PANEL QUESTIONS FOR REGULATORY CONSIDERATION

Biometric Monitoring Devices (BMDs) to Quantitatively Assess Quality-of-Life (QoL) Domains: Mobility/Frailty, Sleep, & Cognition

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QUESTIONS FOR THE PANEL

CAMD and its members have framed some questions to gain a perspective on how BMDs could be used as potential Drug Development Tools and Future Outcome Assessments in Clinical Drug Trials.

The questions are group into the categories of:

• General Use
• Data Collection
• Clinical Validation/ Regulatory Path
QUESTIONS FOR THE PANEL (continued)

GENERAL USE

• Do you agree that input from patients on which functional aspects of mobility/frailty, sleep, cognition, and mood should drive where focus should be given in validating BMD assessments? Should the data be derived from caregivers too?

• Given that both neurologic and psychiatric diseases have symptoms of altered mobility/frailty, sleep and cognition, would an assessment based on BMD measurements be faced with pseudo-specificity issues?

• What regulatory conversations are encouraged to ensure that that use is developed for a specific context-of-use?

• What are the considerations between deciding to use a commercial grade device and a medical device for a regulatory submission?
  - Would this be influenced by use in a label claim?
QUESTIONs FOR THE PANEL (continued)

DATA COLLECTION

• What practices must be put into place that ensures data collected is from the intended research subject?
  - Fingerprint; Facial recognition; Behavioral phenotyping; Voice recognition

• As more technologies enter the clinical arena, comparative effectiveness studies should consider the impact of user-centric dimensions that have historically not been prominent considerations (e.g., easy user interface and user accessibility).
  - What is FDA’s perspective about defining metrics to capture usage patterns, learnability, and other crucial traits of consumer-grade technologies?
QUESTIONS FOR THE PANEL (continued)

DATA COLLECTION (continued)

• How critical is it to collect contextual metadata to integrate into the BMD assessment for interpretation?
  – Case 1: Recent knee replacement;
  – Case 2: Hiking the Appalachian trail;
  – Case 3: -40°F outside in Minneapolis/ +100°F outside in Phoenix;
  – Case 4: Wheelchair bound;
  – Case 5: Depression

• Many mHealth technologies have started incorporating more active components such as notifications and reminders that inevitably affect data collection and, potentially, outcomes.
  – How can study reproducibility be improved in cases where prompting is not standardized? Is this a concern?
  – Will use the type of assessment influence whether this is important?
QUESTIONS FOR THE PANEL (continued)

CLINICAL VALIDATION

• How should the reliability of a BMD be established?
  – How should test, re-test, and analytical reliability be documented?
    • Should this be done across all intended patient populations?
  – Are longitudinal studies required?

• In making assessment with BMDs, is it more important to compare results to normal populations, or is it more important to analyze the rate of change for an individual?
  – **Case in Point:** If an individual normally resides 1.5 to 2 standard deviations above the norm for cognition, but deteriorates to the mean within 3 months, would this be a potential signal for acute brain dysfunction?
CLINICAL VALIDATION (continued)

• For clinical validation of a BMD would patients at each stage of disease need to be specifically explored?
  - e.g., pre-symptomatic, MCI, mild-to-moderate

• How are individual and patient population differences handled in guiding the assessment of ‘normal’?
  – Case in Point: An algorithm may work well in non-obese, non-frail, etc. Will each patient population need to be studied for validity, or would reliability for a range of ‘normals’ be sufficient to warrant immediate use?
QUESTIONS FOR THE PANEL (continued)

CLINICAL VALIDATION (continued)

• Given the multi-dimensional impact of psychiatric and neurologic disease on the physiology supporting mobility, sleep, mood, and cognition, should future work focus on individual measures, or should composite assessments that probe the constellation of pathophysiologic dimensions most important to those affected by a disease drive where the field goes?

• For BMD tests that have already received FDA approval for assessing cognitive impairment for one type of brain dysfunction, what general considerations would need to be addressed to advance the use of this device for another brain disease that affects cognitive function?

• By what regulatory endorsement pathway should these assessments best progress:
  – Fit-for-Purpose (e.g., Physiologically Based Model of Disease Progression)?
  – Biomarker Qualification?
  – COA Qualification?
  – Individual Review Divisions within CDER (e.g., Psychiatry or Neurology)?
Thank you!

Pharmaceutical Industry
- AbbVie Inc.
- Biogen
- Boehringer Ingelheim Pharmaceuticals, Inc.
- Eisai
- Eli Lilly and Company
- Roche/ Genentech
- Johnson & Johnson Pharmaceutical Research & Development, LLC
- Merck, Sharp & Dohme Corp.
- Novartis Pharmaceutical
- Pfizer, Inc.
- Takeda

Government and Regulatory Agencies
- European Medicines Agency (EMA)
- National Institute of Neurological Disorders and Stroke (NINDS)
- National Institute on Aging (NIA)
- U.S. Food and Drug Administration (FDA)
- National Institutes of Health (NIH)

Non-profit Research Organizations
- Alzheimer’s Association
- UsAgainstAlzheimer’s Network
- Alzheimer’s Research UK
- Alzheimer’s Drug Discovery Foundation
- CHDI Foundation