The National Academies of SCIENCES ENGINEERING MEDICINE

Forum on DRUG DISCOVERY, DEVELOPMENT, and TRANSLATION

Examining the Impact of Real-World Evidence on Medical Product Development: A Three-Part Workshop Series

Workshop Three: Application

July 17 – 18, 2018

National Academy of Sciences Building, Lecture Room
2101 Constitution Ave. NW, Washington, DC 20418

The National Academies of Sciences, Engineering, and Medicine (National Academies) is convening a three-part workshop series examining how real-world evidence development and uptake can enhance medical product development and evaluation. The workshops will advance discussions and common knowledge about complex issues relating to the generation and utilization of real-world evidence, including fostering development and implementation of the science and technology of real-world evidence generation and utilization.

- Workshop One (*September 19-20, 2017*) focused on how to align incentives to support collection and use of real-world evidence in health product review, payment, and delivery. Incentives need to address barriers impeding the uptake of real-world evidence, including barriers to transparency.
- Workshop Two (*March 6-7, 2018*) illuminated what types of data are appropriate for what specific purposes and suggested practical approaches for data collection and evidence use by developing and working through example use cases.
- **Workshop Three (*July 17-18, 2018*) will examine and suggest approaches for operationalizing the collection and use of real-world evidence through discussing and revising "decision aids" about specific topics in study design. The decision aids will be question lists to help inform stakeholders about study design choices, including potential risks, costs, and reporting/transparency expectations.**

DAY 1: July 17, 2018

8:00 a.m. Breakfast available outside the Lecture Room

8:15 a.m. **Welcome and opening remarks**

MARK MCCLELLAN , *Workshop Series Co-Chair*
Director
Duke-Margolis Center for Health Policy

GREG SIMON, *Workshop Series Co-Chair*
Investigator
Kaiser Permanente Washington Health Research Institute

SESSION I KEY CONSIDERATIONS FOR REAL-WORLD EVIDENCE APPLICATION

Session Objectives:

- Examine how some organizations are currently considering traditional and real-world evidence.
- Discuss factors that may be influencing overall cost and time investment required by traditional evidence generation.
- Consider when nontraditional datasources may be beneficial to assess outcomes.

8:45 a.m. **Update on IMI's GetReal and view from NICE**

PALL JONSSON
Associate Director, Research and Development
National Institute for Health and Care Excellence

9:05 a.m. **Drivers of expense and delay**

ELLIOTT LEVY
Senior Vice President, Global Development
Amgen, Inc.

9:25 a.m. **Patient-collected and owned data**

KOMATHI STEM
Chief Executive Officer and Founder
monARC Bionetworks

9:45 a.m. **BREAK**

SESSION II WHEN ARE REAL-WORLD DATA FIT FOR PURPOSE?

Session Objectives:

- Discuss potential bias-introducing steps in evidence generation from real-world data.
- Suggest key considerations in the data collection and evidence generation processes that influence reliability of RWD.
- Discuss how a decision aid laying out key questions and considerations might help inform current and future studies.

Moderator: Pall Jonsson, National Institute for Health and Care Excellence

10:05 a.m. **Introduction: A proposed framework for a decision aid**

10:15 a.m. **Looking back: How might a decision aid inform a real-world example?**

JEFF ALLEN
President and Chief Executive Officer
Friends of Cancer Research

10:35 a.m. **Looking forward: How decision aid might apply to future studies?**
Panel discussion and audience Q&A

AYLIN ALTAN
Senior Vice President of Research
OptumLabs

ROBERT BALL
Deputy Director, Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

LUCA FOSCHINI
Co-founder and Chief Data Scientist
Evidation Health

BRANDE YAIST
Sr. Director, Global Patient outcomes and Real-World Evidence
Eli Lilly and Company

12:00 p.m. **BREAK** (Lunch available Outside the Lecture Room)

SESSION III BLINDING: WHY, WHO, AND WHEN?

Session Objectives:

- Discuss how variability in knowledge of treatment assignment group affects
  - Provider and patient adherence and outcomes
  - Study cost and reliability.
- Suggest key factors that could affect blinding assignment.
- Discuss how a decision aid laying out key questions and considerations might help inform current and future studies.

Moderator: Jonathan Watanabe, University of California San Diego

1:00 p.m. **Introduction: A proposed framework for a decision aid**

1:10 p.m. **Looking back: How might a decision aid inform a real-world example?**

JOHN GRAHAM (*invited*)
Head, Value Evidence and Outcomes
GlaxoSmithKline

ORLY VARDENY
Minneapolis VA Center for Chronic Disease outcomes Research
Associate Professor of Medicine
University of Minnesota

1:30 p.m. **Looking forward: How decision aid might apply to future studies?**
Panel discussion and audience Q&A

CATHY CRITCHLOW
Vice President, Center for Observational Research
Amgen, Inc.

NANCY DREYER
Chief Scientific Officer
IQVIA

ALEX JOHN LONDON
Clara L. West Professor of Ethics and Philosophy
Carnegie Mellon University

JAMES P. SMITH
Deputy Director, Division of Metabolism and Endocrinology Products
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

2:30 p.m. **BREAK**

SESSION IV TREATMENT QUALITY AND PARTICIPANT SAFETY IN PRAGMATIC TRIALS

Session Objectives:

- Discuss how variability in treatment delivery and adherence can affect results, including
  - Potential influence of variation in standard treatment practice, and
  - Considerations for balancing participant autonomy and safety.
- Suggest key factors that could help determine the base comparison and level of control suited to a particular trial.
- Discuss how a decision aid laying out key questions and considerations might help inform current and future studies.

Moderator: Jennifer Graff, National Pharmaceutical Council

2:50 p.m. **Introduction: A proposed framework for a decision aid**

3:00 p.m. **Looking back: How might a decision aid inform a real-world example?**

LARRY ALPHS
Newron Pharmaceuticals

3:20 p.m. **Looking forward: How decision aid might apply to future studies?**
Panel discussion and audience Q&A

JUDITH CARRITHERS
Director of Oncology Services, Central Oncology Review
Advarra

BEN NOWELL
Director, Patient Centered Research
Global Healthy Living Foundation

PETER STEIN
Deputy Director, Office of New Drugs
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

4:40 p.m. **Day 1 wrap up and concluding thoughts/discussion with audience**

5:00 p.m. **ADJOURN WORKSHOP DAY 1**

DAY 2: July 18, 2018

7:30 a.m. Breakfast Available Outside the Lecture Room

8:00 a.m. **Welcome**

MARK MCCLELLAN , *Workshop Series Co-Chair*
Director
Duke-Margolis Center for Health Policy

GREG SIMON, *Workshop Series Co-Chair*
Investigator
Kaiser Permanente Washington Health Research Institute

SESSION V ASSESSING AND MINIMIZING BIAS IN OBSERVATIONAL COMPARISONS

Session Objectives:

- Discuss methods to assess presence of and optimally reduce bias from unmeasured confounding.
- Suggest key considerations for assessing—and communicating—uncertainty in observational studies.
- Discuss how a decision aid laying out key questions and considerations might help inform current and future studies.

Moderator: Greg Daniel, Duke-Margolis Center for Health Policy

8:10 a.m. **Introduction: A proposed framework for a decision aid**

DAVID MARTIN
Associate Director for Real-World Evidence Analytics
U.S Food and Drug Administration

8:20 a.m. **Looking back: How might a decision aid inform a real-world example?**

HECTOR IZURIETA
Epidemiologist, Office of Biostatistics and Epidemiology
Center for Biologics Evaluation and Research
U.S. Food and Drug Administration

8:35 a.m. **Looking forward: How decision aid might apply to future studies?**
Panel discussion and audience Q&A

GREG DANIEL
Deputy Director
Duke-Margolis Center for Health Policy

JESSICA FRANKLIN
Assistant Professor of Medicine
Harvard Medical School

NICOLE GORMLEY
Team Lead, Division of Hematologic Products
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

JAVIER JIMENEZ
Vice President and Global Head for Real-World Evidence and Clinical Outcomes
Sanofi

HENG LI
Mathematical Statistician
Center for Devices and Radiological Health
U.S. Food and Drug Administration

MARK VAN DER LAAN
Professor, Biostatistics and Statistics
University of California Berkeley

10:00 a.m. **BREAK**

SESSION VI FDA PANEL

Moderator: Alasdair Breckenridge, University of Liverpool

10:15 a.m. **A European perspective**

ALASDAIR BRECKENRIDGE
Emeritus Professor of Clinical Pharmacology
University of Liverpool

10:30 a.m. **Reflections from the FDA Center Directors**

JACQUELINE CORRIGAN-CURAY
Director, Office of Medical Policy, Center for Drug Evaluation and Research
U.S. Food and Drug Administration

PETER MARKS
Director, Center for Biologics Evaluation and Research
U.S. Food and Drug Administration

JEFF SHUREN
Director, Center for Devices and Radiological Health
U.S. Food and Drug Administration

11:35 a.m. **Panel discussion with audience**

11:50 p.m. **Synthesis of workshop discussions**

MARK MCCLELLAN , *Workshop Series Co-Chair*
Director
Duke-Margolis Center for Health Policy

GREG SIMON, *Workshop Series Co-Chair*
Investigator
Kaiser Permanente Washington Health Research Institute

12:00 p.m. **ADJOURN WORKSHOP DAY 2**