

# Digital Biomarkers Decision Process Working Group

17th Feb 2023

Chairs:

Diane Hoffman

Vikas Mohan Sharma

## Disclosures:

- Vikas Sharma: Employee Boehringer Ingelheim International GmbH; Independent Ethics Expert; European Research Council Honorary Trustee; Comm DEALL Trust
  
- Diane Hoffman: Consultant for Quantic Innovation, a digital biomarkers/phenotyping company; Johnson & Johnson stockholder

# Financial Disclosures Core Team Members

- Jeff Cohn is a professor at the University of Pittsburgh, adjunct faculty at Carnegie Mellon University, and chief scientist and a shareholder at Deliberate AI. He holds options at Embodied, Inc., and is a member of advisory boards at SPRING; Embodied, Inc.; and RealEyes, Inc.
- Louise Steinberg: Employee of ICON Plc.
- Cara Pendergrass, Ph.D: Owner of Avanti Clinical Research Consulting; Consultant for BioXcel Therapeutics; Functional Neuromodulation; EMA Wellness
- Marc Aafjes is a shareholder and employee of Deliberate Solutions, Inc ("Deliberate AI"), and a shareholder of Topia, Inc, and Vodafone Group plc.
- Brian Kirkpatrick: CEO & part owner of Quantic Innovations; Karuna; Sunovion; ProPhase/MedAvante; Lundbeck; Acadia; Otsuka; Minerva Neurosciences; PPD Biotech; use of the Brief Negative Symptom Scale

# Agenda

- Introduction: Core WG members
- Summary last WG meeting Autumn 2022
- Introduction: Core WG members
- Proposals from WG
- Breakout sessions with WG leads
- Overview and next steps

# Introduction of the Core WG members

- Diane Hoffman
- Vikas Mohan Sharma
- Brian Kirkpatrick
- Cara Pendergrass
- Jeffrey Cohn
- Marc Aafjes
- Louisa Steinberg
- Hopefully more will join today 😊

# Summary from our last meeting in Sep 2022

- In Sep 2022 we met in Boston for f2f discussion
- Breakout sessions in smaller groups
  - Start building Digital BMx database/Focus
  - Domain/Disease focused BMx guidance
  - Use cases of Digital BMx (Clinical development, clinical practice etc.)
  - Challenges in validation/framework of validation
  - Learnings from other efforts in same direction e.g. Digital Medicine Society
- Smaller group of WG members volunteered to support offline activities
- Multiple telecons in preparation of today's meeting

# Contents

- Open Questions re: Digital Biomarkers
- Proposed Work Streams:
  1. Glossary and existing Resources Synthesis
  2. Clinical Validation: Neuropsychiatric disorders
  3. Clinical Validation: Movement disorders
  4. Regulatory Adoption

# Existing resources **lack CNS-specific details regarding clinical validation and regulatory acceptance of digital biomarkers**

- 1) What is the **current state of clinical validation** of digital biomarkers and clinical outcome assessments in CNS?
  - What novel PerfO are used for digital assessments
  
- 2) What is the **current state of regulatory acceptance** of biomarkers in CNS drug or device approvals?
  - Status of CNS drug and medical device approvals supported by (digital) biomarkers
  - Best practices to generate evidence for qualifications or acceptance of CNS (digital) biomarkers, COAs (clinical outcome assessments) or ‘software as a medical device’ (SaMD)



# 1. What **resources are already available**, and how do we establish a common **glossary**?

- **Objective:**

- Gather and synthesize existing resources, specifically for CNS use cases
- Establish a common Glossary

- **Method:**

- Desk research for resources

- **Deliverables:**

- Website page with linked resources
- Synthesis publication (website or PowerPoint) of key materials with CNS use cases in mind

- **Team:**

- Cara Pendergrass
- Members:

## 2. What is the **current state of clinical validation** of (digital) biomarkers and COAs for **Neuropsychiatric disorders**

### ▪ **Objective:**

- Understand the degree of clinical validation, assess the strength of evidence, and identify any gaps

### ▪ **Method:**

- A: Create a Scoping review of clinical validation of novel biomarkers and digital PerfOs for Neuropsychiatric disorders
- B: Create a Structured review of clinical validation of novel biomarkers and digital PerfOs for Neuropsychiatric disorders
- (C: Undertake a meta-analysis to assess the strength of evidence)

### ▪ **Deliverables:**

- Academic publication
- Executive whitepaper
- Interactive literature infographic/navigator (potentially being kept up to date)

### ▪ **Team:**

- Marc Aafijes
- Members:

### 3. What is the **current state of clinical validation** of (digital) biomarkers and COAs for **Movement Disorders**

- **Objective:**

- Understand the degree of clinical validation, assess the strength of evidence, and identify any gaps

- **Method:**

- A: Create a Scoping review of clinical validation of novel biomarkers and digital PerfOs for Movement disorders
- B: Create a Structured review of clinical validation of novel biomarkers and digital PerfOs for Movement disorders
- (C: Undertake a meta-analysis to assess the strength of evidence)

- **Deliverables:**

- Academic publication
- Executive whitepaper
- Interactive literature infographic/navigator (potentially being kept up to date)

- **Team:**

- Marc Aafijes
- Members:

## 4. What is the current state of regulatory acceptance of biomarkers in CNS drug or device approvals?

### ■ Objective:

- The purpose of the digital biomarker work group is to develop a guide or tool to aid users of digital biomarkers in
  - evaluating and choosing markers
  - implementing markers in CNS clinical trials
- The purpose of the regulatory stream is to develop the regulatory section of this tool

### ■ Methods:

- Review regulatory agency statements
- Interview participants in industry/regulatory discussions of specific proposed biomarkers

### ■ Deliverables:

- A summary of interviews with regulatory discussion participants
- Recommendations for approaching evaluation & choice of markers, & implementation in trials

### ■ Team:

- Brian Kirkpatrick
- Members:

**Appendix**

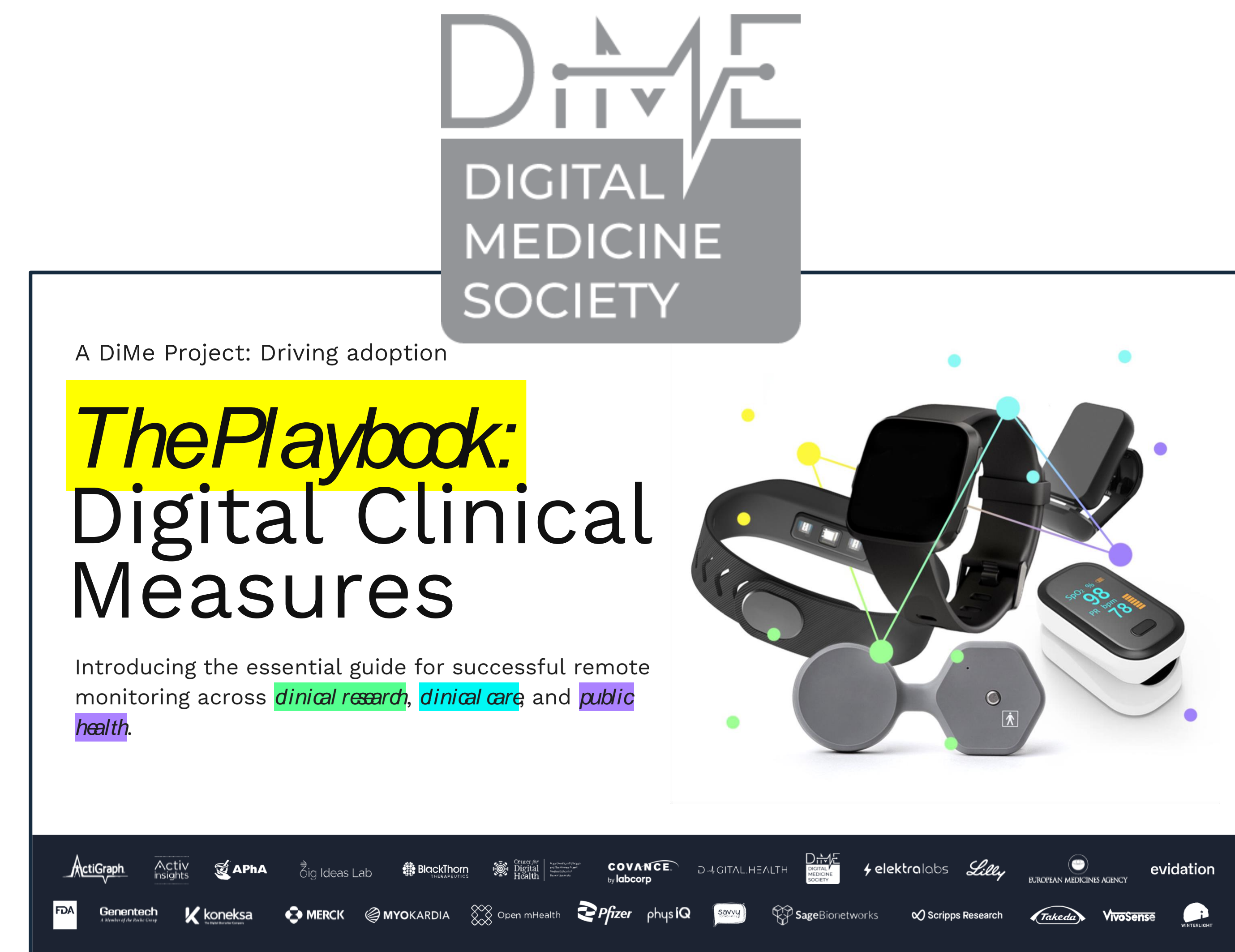


Backup slides

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# DIME's playbook provides frameworks and implementation considerations for **remote monitoring & digital clinical measures**

- The Digital Medicine Society (DiMe) is the professional society for the digital medicine community
- DIME's goal is to build a shared foundation for remote monitoring and digital clinical measures across research, care and public health.
- 'The Playbook' is an industry guide for successfully developing & deploying digital clinical measures and remote monitoring
- It covers measures, technologies and operations, and emphasizes its V3-framework to ensure utility
  - 'Verification, Analytical Validation and Clinical Validation'



# DIME's playbook **lacks a CNS-specific 'lay of the land' regarding clinical validation and regulatory acceptance of biomarkers**

## **DIME Playbook benefits: *Education***

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- Conceptual frameworks to define and implement digital endpoints in clinical trials
- Primary focus on 'digital' ways to measure 'outcomes', through defining "meaningful Aspects of Health" MAH and "Concepts of Interest" (COI)
  - Focus on diagnostic or monitoring biomarkers
- Provides overview of regulatory considerations of digital endpoints in trials
- Considers generic implementation considerations around potential biases and accessibility

## **Open Questions: *'lay of the land' in CNS***

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- 1) What is the **current state of clinical validation** of (digital) biomarkers and COAs in CNS?
  - Across all types, (e.g. diagnostic, predictive,...) and classes (molecular, histologic, radiographic, physiologic) of biomarkers
  - What novel PerfO are used for digital assessments
- 2) What is the **current state of regulatory acceptance** of biomarkers in CNS drug or device approvals?
  - Status of CNS Drug and Medical Device approvals supported by (digital) biomarkers
  - Best practices to generate evidence for qualifications or acceptance of CNS (digital) biomarkers, COAs (clinical outcome assessments) or 'software as a medical device' (SaMD)
- 3) What are **data science best practices** for more complex composite CNS endpoints, beyond simple sensors?
  - What multimodal/computational approaches to use in CNS to achieve meaningful clinical validation?

# 1. What is the **current state of clinical validation** of (digital) biomarkers and COAs in CNS?

## ▪ **Objective:**

- A: Provide a comprehensive overview of clinical validation of novel biomarkers and digital PerFOs for CNS
- B (Expand): Assess the strength of evidence

## ▪ **Method:**

- A: a systematic/scoping review of \peer-reviewed and gray literature; B: meta-analysis

## ▪ **Deliverables:**

- Academic publication
- Interactive literature infographic/navigator (potentially being kept up to date)

## ▪ **Structure:**

- Work packages by indication cluster (using DSM-5, HiTOPS or other transdiagnostic)
- Each work package team needs to be able to cover all biomarker classes; potentially could also organize this way
- Papers are typically not focused on biomarker type/category, so team will cover all (susceptibility/risk, diagnostic, monitoring, prognostic, predictive, pharmacodynamic/response, and safety)

