

Biomarkers Consortium Neuroscience Symposium
Tuesday April 30th – Wednesday May 1st, 2019

Agenda

Tuesday April 30th

7:30 am – 8:30 am **Registration and Breakfast**

8:30 am – 8:45 am **Welcome and Opening Remarks**
Rosa Canet-Aviles (FNIH), Michael Biarnes (FNIH)

8:45 am – 12:00 pm **Session 1: Multimodal Biomarkers in Neuroscience: State of the Science and Key Issues for Consideration when Proposing a Multimodal Biomarker for a Specific COU**

Session 1 Questions

- *What are examples of unimodal biomarkers routinely used in neuroscience clinical trials (e.g., fluid biomarkers; CSF Aβeta, Tau..)?*
- *Does one go stepwise from unimodal biomarkers to a multimodal one?*
- *Do the biomarkers need to be individually qualified to be part of a multimodal biomarker panel or can they be qualified together as part of a multimodal biomarker panel?*
- *How does the complexity of the disorder weigh in on the decision to move from a unimodal biomarker to a multimodal biomarker?*
- *How can pre-competitive consortia efforts be made more effective in moving a promising biomarker toward FDA approval?*

8:45 am – 8:50 am **Session 1 Introduction**
Chris Leptak (FDA), Hartmuth Kolb (Johnson & Johnson)

8:50 am – 9:15 am **Biomarker Qualification and Barriers to Biomarker Development**
Peter Stein (FDA)

9:15 am – 9:40 am **Multimodal Biomarkers: Overview and Strategies – Examples from Other Highly Prevalent Chronic Diseases**
John Wagner (Takeda)

9:40 am – 10:15 am **How far have we progressed in the thinking of multimodal biomarkers in the field of AD - lessons learned**
Maria Carrillo (Alzheimer's Association), Clifford Jack (Mayo Clinic)

10:15 am – 10:30 am **Break**

10:30 am – 10:55 am **Quantitative Peptidomics and proteomics Data on the EMIF Study**
Henrik Zetterberg (University of Gothenburg)

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- 10:55 am – 11:15 am** **Strengths and Limitations of Targeted vs. Discovery Based Approaches**
Ida Grundberg (O-LINK)
- 11:15 am – 12:00 pm** **Multimodal Biomarker Panel Discussion**
Moderator: Chris Leptak (FDA), Hartmuth Kolb (Johnson & Johnson)
Panelists: Maria Carrillo (Alzheimer's Association), Ida Grundberg (O-LINK), Steve Hoffmann (FNIH), Clifford Jack (Mayo Clinic), Kun Jin (FDA Stats), Peter Stein (FDA), John Wagner (Takeda), Henrik Zetterberg (University of Gothenburg)
- 12:00 pm – 1:00 pm** **Lunch**
- 1:00 pm – 4:00 pm** **Session 2: Fluid Biomarkers for Specific COUs and Pre-analytical and Analytical Considerations for Biomarker Technology Platforms**
Session 2 Questions
- *What is the state of the science for fluid biomarkers in neuroscience disorders?*
 - *What are the challenges for qualifying Fluid Biomarkers?*
 - *Is CLIA necessary for qualification?*
 - *What is the state of the science for preanalytics and analytical standards for fluid, imaging, and neurophysiological biomarkers?*
 - *Should the analytics be independent of the technology platform?*
- 1:00 pm – 1:05 pm** **Session 2 Introduction**
Danielle Graham (Biogen), Bill Potter (National Institute of Mental Health)
- 1:05 pm – 1:35 pm** **Fluid Biomarkers in Alzheimer's disease: From Research-Use-Only status to robustly validated tests for detection of underlying neuropathology**
Les Shaw (University of Pennsylvania)
- 1:35 pm – 2:05 pm** **Biochemical Biomarkers in Parkinson's disease**
Samantha Hutten (Michael J. Fox Foundation)
- 2:05 pm – 2:35 pm** **CSF and Plasma Markers: Reference Materials, Preanalytical Standardization, and Method Optimization**
Samantha Hutten (Michael J. Fox Foundation), Charlotte Teunissen (Amsterdam University Medical Center)
- 2:35 pm – 2:45 pm** **Break**
- 2:45 pm – 3:15 pm** **Using EEG Biomarkers in Multi-Site Global Trials**
Gregory Light (University of California San Diego)

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3:15 pm – 4:00 pm Fluid Biomarkers and Analytical Considerations for Biomarker Technology Platforms Panel Discussion

Moderator: Danielle Graham (Biogen), Bill Potter (National Institute of Mental Health)

Panelists: Kaj Blennow (University of Gothenburg), Samantha Hutten (Michael J. Fox Foundation), Mehmet Kosoglu (FDA BQP), Gregory Light (University of California San Diego), Steve Piccoli (GSK), Les Shaw (University of Pennsylvania), Charlotte Teunissen (Amsterdam University Medical Center), Sue-Jane Wang (FDA)

4:00 pm – 5:00 pm Session 3 Imaging Biomarker State of the Science and Proposed COU in Neuroscience

(Session will continue on Day 2)

Session 3 Questions

- *Can we think of a mechanism to get imaging agents qualified for a specific COU without requiring formal FDA approval?*
- *If approval of PET tracer, is the COU also approved?*
- *What would be the path of qualification in the absence of approval?*
- *Why are there so few FDA approved PET tracers? What are the hurdles for approval? Can we discuss mechanisms (e.g. consortia efforts) to drive promising PET tracers toward approval?*
- *Are these imaging measures considered to be automatically qualified as a fit for “use” of what they were approved for?*
- *What is the context of use for neuroinflammation PET tracers?*
- *How do the various neuroinflammation tracers differ? How do we drive consensus, ie identify the “best” tracer and drive its validation forward?*

4:00 pm – 4:15 pm Session 3 Introduction

Hartmuth Kolb (Johnson & Johnson), Anthony Fotenos (FDA)

4:15 pm – 4:30 pm PET Tracers of CNS Neurotransmitter Drug Targets: Applications to Date

Jeff Meyer (University of Toronto)

4:30 pm – 5:00 pm Emerging PET Radiotracers and Targets for Imaging of Neuroinflammation

Neil Vasdev (University of Toronto)

5:00 pm – 5:15 pm Day 1 Closing Remarks

Linda Brady (National Institute of Mental Health), Hartmuth Kolb (Johnson & Johnson)

5:30 pm – 6:30 pm Reception

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Wednesday, May 1st

- 7:30 am – 8:30 am** **Registration and Breakfast**
- 8:30 am – 8:45 am** **Welcome and Opening Remarks**
Linda Brady (National Institute of Mental Health), Hartmuth Kolb (Johnson & Johnson)
- 8:45 am – 10:20 am** **Session 3 Imaging Biomarker State of the Science and Proposed COU in Neuroscience**
Continued from Day 1
Session 3 Questions
- *What is the state of the science for functional imaging biomarkers in neuroscience disorders?*
 - *What are the challenges for qualifying imaging biomarkers for specific COUs?*
 - *Are there ways to improve the qualification process to improve the business case for imaging agents?*
 - *What are the key differences and similarities between approval for imaging agents and fluid biomarkers?*
- 8:45 am – 9:20 am** **Cortical Thinning and Cerebello-Thalamo-Cortical Circuitry Hyperconnectivity in Psychosis Prodrome**
Tyrone Cannon (Yale University)
Alan Anticevic (Yale University)
- 9:20 am – 9:45 am** **DAT Imaging as an enrichment biomarker for PD clinical trials**
Diane Stephenson (Critical Path Institute)
- 9:45 am – 10:20 am** **Imaging Biomarker Qualification Panel Discussion – Next Steps**
Moderator: Hartmuth Kolb (Johnson & Johnson), Anthony Fotenos (FDA)
Panelists: Dan Krainak (FDA), Alan Anticevic (Yale University), Tyrone Cannon (Yale University), Jeff Meyer (University of Toronto), Diane Stephenson (Critical Path Institute), Neil Vasdev (University of Toronto), Sue-Jane Wang (FDA)
- 10:20 am – 10:30 am** **Break**

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10:30 am – 12:30 pm **Session 4: EEG Biomarker State of the Science and Proposed COU in Neuroscience**

Session 4 Questions

- *What is the state of the science for resting state and task-based neurophysiological biomarkers in neuroscience disorders?*
- *What are the challenges for qualifying neurophysiological biomarkers for specific COUs?*
- *Are there ways to improve the qualification process to improve the business case for neurophysiological biomarkers?*
- *What are the key differences and similarities between approval for neurophysiological and imaging biomarkers?*

10:30 am – 10:35 am **Session Introduction**

Linda Brady (National Institute of Mental Health), Bernard Fischer (FDA)

10:35 am – 11:00 am **EEG Biomarkers in Combination with Clinical Measures as a Predictor of Outcome in MDD (the EMBARC Study)**

Amit Etkin (Stanford University)

11:00 am – 11:25 am **EEG Based Measures: Mismatch negativity (MMN) and P300 in psychosis prodrome**

John Sweeney (University of Texas Southwestern)

11:25 am – 11:50 am **EEG Based Measures in Autism Spectrum Disorder**

Jamie McPartland (Yale University)

11:50 am – 12:30 pm **EEG Biomarkers Panel Discussion**

Moderator: Linda Brady (National Institute of Mental Health), Bernard Fischer (FDA)

Panelists: Amit Etkin (Stanford University), Jay Gupta (FDA), Jamie McPartland (Yale University), John Sweeney (UTSW)

12:30 pm – 1:15 pm **Lunch**

1:15 pm – 3:50 pm **Session 5: Clinical Measures in Drug Development**

Session 5 Questions

- *What are the best cognitive measures to measure minute changes of disease progression in neuroscience?*
- *What are the most robust, reliable cognitive measures for selection of subjects for clinical trials in AD/MCI or depression, etc (not as endpoints); can the same set of cognitive measures be used across neuroscience disorders?*

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- *How rigorously is reproducibility and test/retest variability of clinical measures assessed and how do these factors affect the utility of the markers?*

1:15 pm – 1:20 pm	Session Introduction <i>Bernard Fischer (FDA), Bill Potter (National Institute of Mental Health)</i>
1:20 pm – 1:45 pm	Task-based Behavioral Markers <i>Stephane Pollentier (Boehringer Ingelheim)</i>
1:45 pm – 2:10 pm	Cognitive Measures <i>Raquel Gur (University of Pennsylvania)</i>
2:10 pm – 2:35 pm	Multivariate biomarker for enrichment/patient selection <i>Laurel Beckett (University of California, Davis)</i>
2:35 pm – 2:45 pm	Break
2:45 pm – 3:10 pm	Genomic markers – Polygenic Risk Scores (PRS) <i>Lea Davis (Vanderbilt University)</i>
3:10 pm – 3:50 pm	Clinical Measures in Drug Development Panel Discussion <i><u>Moderator:</u> Bernard Fischer (FDA), Bill Potter (National Institute of Mental Health)</i> <i><u>Panelists:</u> Laurel Beckett (University of California, Davis), Lea Davis (Vanderbilt University), Raquel Gur (University of Pennsylvania), Stephane Pollentier (Boehringer Ingelheim)</i>
3:50 pm – 4:50 pm	<u>Symposium Summary and Next Steps</u>
3:50 pm – 4:20 pm	Summary <i>Linda Brady (National Institute of Mental Health), Hartmuth Kolb (Johnson & Johnson)</i>
4:20 pm – 4:50 pm	Session Co-Chair Panel Discussion <i>Linda Brady (National Institute of Mental Health), Bernard Fischer (FDA), Anthony Fotenos (FDA), Danielle Graham (Biogen), Hartmuth Kolb (Johnson & Johnson), Chris Leptak (FDA), Bill Potter (National Institute of Mental Health)</i>
4:50 pm	Meeting Adjourns