

Considerations for the Use of Real-World Evidence (RWE) to Assess the Effectiveness of Preventive Vaccines

Background and meeting objectives:

The 21st Century Cures Act directs the FDA to establish a program to evaluate the potential use of **real-world evidence (RWE)** to a) support the approval of a new indication for a drug approved under section 505(c) of the Federal Food, Drug, and Cosmetic Act; and b) to support or satisfy post-approval study requirements. Details on the framework for FDA's RWE Program are available here: <https://www.fda.gov/media/120060/download>.

The FDA's Office of Vaccines Research and Review (OVRR) is considering how RWE can be used for regulatory decision-making (e.g., to confirm the clinical benefit of vaccines and to support labeling changes for licensed vaccines). The purpose of this online workshop is to exchange information with stakeholders from industry, academia, and government about the scientific, clinical, and regulatory challenges and opportunities in using RWE to assess the **effectiveness of preventive vaccines**. Given the limitations inherent to the virtual-only format, the goal is to identify and frame the important issues. We anticipate that detailed discussions about these topics will be needed at more comprehensive meeting(s) in the future.

The **goals/objectives** of the workshop include:

- Clarify the FDA's current thinking and the **regulatory framework** that informs the use of RWE in vaccine development and licensure. Provide context and illustrate the importance of RWE in vaccine development, including through a review of relevant case examples.
- Focusing on **observational studies**:
 - Identify and discuss features of RWE studies (design/methodology, study conduct, analysis, and fitness of data for proposed study populations and endpoints) that would tend to increase (or decrease) confidence in conclusions about vaccine effectiveness.
 - Discuss the potential uses of methods to identify, measure, and/or correct for the effect of bias and confounding.
- Identify challenges and opportunities for incorporating RWE into **innovative trial designs** (e.g., cluster-randomization, decentralized trials, "pragmatic" or "large simple trials") that maintain **randomization**.
- Discuss emerging infectious diseases (e.g., coronavirus, ebola, influenza pandemics) and other scenarios (e.g., maternal immunization to prevent disease in infants through the use of licensed/recommended vaccines) in which traditional clinical trials could be impractical or ethically unacceptable. Consider the role of RWE approaches in these scenarios.
- Understand **stakeholders' perspectives/priorities/expectations** concerning the use of RWE for preventive vaccine development, licensure, and implementation.

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DRAFT AGENDA

DAY 1

September 17, 2020

9:00 AM – 12:00 PM

Session 1: Regulatory perspective

Welcome, background and CBER objectives for the meeting

Marion Gruber, PhD, Director, Office of Vaccines Research and Review (OVRR), Center for Biologics Evaluation and Research (CBER)

5 min

Regulatory framework, case examples, and potential future applications for RWE/RWD

Dr. Jeff Roberts, MD, Associate Director, Medical Countermeasures and Scientific Affairs, OVRR, CBER

15 min

CBER partnerships to develop the use of RWE for regulatory purposes

Rich Forshee, PhD, Associate Director for Research, Office of Biostatistics and Epidemiology (OBE), CBER

10 min

EMA perspective on the role of RWE studies and current uses of RWE in EU vaccine labeling

Marco Cavaleri, PhD, Head of Anti-infectives and Vaccines, European Medicines Agency (EMA)

10 min

Q&As – 15 min

Break – 10min

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Session 2: Observational study methodology and approaches to quantifying and correcting for bias and confounding

CBER experience with the development of methods for the use of RWE for comparative effectiveness studies in Medicare, preliminary perspective on their usefulness, limitations, and progress in using methods to address bias and confounding.

Hector S. Izurieta, MD, MPH, Senior Epidemiologist, OBE, CBER
15 min

Clarifying questions (5 min)

Observational vaccine study case examples: design choices to fit the population, the vaccine, and the available endpoint data

Nick Andrews, Deputy Head of the Statistics Unit, Public Health England
15 min

Clarifying questions (5 min)

Use of an instrumental variable method to address unmeasured confounding and bias: experience from the study of high dose influenza vaccine in the VA system

Yinong Young-Xu, SCD, Assistant Professor of Psychiatry, Department of Psychiatry, Geisel School of Medicine at Dartmouth
15 min

Clarifying questions (5 min)

Panel Discussion – 30 min

End

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9:00 AM – 12:00 PM

Session 3: External stakeholder experiences and perspective

Lessons learned from the Zostavax long-term effectiveness study

Patricia Saddier, MD, PhD, Executive Director, Pharmacoepidemiology, Center for Observational and Real-world Evidence (CORE), Merck & Co., Inc.

15 min

Clarifying questions (5 min)

Individually randomized large pragmatic trials: the Fluzone HD experience in the Finnish health care system

Iris De Bruijn, MSc, PhD, Clinical Franchise Leader, Influenza, Sanofi Pasteur

15 min

Clarifying questions (5 min)

COVID-19 Vaccine Development: A Case Study in decentralized clinical trials (DCT) design opportunities

Kourtney J. Davis, PhD, Senior Director and Head, Therapy Area Matrix, Epidemiology, Janssen Research and Development

15 min

Clarifying questions (5 min)

Panel discussion – 30 min

Break – 10 min

Session 4: Panel discussion on COVID-19 and prospects for the use of RWE to support vaccine effectiveness for pandemic/emerging infectious diseases: lessons learned and next steps

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Repurposing data from the CDC influenza vaccine effectiveness surveillance and other CDC sources to evaluate the effectiveness of Covid-19 vaccines

Jennifer Verani, MD, MPH, Medical Epidemiologist, Division of Bacterial Diseases in the National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention

15 min

Clarifying questions (5 min)

The DRIVE initiative: progress toward product-specific influenza vaccine effectiveness in the European Union

Thomas Verstraeten, MSc, MD, Managing Director, P95 Pharmacovigilance and Epidemiology Services

15 min

Clarifying questions (5 min)

Panel discussion – 40 min

End