RWD/RWE – Introduction, Challenges and Best practices from Programmer's perspective,

PHUSE India Summer SDE, 12Jun2021

Sasidhar Amilineni, Principal Programmer, Navitas Data Sciences

Disclaimer

This Presentation does not represent views of Navitas Data Sciences and belong solely to the author.

I take full responsibility for the work and errors if any.

Agenda

- Introduction
  - What is RWD/RWE?
  - Why RWD in Drug Development?
- Regulatory Guidelines for RWD/RWE submission
- CDISC and HL7
- Case Studies for RWE
  - Using EHR Data
  - Using Clinical Trial Data
- Role of Programmers and Challenges in RWD/RWE
- Best Practices in RWD/RWE
- Key Takeaways
- Q&A

Source: https://www.fda.gov/news-events/fda-voices/leveraging-real-world-evidence-regulatory-submissions-medical-devices

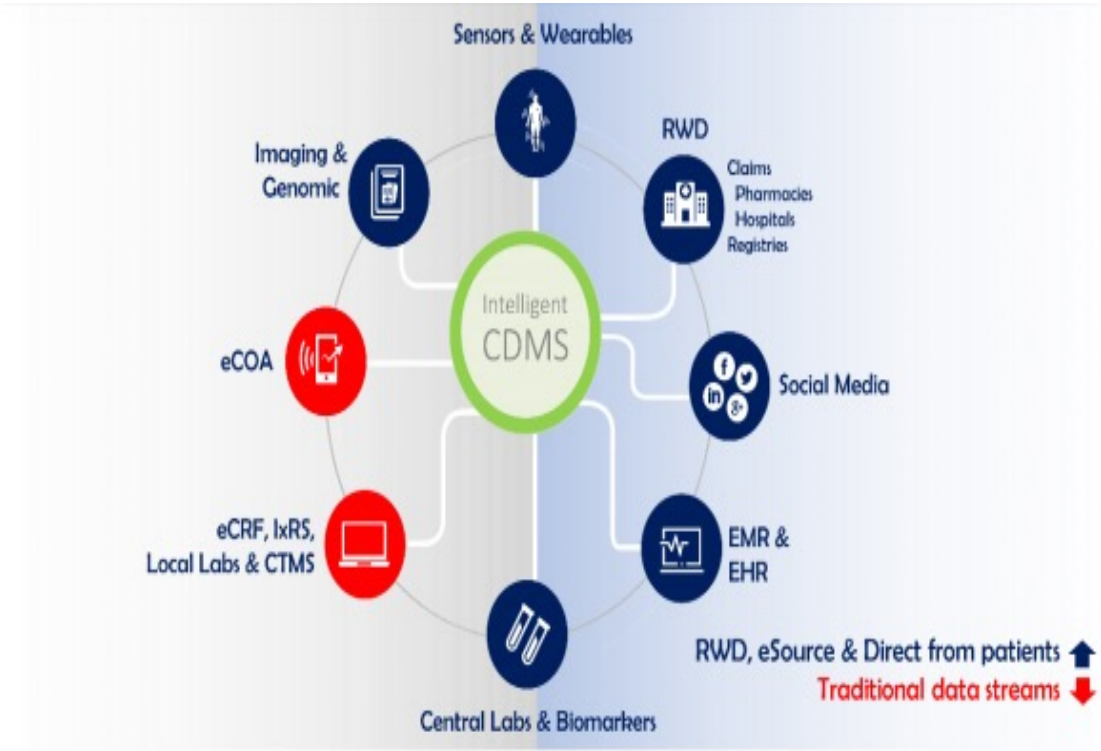
What is RWD/RWE?

RWD

Real-world data are the data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources such as Electronic health records (EHRs), Claims and billing activities, Product and disease registries, Data gathered from other sources that can inform on health status like mobile devices/applications.

RWE

RWE is the clinical evidence regarding the usage and potential benefits or risks of a medical product derived from analysis of RWD. RWE can be generated, for example, by collecting information about effectiveness or safety outcomes from an RWD source in randomized clinical trials or in observational studies.



Source: https://scdm.org/white-papers/

Why RWD in Drug Development?

- In the last twenty-five years we have seen a dramatic shift in the way the pharmaceutical, healthcare, and insurance industries collect, analyze and report data. The rapid adoption and advancement of technology, has brought an explosion of data that may be purposefully curated, combined, and analyzed to provide very useful and timely information.

- The **21st Century Cures Act** was passed in 2016 with the remit to accelerate the **discovery**, **development**, and **delivery** of 21st century cures, and for other purposes. This act also laid the Framework for FDA's **Real-World Evidence Program** to help support approvals for new indications and support or satisfy post approval study requirements.

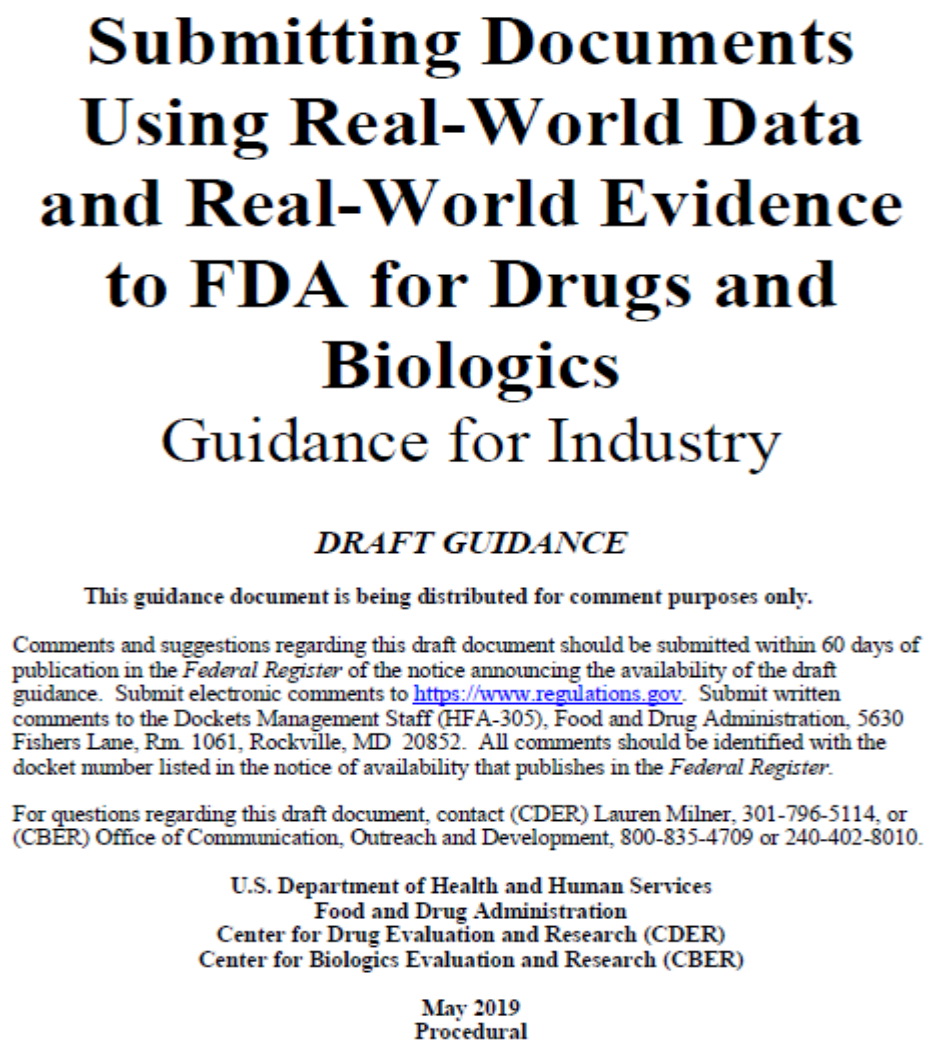
Source: https://smarthealthit.org/wp-content/uploads/CuresActCongress-300x265.png

Regulatory Guidelines for RWD/RWE submission

List of Study objectives which may include RWD/RWE as relevant submission package:

- **IND submissions** for randomized clinical trials that use RWD to **capture clinical outcomes** or **safety data**, including pragmatic and large simple trials.
- New protocols for single arm trials that use **RWE** as an **external control**
- **Observational** studies that generate RWE intended to help to support an **efficacy supplement**
- **Clinical trials** or using RWE to fulfill a **post marketing** requirement to **observational studies** further evaluate safety or effectiveness and support a regulatory decision

FDA encourages sponsors and applicants to consult the appropriate **review division** with questions about whether a specific submission should be identified as containing RWE.



Submitting Documents Using Real-World Data and Real-World Evidence to FDA for Drugs and Biologics

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Lauren Milner, 301-796-5114, or (CBER) Office of Communication, Outreach and Development, 800-835-4709 or 240-402-8010.

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)

May 2019
Procedural

CDISC and HL7

- **CDISC** is focused on **Clinical trial Data standardization**, whereas **Health Level 7** (HL7) standards focus on standards utilized in **real-life healthcare services**. With the advent of RWE or the inclusion of electronic health records in clinical trials, these two worlds now merge together.

- With the publication of the **Fast Healthcare Interoperability Resources** (FHIR) draft standard, a paradigm change was introduced.

- The **HL7 FHIR(**Fast Healthcare Interoperability Resources) standard can serve as an interface between diverse EHR applications delivering real world data in support of RWE.

- Leveraging RWD, CDISC and other established and emerging standards (e.g., HL7-FHIR, BRIDG, OHDSI-OMOP, Sentinel, etc.) have the potential to transform the healthcare industry.

Source: https://www.cdisc.org

Source: https://www.fhir.org

CDISC Partners with Gevity to Facilitate Use of **Electronic Health Record Data** in Clinical Research

- The **FHIR to CDISC project** will leverage Fast Healthcare Interoperability Resources (FHIR), HL7's standard for exchanging healthcare information electronically and CDISC's standards for data collection (CDASH) and data tabulation (SDTM) **to streamline the flow of data from EHRs to CDISC submission-ready datasets**. The mapping and Implementation Guide will be available via the CDISC Library API (source of CDISC standards metadata).

- "As EHRs and other real world data sources play an increasingly important role in clinical research and healthcare decision making, our FHIR to CDISC project is timelier than ever," said Rhonda Facile, Vice President, Development Opportunities.

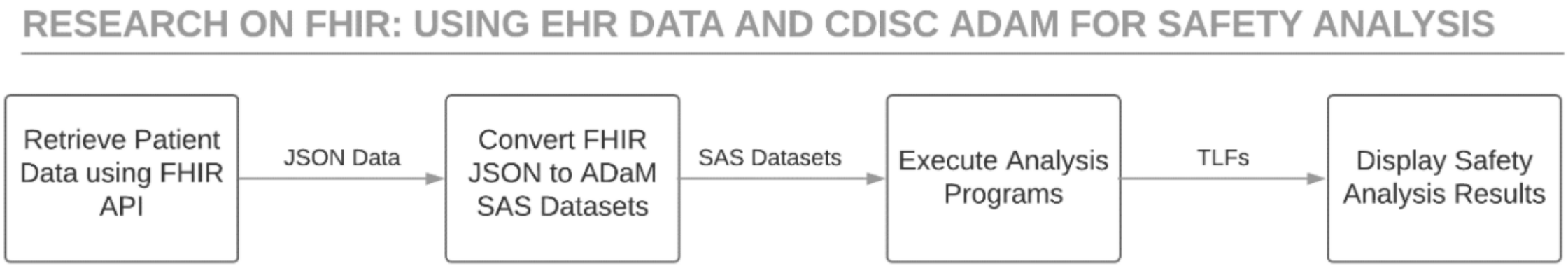
"*Facilitating the development of quality tools to help unlock the benefits of standardization is an essential component of CDISC's Strategic Plan*," stated David R. Bobbitt, CDISC President and CEO.

Source: https://www.cdisc.org/news/cdisc-partners-gevity-facilitate-use-electronic-health-record-data-clinical-research

Case study for RWE using EHR Data

- The **PHUSE Working Group** has demonstrated through a **case study** in 2019 that data typically collected in real world(Eg. diabetes) studies can be extracted from medical records through FHIR resources and the process can be automated to populate eCRFs.

- They have developed a **model** and automated process to extract data from **EHRs** using **FHIR** resources and **APIs** (application programming interface), use these data as input for creating CDISC ADaM analysis datasets, which in turn are used to generate analytics/reports.



Source: PhUSE EU Connect 2019

Case study for RWE using Clinical Trial Data

- Pharmaceutical companies have been working with the US Food and Drug Administration (FDA) to explore new ways to use RWE to support new drug applications (NDAs), supplemental new drug applications (sNDAs), and pre-marketing approvals (PMAs) for medical devices.

- This can be important for new therapies that target rare but serious illnesses with unmet need and low feasibility of a parallel-arm controlled trial. In these and other cases, RWE can play a role in complementing and contextualizing a drug's usage, benefits (in terms of efficacy), and risks (in terms of safety) in order to support accelerated approval.

Six areas where RWE provides advantage

Source: https://www.clinicalleader.com/doc/the-impact-of-mhealth-on-real-world-data-collection-0001

Case study for RWE using Clinical Trial Data

- **Bavencio® (Avelumab),** a drug used to treat Merkel cell carcinoma, a rare and lethal form of skin cancer, provides an example of considering RWE for accelerated regulatory approval.

- **Merck KGaA** and **Pfizer** used RWE from a retrospective observational study to benchmark and contextualize results from their single-arm trial with respect to real-world outcomes in patients treated with chemotherapy.

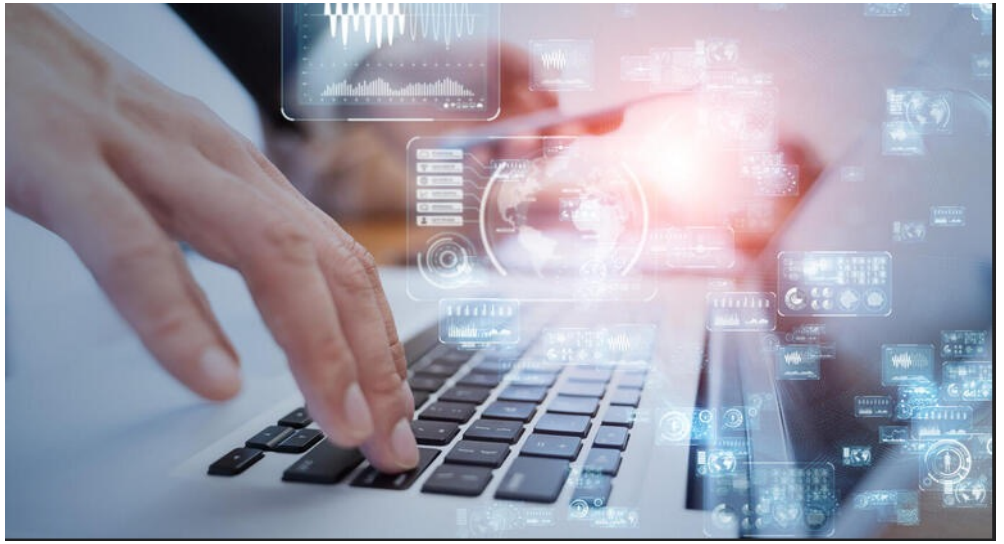
- The **FDA** agreed that the trial efficacy and safety data presented in conjunction with RWE were sufficient to support avelumab's accelerated approval. As a result, avelumab gained accelerated approval only **3 years** after its investigational new drug **(IND)** filing, approximately **1.8 years shorter** than the median for other drugs in expedited programs. (See timeline.)

Source: https://www.analysisgroup.com/Insights/ag-feature/health-care-bulletin/winterspring-2019

Role of Programmers and Challenges in RWD/RWE

In RWD, we receive data from multiple sources like Electronic health records (EHRs), Claims and billing activities, Product and disease registries, mobile devices/applications etc. One of the challenges in obtaining RWE from existing data sources stems from the diverse array of applications used to collect and store healthcare data.

- **Data Reliability**
- **Data Integration**
- **Lack of Clinical Effectiveness**
- **Expertise**



Source: https://www.c-sharpcorner.com/blogs/what-are-some-of-the-best-ways-to-learn-programming

Best Practices in RWD/RWE

- The **International Society for Pharmacoeconomics and Outcomes Research** (ISPOR) and the **International Society for Pharmacoepidemiology** (ISPE) created a task force to make recommendations regarding good procedural practices that would enhance decision makers' confidence in evidence derived from RWD studies.

- Peer review by **ISPOR/ISPE** members and task force participants provided a consensus-building iterative process for the topics and framing of recommendations.

- Seven recommendation by the task force can be found in **https://pubmed.ncbi.nlm.nih.gov/28913966/**

Key Takeaway

RWD/RWE has great promise to transform Research

Leveraging RWD, CDISC, and other established and emerging standards (e.g., HL7-FHIR), have the potential to transform the healthcare industry

FHIR to CDISC

FHIR to CDISC project will streamline the flow of data from EHRs to CDISC submission-ready datasets.

Managing Challenges

RWD is not collected with research as its primary purpose, there are significant challenges in using and representing the data

Helpful Case studies

Learning from Case studies or Live examples will be very helpful for implementation

References

- FDA https://www.fda.gov
- SCDM https://scdm.org/white-papers/
- PHUSE https://phuse.global/Education
- CDISC https://www.cdisc.org
- PUBMED https://pubmed.ncbi.nlm.nih.gov

A TAKE Solutions Enterprise

NAVITAS LIFE SCIENCES

Questions And Answers

Feel free to Ask Us Any Question

A TAKE Solutions Enterprise

NAVITAS LIFE SCIENCES

Driving better outcomes through insights