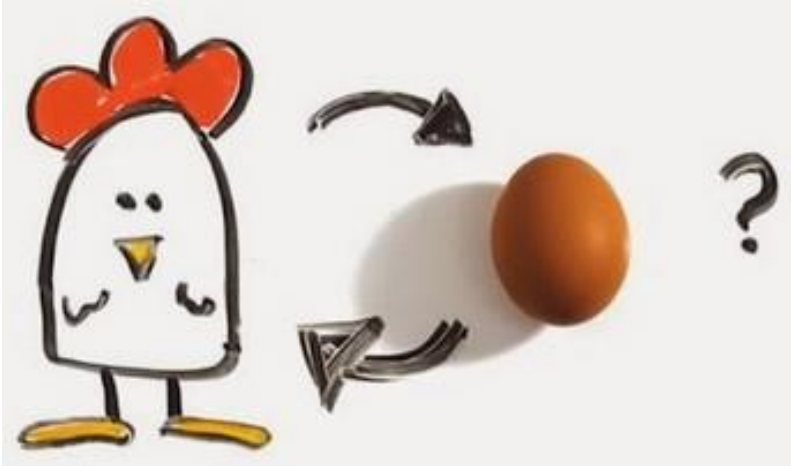
# Reward Processing Tasks in Clinical Trials

- Potential probe for apathy, anhedonia, or negative symptoms
- More closely linked to pathophysiology
- Clinical relevance
- Can reward processing task ever be a primary endpoint?

# Anhedonia, Apathy, Negative Symptoms

- As clinical constructs, these are qualitatively different
- How similar is the underlying circuitry?



# Understanding Pathophysiology

- Goal: Move from subjective/descriptive constructs to pathophysiology
  - "Activation" (e.g., BOLD signal) is a gross phenomenon
  - Underlying cascade of events not characterized
  - But, closer to pathophysiology than rating scales

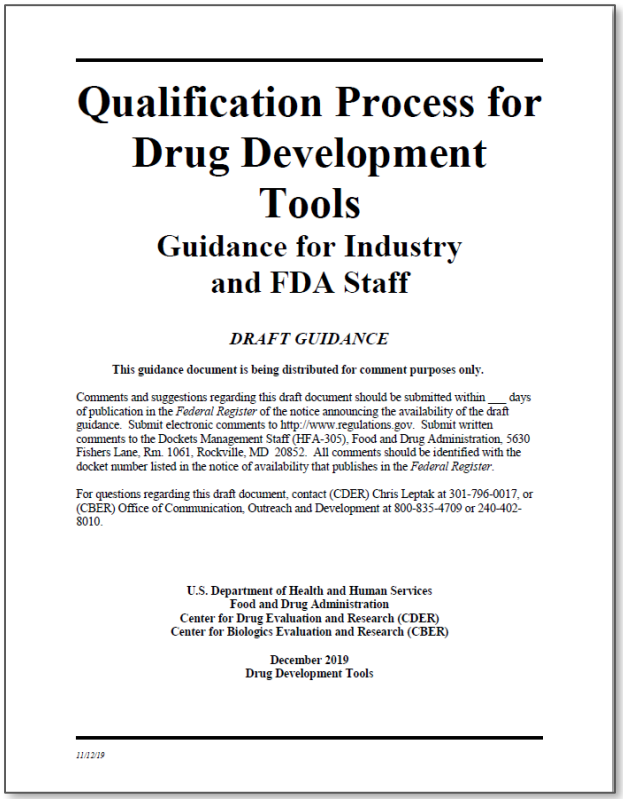
# Clinical Relevance?

- Current assessments based on rating scales
- Imaging measures are putative biomarkers
  - A biomarker is a defined characteristic that is measured as an indicator of normal biological processes, pathogenic processes, or responses to an exposure or intervention, including therapeutic interventions. Molecular, histologic, radiographic, or physiologic characteristics are types of biomarkers. A biomarker is not an assessment of how an individual feels, functions, or survives.

# Reward Processing as Primary Endpoint?

# Biomarker Qualification

- Multistep process with *lots* of feedback and interaction along the way
  - Letter of Intent
  - Qualification Plan
  - Full Qualification Package



**Qualification Process for Drug Development Tools**

**Guidance for Industry and FDA Staff**

***DRAFT GUIDANCE***

**This guidance document is being distributed for comment purposes only.**

Comments and suggestions regarding this draft document should be submitted within ___ days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to http://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Chris Leptak at 301-796-0017, or (CBER) Office of Communication, Outreach and Development at 800-835-4709 or 240-402-8010.

**U.S. Department of Health and Human Services**
**Food and Drug Administration**
**Center for Drug Evaluation and Research (CDER)**
**Center for Biologics Evaluation and Research (CBER)**

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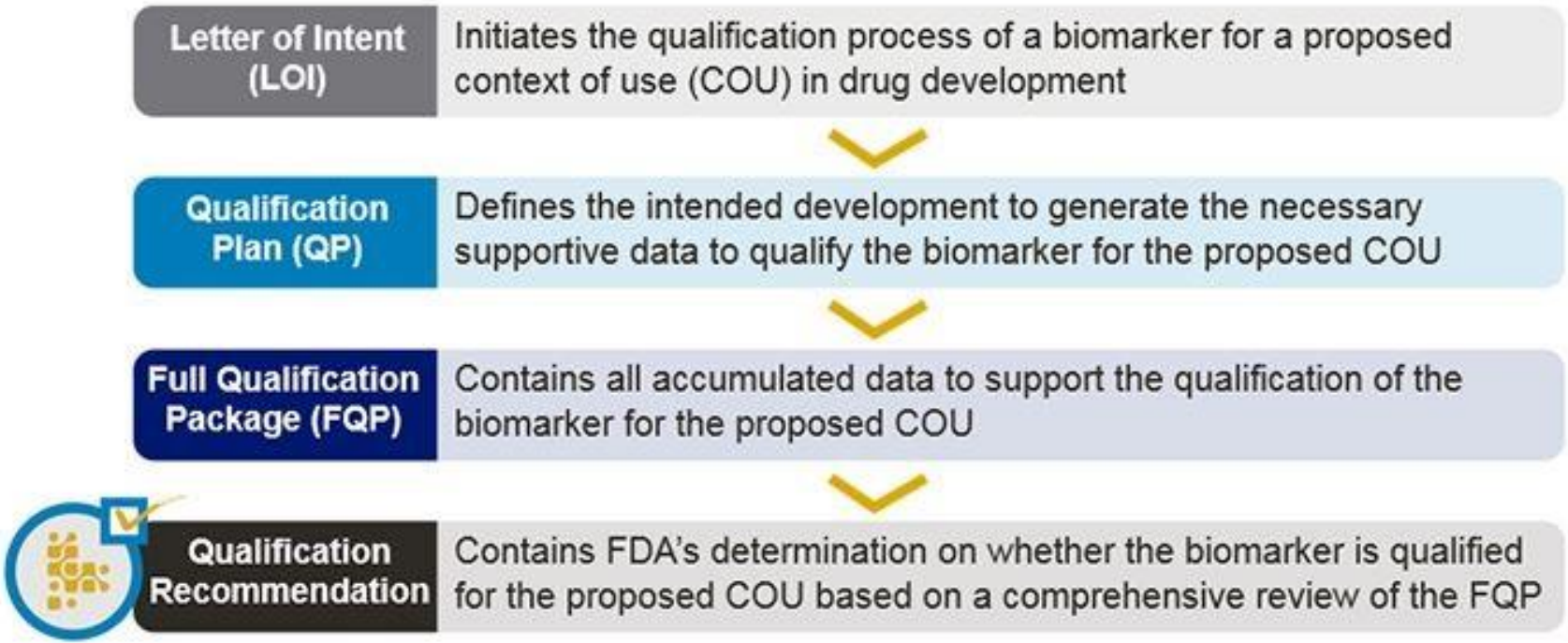
# Qualification Process




www.fda.gov *https://www.fda.gov/drugs/cder-biomarker-qualification-program/about-biomarkers-and-qualification

# Letter of Intent

- The LOI provides initial information about the biomarker proposal including:
  - Drug development need the biomarker is intended to address
  - Biomarker information
  - Context of Use (COU)
  - Information on how the biomarker will be measured

# Context of Use

- [BEST biomarker category] that [action] [purpose of intervention] of [target populations] in [type of study].
- Types of biomarkers:
  - Diagnostic
  - Monitoring
  - PD/Response
  - Prognostic
  - Reasonably likely surrogate
  - Safety
  - Susceptibility/Risk

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