Real-World Data Considerations

CDISC US Interchange, October 26, 2022

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Meet the Speaker

G. Scott Gordon, PhD

Title: Senior Health Informatics Officer

Organization: U.S. Food and Drug Administration, Center for Drug Evaluation and Research, Office of Strategic Programs

Since 2016, Dr. Gordon has been responsible for a range of activities to standardize data including “real-world data” derived from health information technology for use in clinical research and pharmacovigilance as well as standardization of pharmaceutical quality and manufacturing data for submission to FDA.

Previously, Dr. Gordon worked from 2011 with a focus on public health informatics and entered the public health domain in 2005 in public health emergency preparedness. Prior to a post-doctoral position at the Whitehead Institute for Biomedical Sciences, Dr. Gordon received his core scientific training with a Ph.D. in Molecular Microbiology from Tufts University Medical School.

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- *The views and opinions expressed in this presentation are those of the author and do not necessarily reflect the official policy or position of FDA.*
- *The author(s) have no real or apparent conflicts of interest to report.*
- *This presentation should not be considered guidance, nor a change in guidance, nor does it necessarily reflect FDA's positions*

Agenda

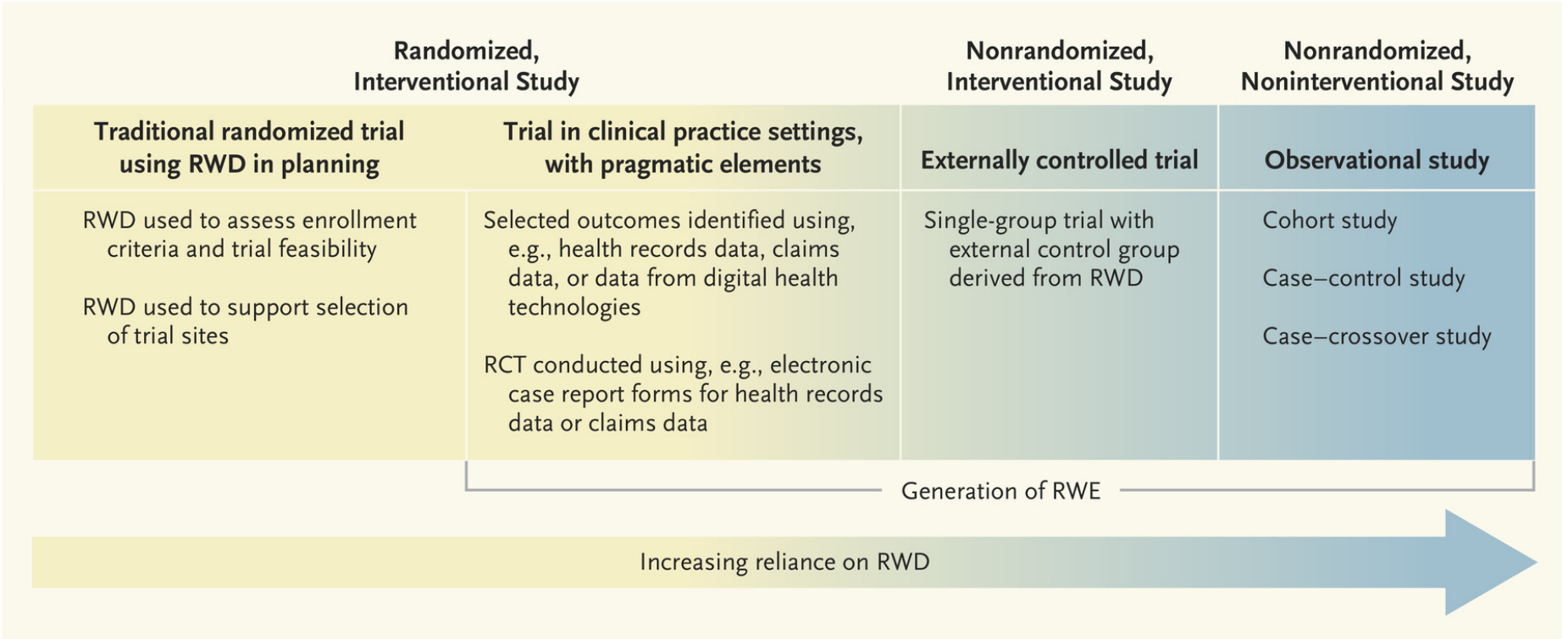
- RWD standards from a CDER-CBER RWE Framework perspective
- Challenges
- Activities

RWD STANDARDS FROM A CDER-CBER RWE FRAMEWORK PERSPECTIVE

Universe of Digital RWD

Real-World Evidence — Where Are We Now?

John Concato, M.D., M.P.H., and Jacqueline Corrigan-Curay, J.D., M.D.

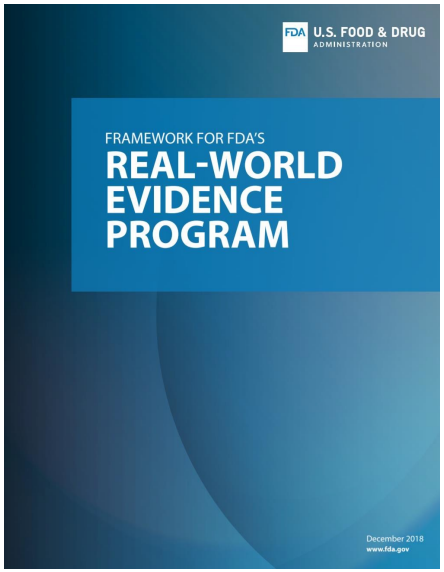


Reliance on RWD in Representative Types of Study Design.

RCT denotes randomized, controlled trial; RWD real-world data; and RWE real-world evidence.

N ENGL J MED 386;18 NEJM.ORG MAY 5, 2022

21st Century Cures – A Path forward for RWE



Scope of RWE Program Under 21st Century Cures Act

Under the Cures Act, FDA's RWE Program must evaluate the potential use of RWD to generate RWE of product effectiveness to help support approval of new indications for drugs approved under FD&C Act Section 505(c) or to help to support or satisfy postapproval study requirements. FDA's RWE Program will also apply to biological products licensed under section 351 of the Public Health Service Act.

https://www.fda.gov/downloads/ScienceResearch/SpecialTopics/RealWorldEvidence/UCM627769.pdf

FDA Draft 'RWE' Guidance: Sep-Dec 2021

Guidance for Industry

DRAFT GUIDANCE

Real-World Data: Assessing Electronic Health Records and Medical Claims Data To Support Regulatory Decision-Making for Drug and Biological Products

Real-World Data: Assessing Registries to Support Regulatory Decision-Making for Drug and Biological Products

Data Standards for Drug and Biological Product Submissions Containing Real-World Data

Considerations for the Use of Real-World Data and Real-World Evidence to Support Regulatory Decision-Making for Drug and Biological Products

https://www.fda.gov/science-research/science-and-research-special-topics/real-world-evidence

‘Data Standards’ Guidance

Data Standards for Drug and Biological Product Submissions Containing Real-World Data

Guidance for Industry

DRAFT GUIDANCE

October 2021
Real-World Data/Real-World Evidence (RWD/RWE)

From Public Presentation:
Real-World Data Webinar Series: Data Standards

Regulatory background and central message of guidance – 3 of 3

Section II

Currently, as stated in the Study Data Guidance, the Agency can process, review, and archive electronic submissions of clinical and nonclinical study data (including those derived from RWD sources) that use the standards specified in the Data Standards Catalog (Catalog).[11] As that guidance explains, the Catalog provides a listing of currently supported[12] and/or required standards, their uses, the date FDA will begin (or has begun) to support a particular standard, the date such support ends (or will end), the date the requirement to use a particular standard will begin (or has begun), the date such requirement ends (or will end), and other pertinent information. FDA is issuing this guidance to provide recommendations to sponsors for complying with section 745A(a) of the FD&C Act using standards specified in the Catalog when submitting study data derived from RWD sources in applicable drug submissions.

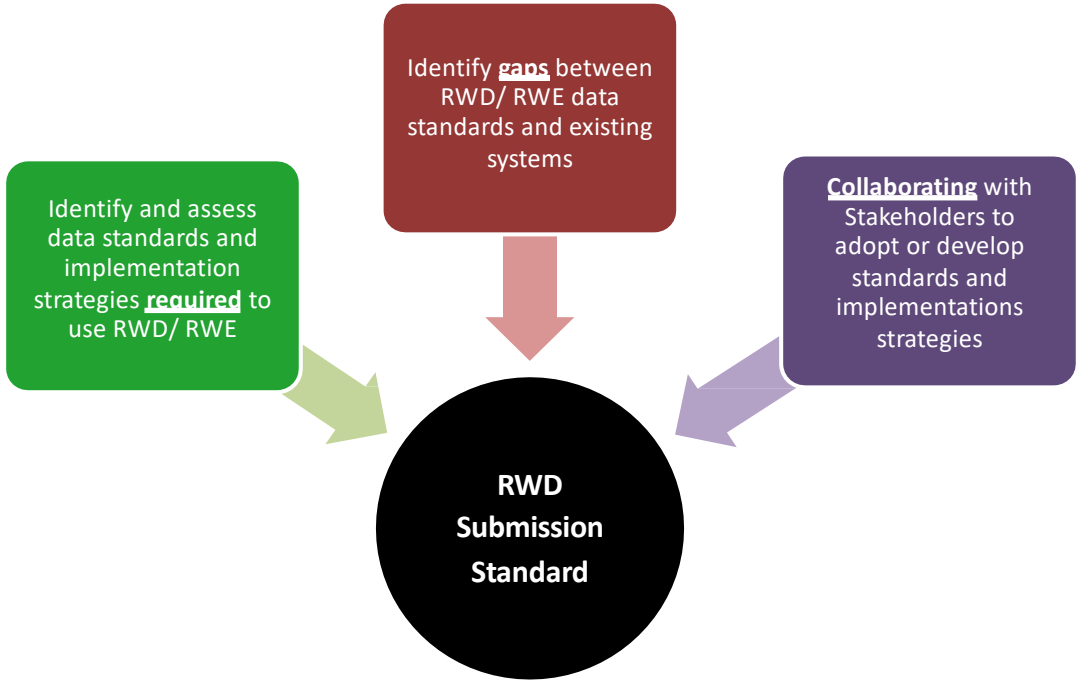
FDA specifies the data standards that must be used for submission of study data

Study data standards requirements apply to RWD submitted as study data

Current allowable study data standards are found in the Data Standards Catalog

From Public Presentation:
Real-World Data Webinar Series: Data Standards

Real-World Evidence Framework: gaps between current submission standards and RWD need to be addressed



CHALLENGES

Overarching Challenges with RWD

- Clinical trials require very specific information collected in clearly specified ways at specified times for specified reasons – all determined by a clinical trial protocol
- Existing standards reflect this
- None of this drives the recording of healthcare data. Healthcare has its own business needs and data requirements.
- Ambiguities abound

From Vulcan RWD Track Report-Out September 2022

Data Standards: Where we are now?

- Current versions of SDTM and ADaM are optimized for expectations of protocol-driven clinical trials with clear data collection mechanism.
- This is different than how typical healthcare practice works
- Current options for sponsors giving data to FDA
  - Use data formats/standards that work for them and their data
    - Case-by-case
    - Massive effort for FDA staff (IT and reviewers)
    - Potential delays in completing reviews
  - Map/transform to CDISC standards that we currently can accept
    - Current versions used at FDA (for example SDTM v1.7, IG v3.3) optimized for clinical research business concepts
    - Mapping of healthcare (or clinical care) concepts = Highly subjective decisions
    - case-by-case
    - Demands extensive documentation
- Both options are non-scalable and will be hard to sustain

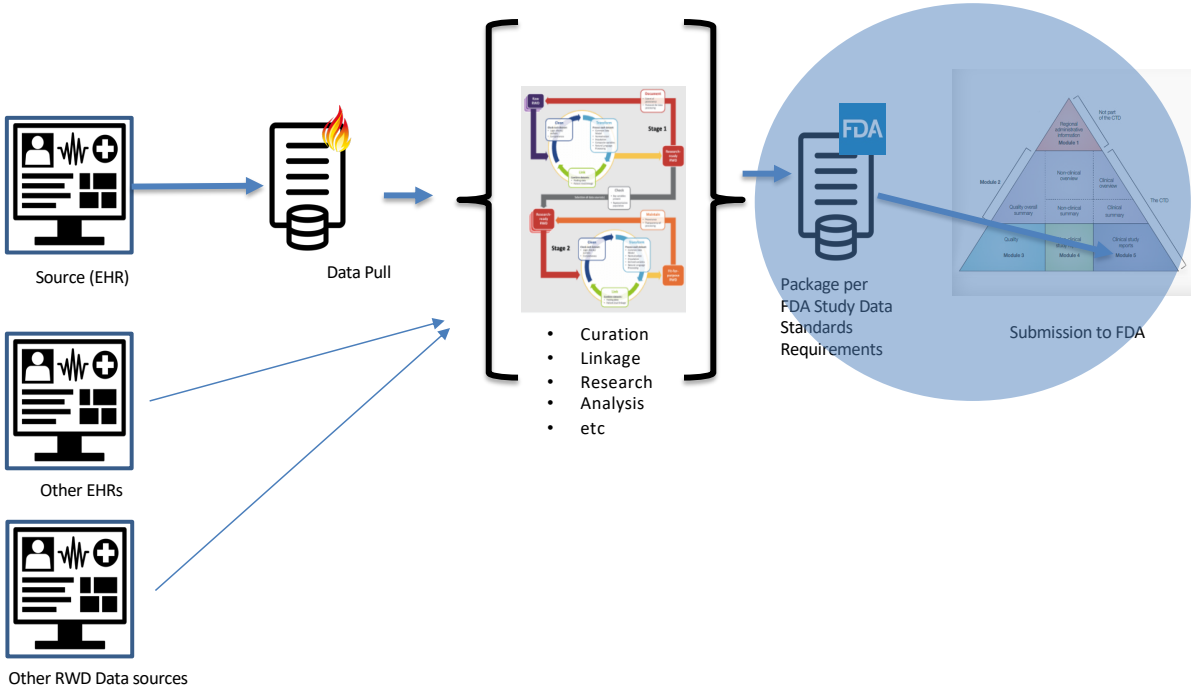
ACTIVITIES

How are we working on this situation?

We are currently working to:

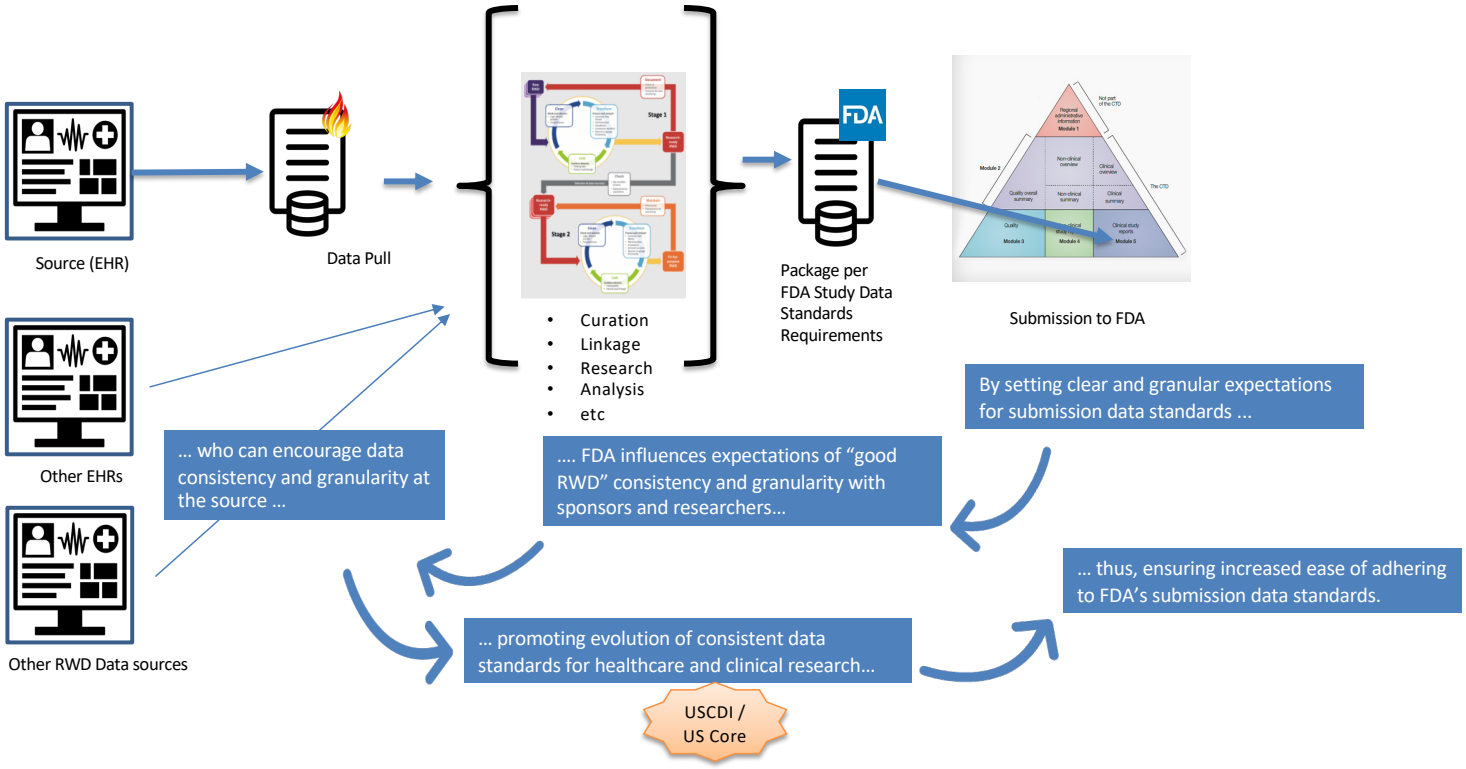
- Evaluate types of research done with RWD
- Evaluate data needed for RWD-based research
- Evaluate how RWD sources supply needed data
- Establish reasonable requirements for data needed from RWD source
- Establish reasonable granular structure, terminologies, etc
- → A first draft table of standardized “content”
  - List of data elements, definitions, cardinalates, etc
- Review proposed content data elements
- Determine approach to a consensus-driven data exchange standard

Focus of our work



Original Data → Preparation/Analysis → Submission to FDA

Potential impact of our work



Participation in Vulcan FHIR Accelerator

Vulcan Vision Statement

Why Vulcan?

Fully integrate research into the delivery of healthcare by streamlining data collection and exchange into a singular process.

What are we doing to reach that vision?

- Collaborating with the international research community to align clinical data and clinical research data at the point of collection.
- Developing out the HL7 FHIR standard to support the bidirectional flow of data.

How will we accomplish this?

- Bridge existing gaps
- Strategically connect industry collaborations
- Maximize collective resources
- Deliver integrated tools and solutions

From Vulcan Overview Slides
https://confluence.hl7.org/display/VA/Vulcan+Accelerator+Home

Vulcan connectathon track:
RWD for Research and Regulatory Submissions

Purpose of Vulcan RWD Connectathon Track

- Develop Implementation Guide with FHIR profiles to represent data that will be supportive of RWD research needs
- Promote standardized use of the FHIR standard at the source
- Facilitate consistent and reliable results from the use of standardized queries
- Ensure retrievable of granular, interoperable data from many RWD sources
- Support the standardization of downstream uses (directly or after transformation) for research submissions to pharmaceutical regulatory agencies.

Participants

These organizations were present at the in-person connectathon Vulcan RWD table on September 17-18, 2022

BioVeras BLOCKCHAIN FOR LIFE SCIENCE

Pfizer

FDA

InterSystems Creative data technology

cdisc

parexel

Droice Labs

VULCAN

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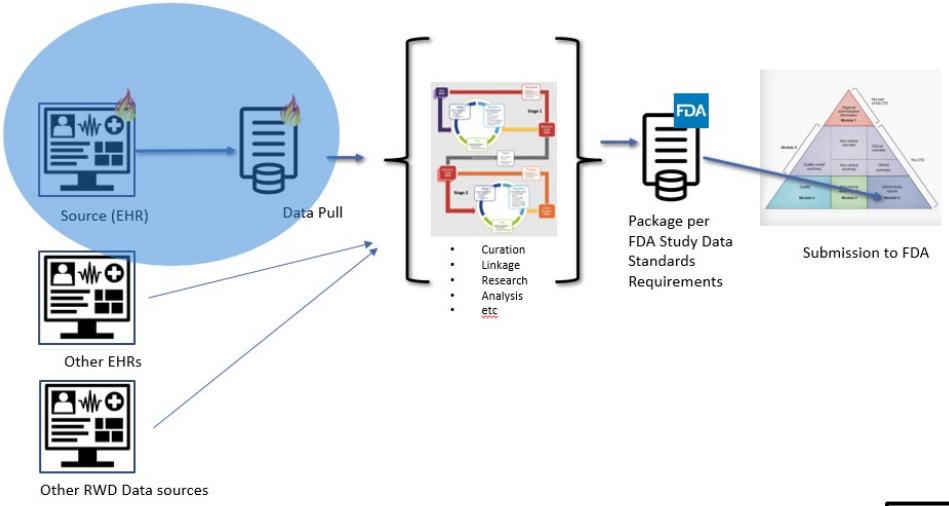
Complementary work with the Vulcan FHIR Accelerator RWD track

Current Scope of Vulcan Real World Data Track



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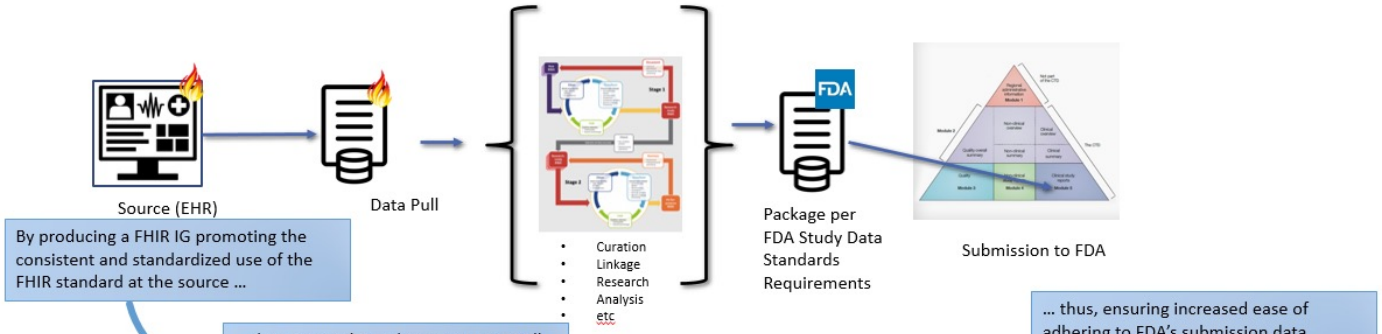
Potential Impact of Vulcan FHIR Accelerator RWD Track



From Vulcan Overview Slides
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Long Term Scope for RWD Submission Standards

- 21st Century Cures Guidance
  - RWD study data ARE study data: must use standards in the Catalog
- Challenge: evolve approaches and standards that will more closely support RWD concepts
- Activities:
  - Evaluating potential approaches
  - Participating in other overlapping initiatives (e.g., Vulcan FHIR Accelerator)
  - One or more of: additional informational guidance, Federal Register Notices, and/or public meetings

Q&A