



## Memorandum

**Date:** April 28, 2016

**Subject:** Critical Path Innovation Meeting: Regulatory Pathways for Biomarkers in Traumatic Brain Injury

**Date of meeting:** March 22, 2016

**Requestor:** Dr. Geoffrey T. Manley on behalf of the Traumatic Brain Injury (TBI) Endpoints Development (TED) Initiative Investigators

Note: Discussions at Critical Path Innovation Meetings are informal. All opinions, recommendations, and proposals are unofficial and nonbinding on FDA and all other participants.

### **ATTENDEES**

#### **FDA**

##### **Office of the Commissioner**

**Office of the Chief Scientist, Office of Scientific Professional Development**  
Lakshmi Kannan, Commissioner Fellow

##### **Center for Drug Evaluation and Research**

##### **Office of Translational Sciences (OTS) Immediate Office**

Shashi Amur, Ph.D., Biomarker Qualification Program Scientific Coordinator  
Kylie Haskins, Ph.D., Biologist  
Suzie McCune, M.D., Deputy Director  
Marianne Noone, R.N., Senior Regulatory Project Manager  
Ameeta Parekh, Ph.D., Senior Advisor for Scientific Collaborations  
Sarmistha Sanyal, Ph.D., Staff Fellow  
Alicia Stuart, Project Manager

##### **OTS Office of Clinical Pharmacology**

Hobart Rogers, Pharm.D., Ph.D., Reviewer, Genomics and Targeted Therapy Group, Biomarker Qualification Liaison to OTS  
Xiaofeng Wang, Ph.D., Visiting Associate, Division of Pharmacometrics

##### **OTS Office of Biostatistics**

Sue-Jane Wang, Ph.D., Associate Director for Pharmacogenomics and Adaptive Design, Biomarker Qualification Liaison to OTS

##### **Office of New Drugs (OND) Office of Drug Evaluation I**

William Dunn, M.D., Director, Division of Neurology Products  
Heather Fitter, M.D., Medical Officer, Division of Neurology Products

Nicholas Kozauer, M.D., Medical Officer, Division of Neurology Products  
John Marler, M.D., Medical Officer, Division of Neurology Products

**OND Office of Drug Evaluation IV**

Brenda Ye, M.D., Medical Officer

**Center for Devices and Radiological Health**

**Office of the Center Director**

Peter Como, Ph.D., Division of Neurological and Physical Medicine Devices, Neurostimulation Devices Branch

Allison Kumar, Senior Project Manager

**REQUESTER**

**The Traumatic Brain Injury Endpoints Development (TED) Team**

General Peter Chiarelli - U.S. Army General (Retired), CEO, One Mind

Sureyya Dikmen, PhD - University of Washington

Joe Giacino, PhD - Spaulding Rehabilitation Hospital

Ramon Diaz-Arrastia, MD PhD - Uniformed Services University

Harvey Levin, PhD - Baylor College of Medicine

Christine Mac Donald, PhD - University of Washington

Geoff Manley, MD PhD - University of California, San Francisco (Contact PI)

Amy Markowitz, JD - University of California, San Francisco

Mike McCrea, PhD - Medical College of Wisconsin

Pratik Mukherjee, MD PhD - University of California, San Francisco

Ann Robbins, PhD - Critical Path Institute

Diane Stephenson, PhD - Critical Path Institute

Nancy Temkin, PhD – University of Washington

Kevin Wang, PhD - University of Florida

Steve Wisniewski, PhD - University of Pittsburgh

**1. BACKGROUND**

The Traumatic Brain Injury Endpoints Development (TED) team requested a CPIM to discuss their work to advance therapies for traumatic brain injury (TBI).

**2. DISCUSSION**

The TED team presented information that reviewed the status of neuroimaging and biofluid biomarkers for use in TBI clinical trials. There was discussion about potential regulatory pathways for biomarkers in TBI. MRI was discussed within the context of differing approaches from CDRH and CDER. TED will follow up with CDRH to discuss the approach to clearing diagnostics in this space. The Division of Neurology Products (DNP) in CDER discussed the use of biomarkers (imaging and biofluid) in drug development. There was discussion of how to provide opportunities for communication related to TBI biomarkers including a potential Letter of Support, public workshops with discussion summarized through white papers, and peer-reviewed journal articles. The importance of the meeting was eloquently summarized by General Chiarelli with an example of how a biomarker in this space could be used to prioritize triage for patients with TBI to prevent morbidity and mortality.

### 3. NEXT STEPS

- TED will follow up with CDRH to discuss plans for clearing diagnostics for TBI.
- FDA will provide information about the Letter of Support (LOS) program.
  - LOS information can be found at:  
<http://www.fda.gov/drugs/developmentapprovalprocess/ucm434382.htm>
- FDA will provide information on the Biomarker Qualification Program (BQP). It would be important to identify specific biomarkers for a well-defined context of use for discussion with the BQP.
  - BQP information can be found at:  
<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugDevelopmentToolsQualificationProgram/ucm284076.htm>
- FDA encouraged TED to consider writing a peer reviewed article to help disseminate and promote the advancement of therapies for TBI.
- FDA encouraged TED to consider having another workshop to engage others in the standardization of therapies for TBI. A white paper could be published as an outcome of the workshop.
- FDA encouraged TED to continue engaging with the Division of Neurology Products with questions about biomarkers in the context of individual drug development programs.