Role of Real-World Evidence in Regulatory Decision-Making, Before, During, and After COVID-19

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Declaration of Interest

• I am an employee of Aetion, Inc.
• Opinions are my own and not of my employer or any other entity
Agenda

RWE Before COVID-19

Accelerating the Understanding and Use of RWD and RWE

RWE After COVID-19
RWE Before COVID-19
Study Design vs. Data Collection vs. Study Setting

- **Study Design**: Interventional vs. Non-interventional
  - Randomized vs. Nonrandomized
- **Data Collection**: Primary Data vs. Secondary Data
- **Study Setting**: Real-world vs. Clinical Trial
Study Design vs. Data Collection vs. Study Setting

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It's a spectrum!
What is RWD and RWE and How Can It Be Used for Regulatory Decision-making
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Real-world data

Real-world evidence

Operational

Clinical trial efficiency
What is RWD and RWE and How Can It Be Used for Regulatory Decision-making

Operational  Clinical trial efficiency  Safety  Effectiveness
RWE Can Complement RCT as Part of an Evidence Package

While PDUFA and CURES Mandates FDA to Explore RWE for Effectiveness Decision; RWE is Not New to FDA or to Evidence Packages

About the Food and Drug Administration (FDA) Sentinel Initiative

Navigate to the following sections on this page:
- FDA Sentinel Initiative Infrastructure
- History of the Sentinel Initiative

The U.S. Food and Drug Administration (FDA) leads the Sentinel Initiative. FDA created the Sentinel Initiative to meet a mandate by Congress in the FDA Amendments Act of 2007. Through the Sentinel Initiative, FDA aims to develop new ways to assess the safety of approved medical products including drugs, vaccines, and medical devices.

Sentinel. "About the FDA Sentinel Initiative." https://www.sentinelinitiative.org/about
Growing Use of RWE to Support Regulatory Decision

- In 2019, 49 percent of FDA-approved NDAs and BLAs included an RWE study.
- In 2020, that figure jumped to 75 percent.
- In 72 percent of submissions with an RWE study, the study influenced the FDA’s approval decision.
Why Can't We Use Traditional RCTs to Answer All Research Questions?

Intrinsic Value of RWD

• Represents a broader population, and enables sub-population studies
• Collect outcomes that may be prioritized by patients and providers
• Reflects "real-world" prescribing and care
• Studies longer-term outcomes
• Already being collected

“The COVID-19 pandemic is highlighting longstanding inefficiencies in the US clinical trials enterprise, the result being that only a small fraction of ongoing studies for potential therapeutics are expected to produce actionable data,”

- Janet Woodcock, Director, CDER, US FDA (On-Leave), Therapeutics Lead, Operation Warp Speed

Accelerating the Understanding and Use of RWD and RWE
COVID-19 Disrupted Traditional Care and Evidence Generation Paradigms

Pandemic
COVID-19 Disrupted Traditional Care and Evidence Generation Paradigms

Digital Tools and Technology

Practical Trials

Enhanced Observational Studies

To learn more: Duke Margolis Annual RWE Conference: Applying Lessons Learned from RWE in the Time of COVID-19 to the Future
Digital Tools: Bringing Trial and Real-world Studies to Patients

FDA Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Public Health Emergency

March 2020
Updated on September 21, 2020

Guidance for Industry, Investigators, and Institutional Review Boards


June 2020
Updated October 2020

Guidance for Industry and Food and Drug Administration Staff


Assessing COVID-19-Related Symptoms in Outpatient Adult and Adolescent Subjects in Clinical Trials of Drugs and Biological Products for COVID-19 Prevention or Treatment

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Office of New Drugs (OND)
Office of Biologics Review (OBR)
Office of Combustion Product Evaluation and Quality (OPEQ)

U.S. Department of Health and Human Services
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Practical Trials: Randomization, Objective Endpoints, and Large Sample Sizes for Decisive Results

- Enhanced, large simple trial
- Randomization
- Streamlined data collection
  - Objective endpoints
  - Serious adverse events
- Embedded in routine clinical care (EHRs)
## Side Bar: COVID Emergency Use Authorizations (EUAs) and RWE

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<thead>
<tr>
<th>What Is An EUA¹</th>
<th>EUA vs. Traditional Approval Standard²</th>
<th>What Does This Mean?</th>
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| EUAs "allows the use of unapproved medical products, or unapproved uses of approved medical products to diagnose, treat, or prevent serious or life-threatening diseases when certain criteria are met, including that there are no adequate, approved, and available alternatives" | "If, based on the totality of the scientific evidence available, it is reasonable to believe that the product may be effective for the specified use, FDA may authorize its emergency use, provided that other statutory criteria for issuing an EUA also are met" | **Treatments³**  
• New products may enter the market before trial completion (e.g., pre-planned interim analyses)  
• Safety and effectiveness in specific Covid-19 patients and treatment contexts  
**Vaccines⁴**  
• Safety and effectiveness in a clinical trial with at least 30,000 patients and median 2 months follow-up at study conclusion |

"Vaccine benefit-risk considerations are different from therapeutics used for life-saving purposes because vaccines are given to healthy people"

- Steve Anderson, Director, Office of Biostatistics and Epidemiology, CBER⁵

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Building a National RWD Infrastructure to Generate RWE

Real-World Data for COVID-19

FDA
Real-World Data Approaches

Evidence Accelerator
Reagan-Udall Foundation/Friends of Cancer Research managed workstream

Other Government
NIH, VA, PCORI, etc

Sits within a larger RWD Community

Figure Courtesy of Duke Margolis Center for Health Policy
Building a National RWD Infrastructure to Generate RWE

Figure Courtesy of Duke Margolis Center for Health Policy
COVID-19 Spurred Several FDA RWE Engagements

“We are regularly engaging with stakeholders -- medical product industry leaders and scientists, academic researchers, technology companies, state and local governments and patient groups -- to hear from them on how we can come together as a public/private health community to harness the power of data during this emergency.”

-Amy Abernethy, Principal Deputy Commissioner, US FDA

[Image of an article about FDA action and real-world data surrounding COVID-19]

FDA Collaborates with HealthVerity to Evaluate Real-World Data

June 10, 2020

The FDA has signed a multiyear agreement with Pennsylvania-based HealthVerity to evaluate real-world data to support the agency's response to COVID-19.

The healthcare data company has access to records from more than 190 million patients, which can be mined for insights into treatment patterns and to understand more about the disease.

HealthVerity is collaborating with Aetion, a New York-based healthcare software company that also entered into an agreement with the FDA last month.
RWE After COVID-19
What Have We Learned, What's Transient, What's Permanent?

**Today**
- Utility of RWD and RWE - matching the right data with the right question
- Increased familiarity with RWD and RWE
- Multi-stakeholder collaboration

**The Future**
- Expanding COVID capabilities and experiences to other therapeutic areas
- Adoption of infrastructure and tools to streamline clinical trial and real-world study conduct (e.g., EHR data capture, master protocols, novel technologies)
- Advancing RWD quality and methods to analyze RWD to generate high-quality RWE
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Thank you

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