Clinical Trials and the Use of Real-World Data in Medical Product Development

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Moderated by **John R. Manthei**, Partner, Latham & Watkins LLP

RWE: Challenges and Opportunities

"The more widespread use of [real-world evidence] can make our medical product development process more efficient, and help lower the cost of development. More importantly, it can help make sure doctors and patients are better informed about the clinical use of new products, enabling them to make more effective, efficient medical choices." – former FDA Commissioner Scott Gottlieb

- Real-world evidence (RWE) and real-world data (RWD) have the potential to transform product development and improve patient outcomes
  - RWD relate to patient health status and/or the delivery of health care from a variety of sources
  - RWE is data regarding the usage, or the potential benefits or risks, of a medical product derived from analysis of RWD
- Harnessing RWE presents opportunities and challenges to FDA and industry:
  - Developing a regulatory framework
  - Regulating consumer-reported data
  - Ensuring patient safety and engagement
  - Patient privacy and anonymization of data
  - Interoperability between proprietary systems

Initial Steps

- Conversation has moved from whether RWE should be used in FDA regulatory decision-making to how and in what circumstances
  - Historically used in the context of healthcare delivery, coverage and reimbursement
  - Approvals using RWE to support efficacy claims have occurred when using a parallel control arm is unethical or not feasible
  - Use of prospective observational cohort study to contextualize single-arm efficacy trials expected to increase
- FDA and industry have taken key initial steps, including:
  - Guidance, Use of Electronic Health Record Data in Clinical Investigations (Jul. 2018)
  - Framework for FDA's Real-World-Evidence Program (Dec. 2018)
  - Expansion of RWE Demonstration Project: from RCT replication to prediction

Promise of Further Development

- New Leadership at FDA: backgrounds in and proponents of use of big data
  - Ned Sharpless, Acting FDA Commissioner
    - Previously served as Director of the National Cancer Institute, where he advocated for more extensive use (particularly sharing, integration, and analysis) of big data in the context of cancer research and care
    - Highlighted the use of IBM Watson to support oncology treatment decisions in his time as an academic
  - Amy Abernethy, Principal Deputy Commissioner
    - Joined FDA from Flatiron Health, where she focused on converting EMR data into information that could be submitted to FDA
- FDA and industry are poised to continue to advance the use of RWE
  - Leveraging RWE to support approvals
  - Further guidance contemplated by the Agency's RWE framework

Regulatory Approach to the Use of Real-World Data and Evidence

Eric Solowey
Vice President and Assistant General Counsel
Parexel International
May 2, 2019

Agenda

- 21st Century Cures Act
- Real World Data vs. Real World Evidence
- Framework for FDA's Real World Evidence Program
- Guidance on Use of Electronic Health Record Data in Clinical Investigations

21st Century Cures Act (2016) §3022

PROGRAM

- Establish program to evaluate use of RWE
  - Support approval of a new indication for approved drug
  - Help satisfy post-approval requirements

CONSULTATION

- Consult with interested parties.

FRAMEWORK

- Draft framework for implementation of the program. Framework to include information describing:
  - Sources of RWE
  - Gaps in data collection activities
  - Standards/methods for collection and analysis
  - Priorities, challenges, pilot opportunities

GUIDANCE

- Use program to inform guidance for industry:
  - Circumstances under which RWE would be used within scope of program
  - Standards and methodologies for collection and analysis of RWE
- Draft due Dec. 2021

Real World Data vs. Real World Evidence

REAL WORLD DATA (RWD)

"Data relating to patient health status and/or delivery of health care routinely collected from a variety of sources"

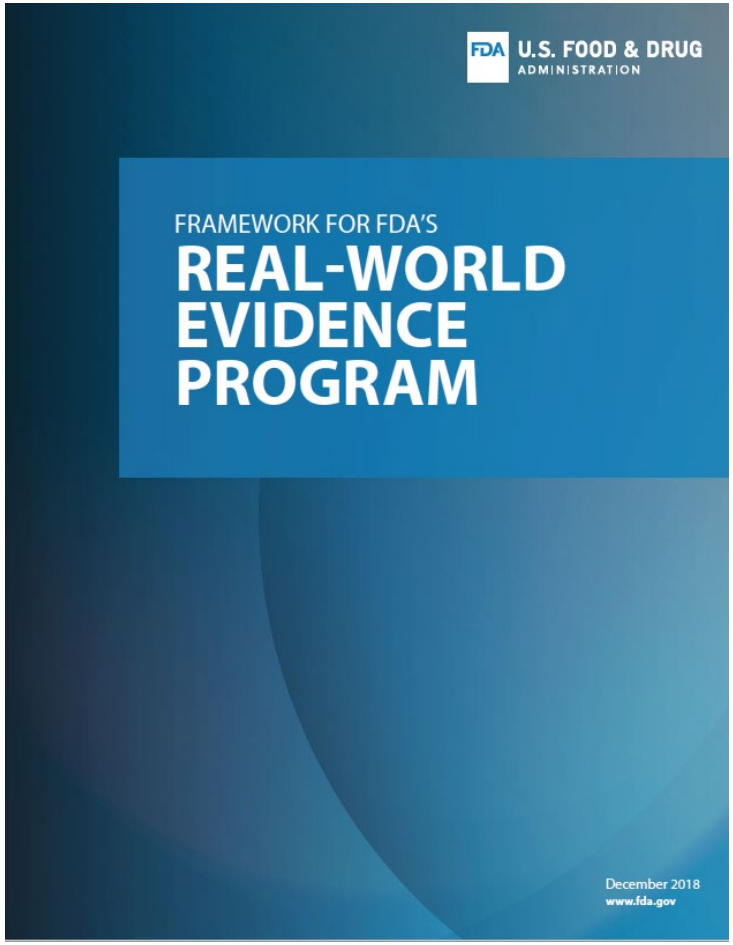
- Electronic health records
- Medical billing and claims
- Product and disease registries
- Data from other sources (e.g. from mobile devices)

[Framework[1] pages 4-5]

REAL WORLD EVIDENCE (RWE)

- "Data regarding the usage, or the potential benefits or risks, of a drug derived from sources other than traditional clinical trials." [21 U.S.C.§ 355g(b)]
- "*Clinical evidence* about the usage and potential benefits or risks of a medical product derived from the analysis of RWD." [Framework page 4]

[1] Framework for FDA's Real World Evidence Program (2018)


FDA U.S. FOOD & DRUG ADMINISTRATION
FRAMEWORK FOR FDA'S
REAL-WORLD EVIDENCE PROGRAM
December 2018
www.fda.gov

Objectives of Framework

Evaluate potential use of RWE to support changes to labeling about drug product effectiveness, including

- Adding or modifying indication
- Change in dose, dose regimen, or route of administration
- Adding new population
- Adding comparative effectiveness or safety information

Framework Considerations

1. Whether RWD are fit for use
2. Whether study design provides adequate evidence to answer the regulatory question
3. Whether study conduct meets FDA regulatory requirements
4. How to develop data standards

1. Whether RWD is Fit for Use

RELIABILITY AND RELEVANCE

- FDA to issue guidance on how to assess reliability and relevance of RWD
  - Medical claims
  - EHR
  - Data from outside US
  - Registries
- Reliability: does data adequately represent underlying medical concepts?
- Relevance: are data fit for the intended purpose?

ADDRESSING GAPS

- FDA to issue guidance on potential gaps in RWD and ways to address
  - RWD may be incomplete or stored in different formats
  - Explore use of mobile technologies, electronic patient reported outcome tools, wearables, and biosensors
  - Explore ways to link data about patient across multiple data sources while protecting patient privacy.

2. Whether Study Design Provides Adequate Evidence for Regulatory Question

PRAGMATIC DESIGN ELEMENTS	*EXTERNAL CONTROL ARMS*	*OBSERVATIONAL STUDIES*
• FDA to develop guidance on trials that include pragmatic design elements for each stage of trial: -recruitment and enrollment; facilitating interventions; assessing outcomes • Pragmatic design = more closely resembles routine clinical practice	• FDA to develop guidance on using RWD to generate external control arms	• FDA to develop guidance about observational study designs • Build upon Pharmacoepidemiologic Guidance (used in safety context) to develop guidance in efficacy context. • Observational Study is a non-interventional clinical study design.

3. Whether Study Conduct meets FDA Regulatory Requirements

ELECTRONIC SOURCE DATA

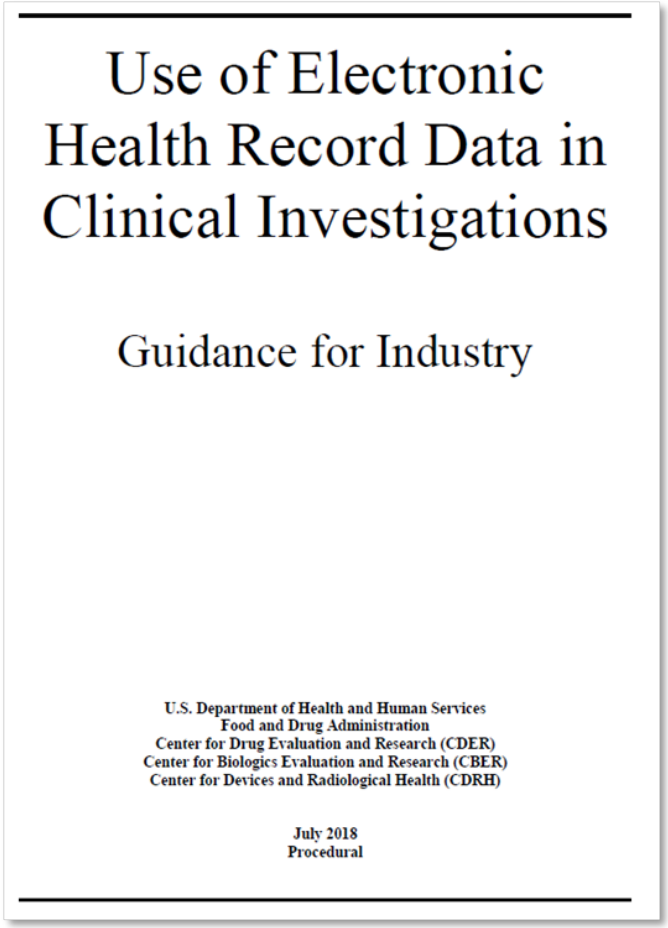
- FDA to consider whether additional requirements are needed on use of electronic source data
- Some standards already exist
  - 21 CFR Part 11
    - Quality, authenticity and reliability of electronic records
  - FDA Guidance (e.g. Electronic Source Data in Clinical Investigations)

STUDIES GENERATING RWE

- FDA to consider new guidance on regulatory considerations raised by different study designs
  - Randomized clinical trials integrated into health care system
  - Observational studies intended to generate RWE for regulatory decision-making
- HIPAA will not be addressed in the Framework

4. Data Standards for RWD and RWE

DATA STANDARDS	*IMPLEMENTATION CONSIDERATIONS*
FDA to identify data standards that apply to proposed uses of RWD/RWE at FDA	FDA to develop implementation strategies, e.g. – Integration with existing FDA systems – Impact on reviewer workload – Tools and training for FDA reviewers


Use of Electronic Health Record Data in Clinical Investigations
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)
Center for Devices and Radiological Health (CDRH)
July 2018
Procedural

FDA Guidance: Using Electronic Health Records in clinical investigations

- FDA expectations when EHR used as a data source in clinical investigations
- Focus on FDA's ability to verify the quality and integrity of the data
- Issued July, 2018
- Guidance issued pursuant to 21st Century Cures Act

FDA Guidance: Using Electronic Health Records in clinical investigations

COVERED	*NOT COVERED*
• Prospective clinical investigations of drugs, biologics and medical devices • Foreign clinical studies not conducted under an investigational new drug application (IND) or investigational device exception (IDE)	• Post-marketing safety studies • Using EHR to evaluate feasibility or for recruitment • Data collected for registries and natural history studies

FDA Guidance: Using Electronic Health Records in clinical investigations (Best Practices)

SECURITY OF EHR SYSTEM

- Policies for use of EHR at site in place
- Appropriate security measures employed to protect study data
- Access limited to authorized users
- Authors of records are identifiable
- Audit trails available to track changes to data
- Records retained for FDA
- FDA encourages use of systems certified in ONC Health IT Program

DATA

- EHR is data originator
- After data entered into eCRF, only investigator or delegated study personnel can modify
- Audit trail of changes
- eCRF signed

UNBLINDING

- Consider whether interoperable EHR and EDC has potential to unblind treatment allocation

INFORMED CONSENT

- Identify parties who can access patient's data

RETENTION/INSPECTION

- Retain EHR records
- Drugs: 2 years after application approved or after investigation discontinued; 21 CFR 312
- Devices: 2 years after investigation end or records not otherwise needed; 21 CFR 812
- Make available to FDA in EHR or certified copies

Thank You

Evaluating Real World Evidence

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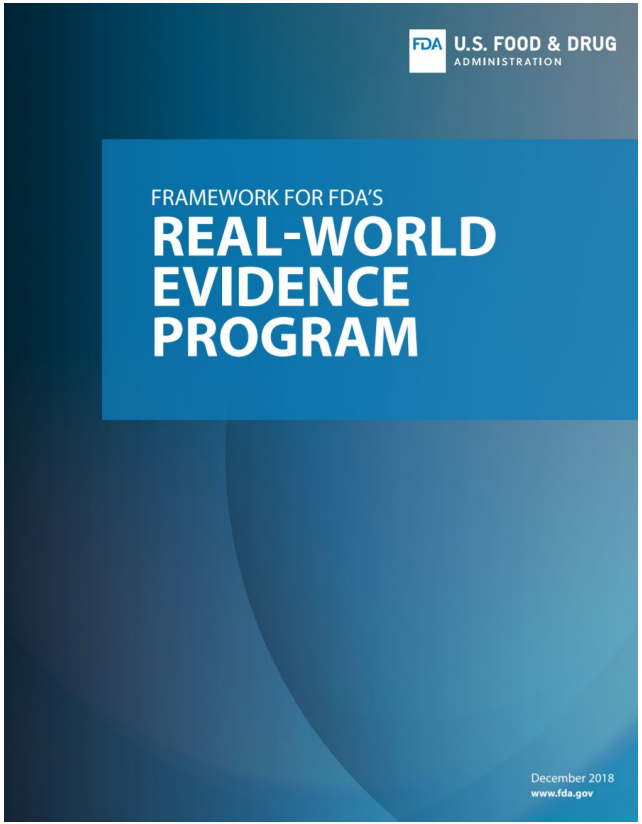
FDLI
May 2, 2019

Disclosure and Disclaimer

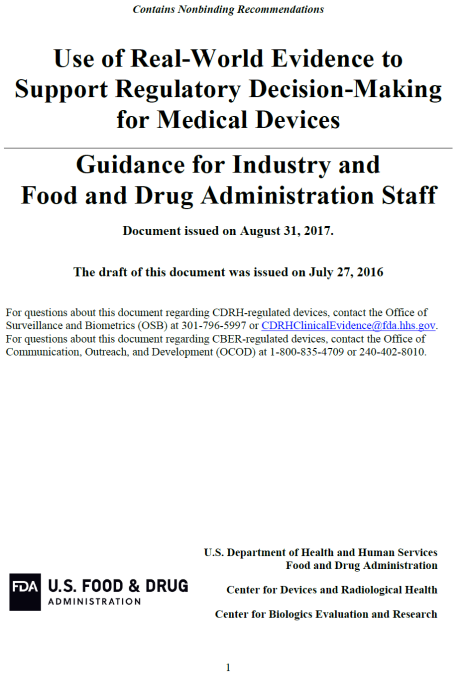
- David Martin received funding from the Patient Centered Outcomes Research Trust Fund to develop the FDA My Studies Mobile App
- No conflicts of interest to disclose
- The views expressed are those of the author and should not be construed as FDA's views or policies
- The mention of commercial products, their sources, or their use in connection with material reported herein is not to be construed as either an actual or implied endorsement of such products by the Department of Health and Human Services



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



Contains Nonbinding Recommendations

Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices

Guidance for Industry and Food and Drug Administration Staff

Document issued on August 31, 2017.

The draft of this document was issued on July 27, 2016

For questions about this document regarding CDRH-regulated devices, contact the Office of Surveillance and Biometrics (OSB) at 301-796-5997 or CDRHClinicalEvidence@fda.hhs.gov. For questions about this document regarding CBER-regulated devices, contact the Office of Communication, Outreach, and Development (OCOD) at 1-800-835-4709 or 240-402-8010.

U.S. FOOD & DRUG ADMINISTRATION

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Center for Biologics Evaluation and Research

1

- FDA guidance document which describes the potential use of Real World Evidence throughout the total product lifecycle for devices
  - Draft issued prior to 21st Century Cures Act
- Definitions of Real World Data and Real World Evidence are harmonized with the FDA Framework
- CDRH, CBER, and CDER are coordinating as the 21st CC RWE program proceeds

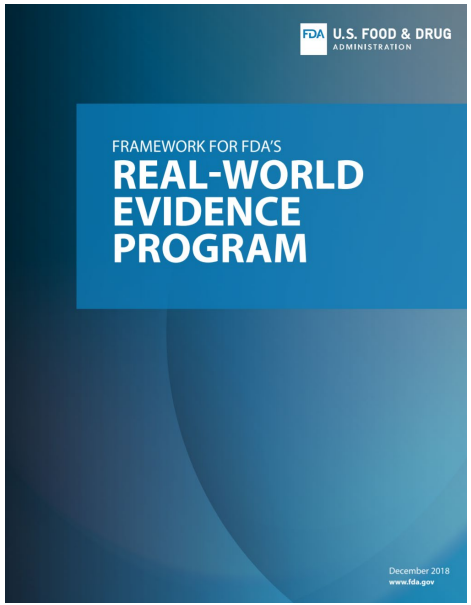
https://www.fda.gov/ScienceResearch/SpecialTopics/RealWorldEvidence/default.htm

Definitions

Real world evidence means data regarding the usage, or the potential benefits or risks, of a drug derived from sources other than *traditional clinical trials*

Real-World Data (RWD) are data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources.

Real-World Evidence (RWE) is the clinical evidence regarding the usage and potential benefits or risks of a medical product derived from analysis of RWD.



- Outlines FDA's plan to implement the RWE program
- Focus on adding or modifying an indication, comparative effectiveness, and comparative safety
- Multifaceted program
  - Internal processes
  - Guidance development
  - Stakeholder engagement
  - Demonstration projects
- Comment period closed April 16, 2019

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

RWE Use is Not New to FDA

Drug	Indication	Status	Data
Lutathera *(lutetium 177 dotate)*	GEP-NET Gastropanc. Neuroendo tumors	Approved 2017	▪ Open label clinical trial ▪ **Analysis of 360 patients in an investigator sponsored, open-label**, single-arm, single institution study of 1214 patients*
Voraxaze *(glucarpidase)*	Treatment of MTX toxicity	Approved 2012	▪ Approval based on open-label, NIH **compassionate Use Protocol**
Uridine Triacetate	Treatment of 5 FU overdose	Approved 2015	▪ Two single-arm, open label expanded access trial of **135 patients compared to case history control**
Blincynto (Blinatumomab)	Treatment of Acute Lymphoblastic Leukemia	Approved 2014	▪ Single arm trial ▪ Reference group weighted analysis of patient level **data on chart review of 694 patients at EU and US study sites***
Carbaglu® (carglumic acid) Tablets	Treatment of NAGS deficiency	Approved 2010	▪ Retrospective, non-random, un-blinded **case series of 23 patients** compared to **historical control group**
Myozyme® (alglucosidase alfa)	Treatment of Pompe disease	Approved 2004	▪ Open-label, non-randomized study of 18 patients compared to **historical control group of 62 untreated patients**
Refludan®	Anti-coagulation in heparin-induced thrombocytopenia	Approved 1998	▪ Two non-randomized, open-label multicenter trials using **historical control comparator group from HIT Registry**

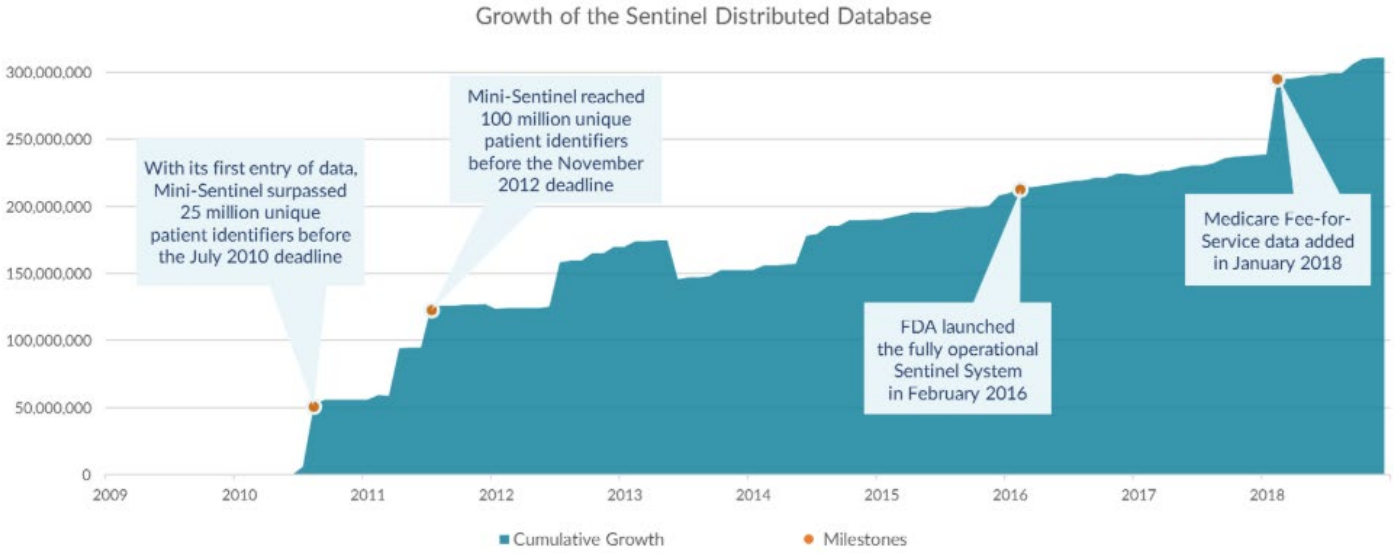
NOT EXHAUSTIVE

Bold = RWE

ANTIZOL (fomepizole) injection

*https://www.nature.com/bcj/journal/v6/n9/full/bcj201684a.html

Sentinel Initiative



310.8 million cumulative patient identifiers between 2000 and 2018

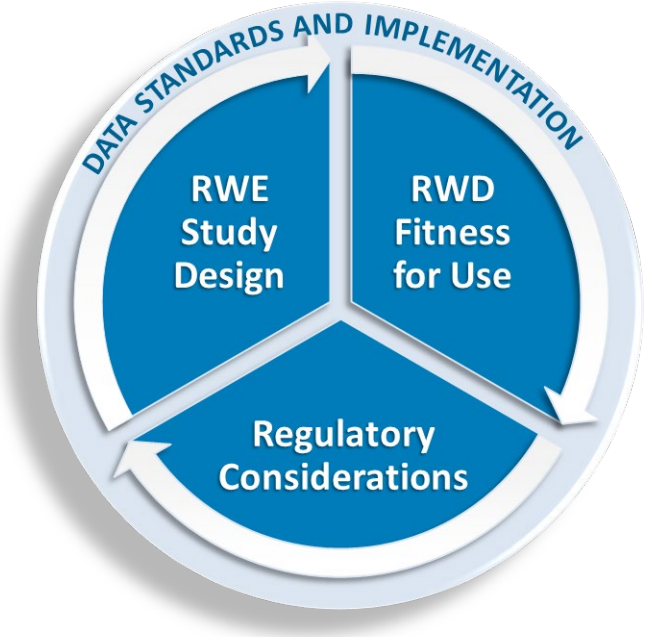
Of members with medical and drug coverage, there are:

- **70.1 million** members are currently accruing new data
- **11.7 billion** pharmacy dispensings
- **15.0 billion** unique medical encounters
- **48.5 million** members with at least one laboratory test result
- **668 million** person-years of data

Benchmark

- Substantial evidence standard unchanged
  - Goal is to distinguish the effect of the drug from other influences such as spontaneous change in disease course, placebo effect, or bias
  - Common practices:
    - Probabilistic control of confounding through randomization
    - Blinding
    - Controlled/Standardized outcome assessment
    - Adjudication criteria
    - Audits

Framework for Evaluating RWD/RWE for Use in Regulatory Decisions



Considerations

- **Whether the RWD are fit for use**
- **Whether the trial or study design used to generate RWE can provide adequate scientific evidence to answer or help answer the regulatory question**
- **Whether the study conduct meets FDA regulatory requirements**

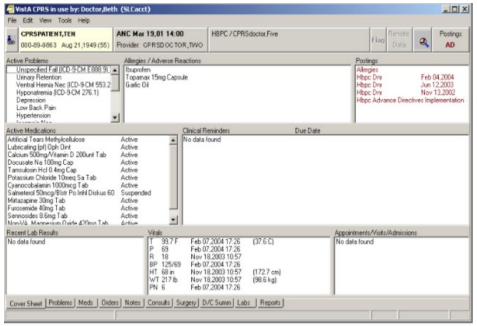
Three Opportunities with Demonstration Projects

- **Expand the quantity, quality, and diversity of RWD**
  - Broaden the range of RCT endpoints that can be captured
  - Increase statistical power
  - Reduce the number of unmeasured confounders
  - Engage with patients through mobile technology
- **Gain practical experience with "Real World" randomized designs and registries**
  - Inform regulatory considerations
- **Assess the performance of non-interventional designs**
  - "Pressure test" widely accepted designs
  - Consider new paradigms

Endpoints in FDA Registrational trials 2007-2015

Type of Endpoint	% of NDA	Examples of Endpoints Measured
Chemistry data	11	HBA1c, pregnancy test, GFR
Hematology	6	Severe neutropenia Apheresis yield > 5 million CD34+ cells/kg
Pathology	2	Increase/decrease of parabasal cells; biopsy proven acute rejection, clearing of anterior chamber cells
Microbiology	6	Sustained virological response, plasma viral load, conversion to negative sputum
Imaging +/- (survival, clinical signs)	17	Bone mineral density; vertebral fractures, spleen volume, progression free survival
Physiological/ functional measurement	9	6 minute walk, normal sinus rhythm, FEV1, sleep studies
Clinical event /clinical sign	19	Death, hospitalization, MACE, MS relapse, Lice free head
CRO/PRO	30	Toronto western spasmodic torticollis rating scale, Hamilton depression rating scale, Rheumatology scale ankylosing spondylitis scale, psoriasis severity index, seizures, sleep, prostate symptom score

EHRs: Potential and Challenge

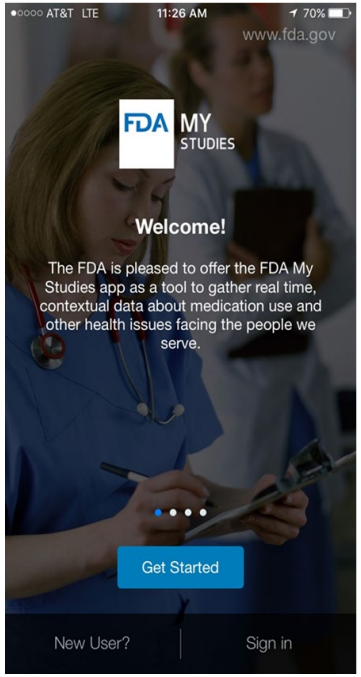


Potential for a more complete and granular clinical picture

Challenges include:

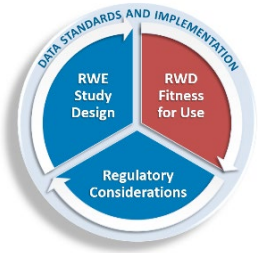
- Data in pathology/ radiology and clinical notes are often unstructured (80%) and images might be necessary
- Structured data ≠ Standardized data
- Typing ≠ consistency/complete documentation
- Clinical outcome measures for drug approvals may not be used or consistently recorded in practice

FDA My Studies



- **Mobile App**
  - Standard frameworks - ResearchKit (iOS), ResearchStack (Android)
  - Gateway capability
- **Web-based configuration portal**
- **Secure Storage Environment**
  - 21 CFR Part 11 and FISMA complaint
  - Partitioned for distributed research
- One private sector research organization has successfully re-purposed the app in a test environment.
- App integral to two new demonstration projects
- **FDA SBIA webinar scheduled for May 9**

FDA MyStudies: now open source

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FDA's MyStudies Application (App)

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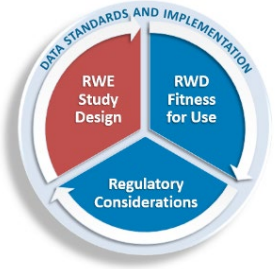
The U.S. Food and Drug Administration (FDA) is posting computer code and a technical roadmap that will allow researchers and developers to customize and use the FDA's newly created MyStudies app. The FDA MyStudies App is designed to facilitate the input of real world data directly by patients which can be linked to electronic health data supporting traditional clinical trials, pragmatic trials, observational studies and registries. It was developed by the FDA and private sector partners, but open source code and technical documentation are being released to the public, so the app and patient data storage system can be reconfigured by organizations conducting clinical research. The app bore the FDA brand while its functionality was tested in a pilot study, but it can now be rebranded by researchers and developers who would like to customize and rebrand the app.

The FDA MyStudies App has several important features, including:

- The data storage environment is secure and supports auditing necessary for compliance with 21 CFR Part 11 and the Federal Information Security Management Act, so it can be used for trials under Investigational New Drug oversight.
- The app is configurable for different therapeutic areas, and health outcomes, which reduces software development hurdles for non-FDA users.
- The data storage environment is partitioned to support multi-site trials or "distributed database" studies.
- The code for MyStudies will be open source so software developers can improve upon its capabilities.

Open source code is being released for two versions of the app. One is built on Apple's ResearchKit (iOS) framework, and the other is built on the open source ResearchStack framework, which runs on Google's Android. (The original FDA-branded app is not currently in app stores because it was removed after being tested in a pilot study.)

- https://www.fda.gov/NewsEvents/Newsroom/FDAInBrief/ucm625228.htm
- https://www.fda.gov/Drugs/ScienceResearch/ucm624785.htm
- https://github.com/PopMedNet-Team/FDA-My-Studies-Mobile-Application-System



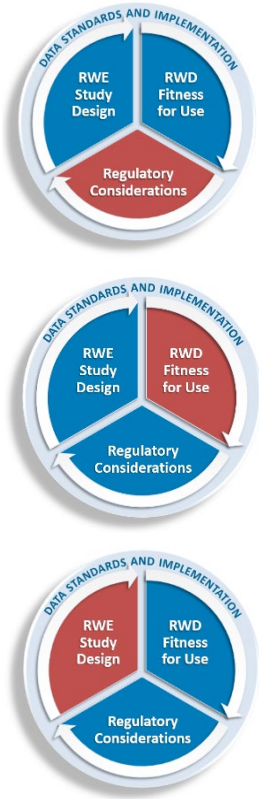
Assessment of Non-Interventional Designs

- High throughput replication of phase 3 & 4 RCTs over three years to provide empirical evidence base to inform the potential level of confidence in high quality non-interventional designs
- FDA reviewers and researchers from the BWH/HMS Division of Pharmacoepidemiology jointly
  - Selected 40 trials in which claims data are sufficiently fit for purpose in a research environment
    - Oral hypoglycemic, novel oral anticoagulant, antiplatelet, antihypertensive, anti-osteoporosis, asthma, COPD, heart failure, anti-arrhythmic, and lipid lowering medications
  - Concurred with pre-specified measures of agreement
  - Reviewed an implementation process
- Goal: 30 attempted replications completed by March 2020

Implementation Process

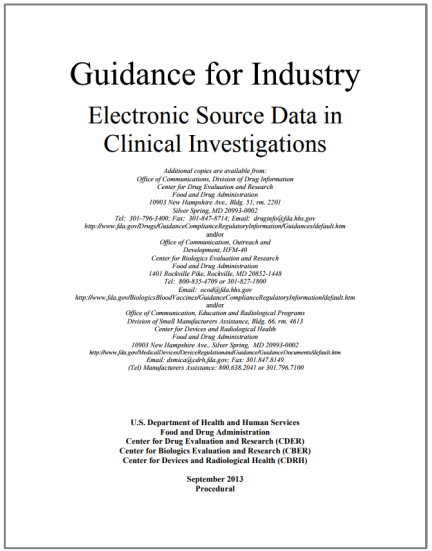
1. Prospective engagement with FDA during protocol development and initial feasibility and power calculations
2. FDA review of final definitions of cohort identification, exposure, outcome, and covariates
3. While blind to differential outcome, final power analyses and covariate balance checks are completed – joint go/no go decision
4. Study protocol registered on ClinicalTrials.gov
5. Analyze outcome data and calculate effect measures
6. Document findings
7. Apply prespecified measures of agreement
8. Audit trail visible to FDA throughout the process – FDA sub-team may at its option engage in additional post-hoc sensitivity analyses for training purposes

RELIANCE trial



- **RofLumilast or Azithromycin to prevent COPD Exacerbations**
  - Randomized "real world" trial; 1,600 adults in each arm
  - **Azithromycin** - macrolide with anti-inflammatory properties
  - **Roflumilast** - noncorticosteroid anti-inflammatory; phosphodiesterase type 4 inhibitor
  - Both guideline recommended but Roflumilast is FDA approved for this indication
- **Primary outcomes**
  - All cause hospitalization
  - All cause mortality
- **Follow-up**
  - 6-36 months, no visits, call center, Patient Portal, Site EMR
  - CMS linkage through FDA-Catalyst for outcomes and exposures
    - Enrollment files: all cause mortality
    - Inpatient claims files: all cause hospitalization for fee for service
    - Part C (Medicare Managed Care): new data source – will request if feasible
    - Part D: medication dispensing
- **FDA-Catalyst privacy-sparing distributed regression validation activity**

Foundation for use of Electronic Data



Guidance for Industry

Electronic Source Data in Clinical Investigations

Additional copies are available from:
Office of Communications, Division of Drug Information
Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Ave., Bldg. 51, rm. 2201
Silver Spring, MD 20993-0002
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Food and Drug Administration
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Email: ocod@fda.hhs.gov
http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/default.htm
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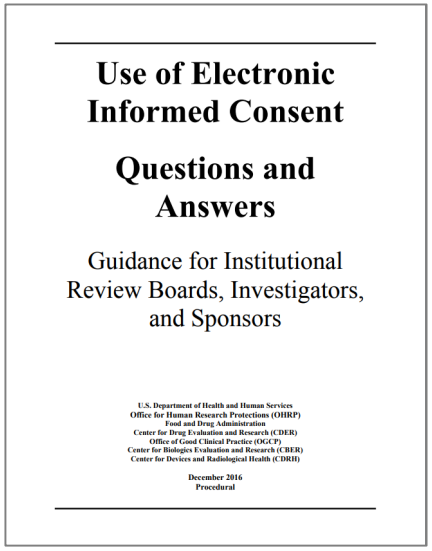
Food and Drug Administration
10903 New Hampshire Ave., Silver Spring, MD 20993-0002
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/default.htm
Email: dsmica@cdrh.fda.gov; Fax: 301.847.8149
(Tel) Manufacturers Assistance: 800.638.2041 or 301.796.7100

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)
Center for Devices and Radiological Health (CDRH)

September 2013
Procedural



Use of Electronic Informed Consent

Questions and Answers

Guidance for Institutional Review Boards, Investigators, and Sponsors

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Office for Human Research Protections (OHRP)
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Office of Good Clinical Practice (OGCP)
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December 2016
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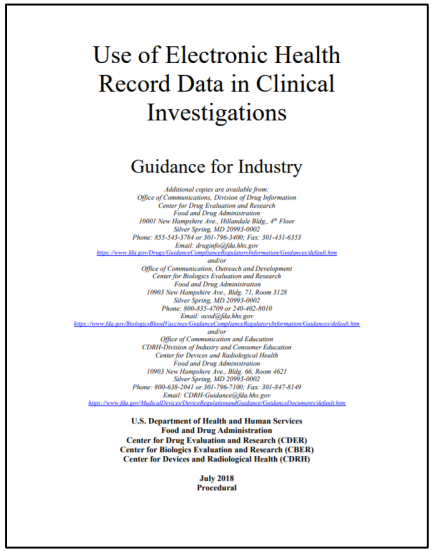

Use of Electronic Health Record Data in Clinical Investigations

Guidance for Industry

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U.S. Department of Health and Human Services
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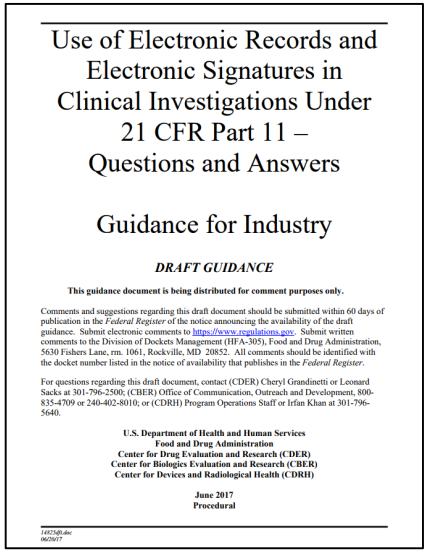

Use of Electronic Records and Electronic Signatures in Clinical Investigations Under 21 CFR Part 11 – Questions and Answers

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 Division of Dockets Management (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) Cheryl Grandinetti or Leonard Sacks at 301-796-2500; (CBER) Office of Communication, Outreach and Development, 800-835-4709 or 240-402-8010; or (CDRH) Program Operations Staff or Irfan Khan at 301-796-5640.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
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June 2017
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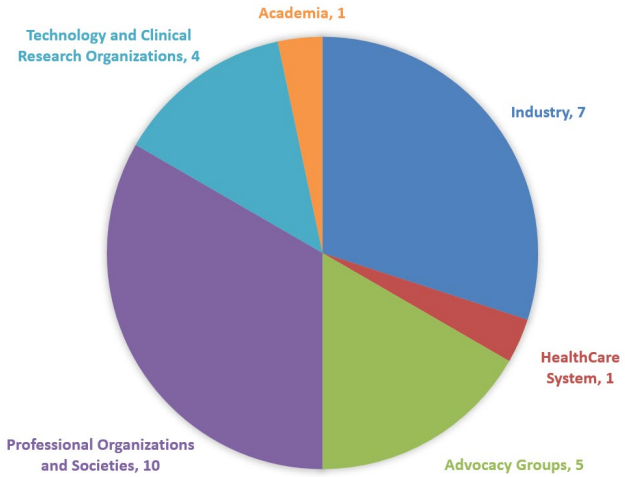
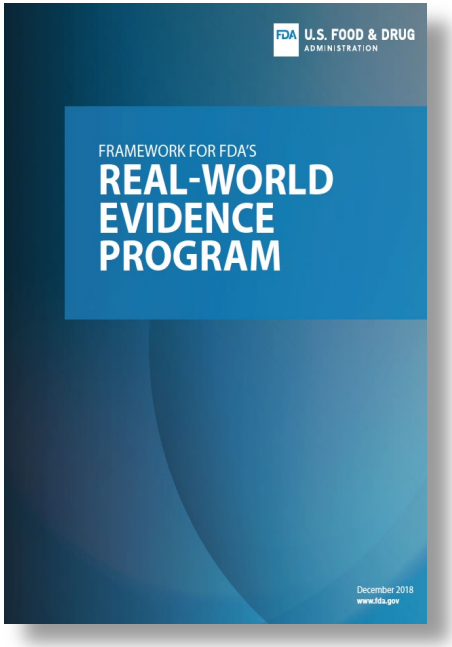
Themes from stakeholder comments



- **Translating regulatory endpoints in real world data sources**
- **Real World Data submission**
- **Data Quality Assessment**
- **Real World study designs**

Conclusion

- Framework serves as a roadmap for more fully incorporating RWD and RWE into the regulatory paradigm
- RWE remains a top FDA priority and it is relevant to other agencies
- FDA is committed to understanding its full potential
- Multi-stakeholder effort and collaborations will benefit everyone



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Use of Real-world Evidence (RWE) for Regulatory Decision-making: An Industry Perspective

Kara Kilpatrick, MPH

Center for Observational Research, Amgen, Inc.

Why should RWE constitute an integral part of the drug development and regulatory cycle?

"As advances are being made in the electronic capture of clinical and patient-reported data, the methods for linking such data to administrative claims and other data types, and the study designs and analytic techniques used to generate evidence, new insights from patient experiences are supporting an array of health care decisions that enable improvement in the quality, safety, and value of care."

Duke Margolis Center for Health Policy

https://healthpolicy.duke.edu/sites/default/files/atoms/files/dg_1_15_16_0.pdf

Ideal incorporation of RWE could facilitate faster, more relevant, and more targeted benefit-risk decision-making.

The evolving regulatory and broader external environment

FDA Expands Real-World Evidence Partnership with Brigham and Women's Hospital and Aetion

RCT DUPLICATE adds new studies to inform FDA - the first to use real-world evidence to predict treatment safety and efficacy

AETION

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TriNetX raises $40M Series D for real-world evidence research platform

The funding will fuel the company's international expansion as well as development of its analytics platform.

By **Dave Muoio (/content/dave-muoio)** | March 14, 2019

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Worldwide Outlook on the Real World Evidence (RWE) Solutions Market 2019-2024 - Emerging Roles of Wearable Devices & AI in RWE Presents Ample Opportunities

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Features

Real World Evidence Developments Across the Globe

This article investigates how Real World Data and Real World Evidence are evolving across the U.S., Europe and Asia.

BIOPHARMA, DIAGNOSTICS

Flatiron, Foundation Medicine study points to real-world data's utility in oncology

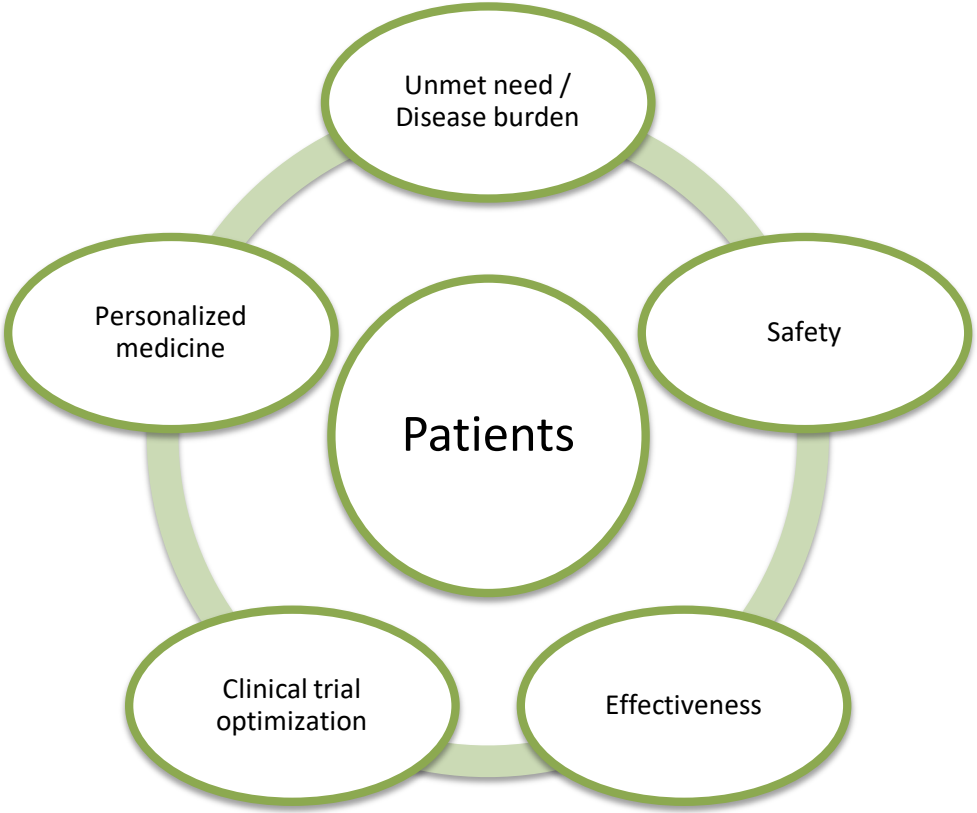
Data published in JAMA on lung cancer patients treated with immunotherapy drugs, gleaned from EHRs and genomic sequencing, backs up clinical trial data and validates clinico-genomic database, the companies said.

By ALARIC DEARMENT

Post a comment / Apr 9, 2019 at 3:00 PM

Madhur Garg, Real World Evidence and Market Access, Sciformix, a Covance Company04.05.19

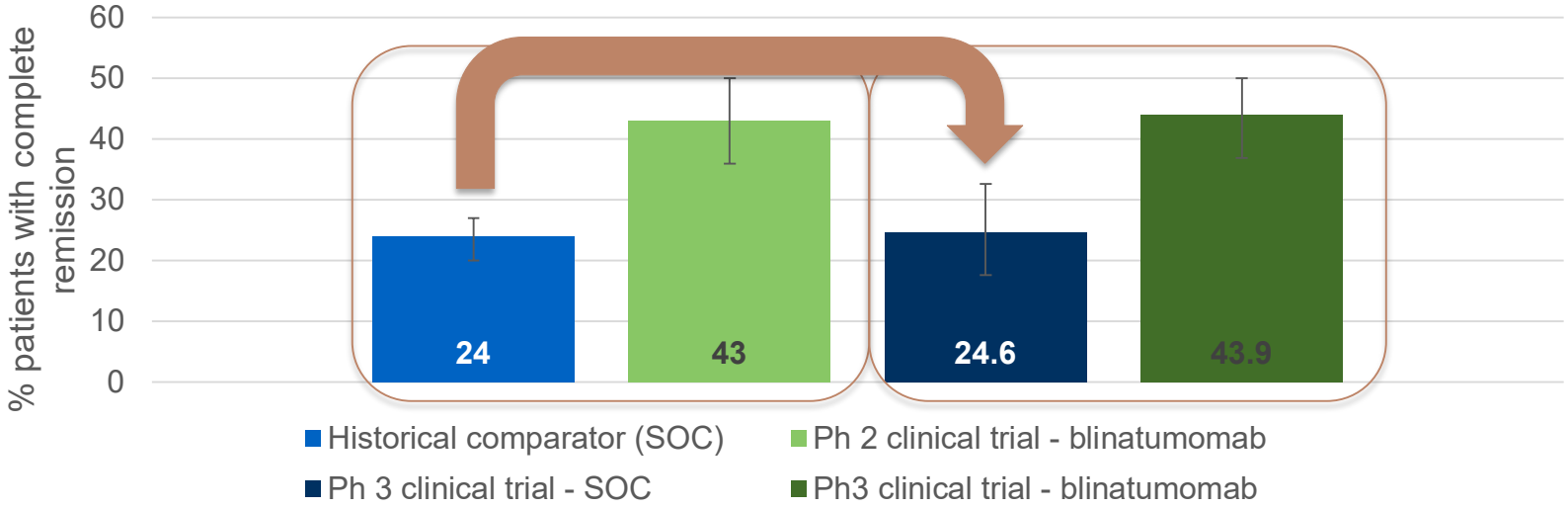
Where is the opportunity?



"As the breadth and reliability of RWE increases, so do the opportunities for FDA to make use of this information."

Scott Gottlieb, Former FDA Commissioner, *National Academies of Science, Engineering, and Medicine*, Examining the Impact of RWE on Medical Product Development. September 19, 2017.

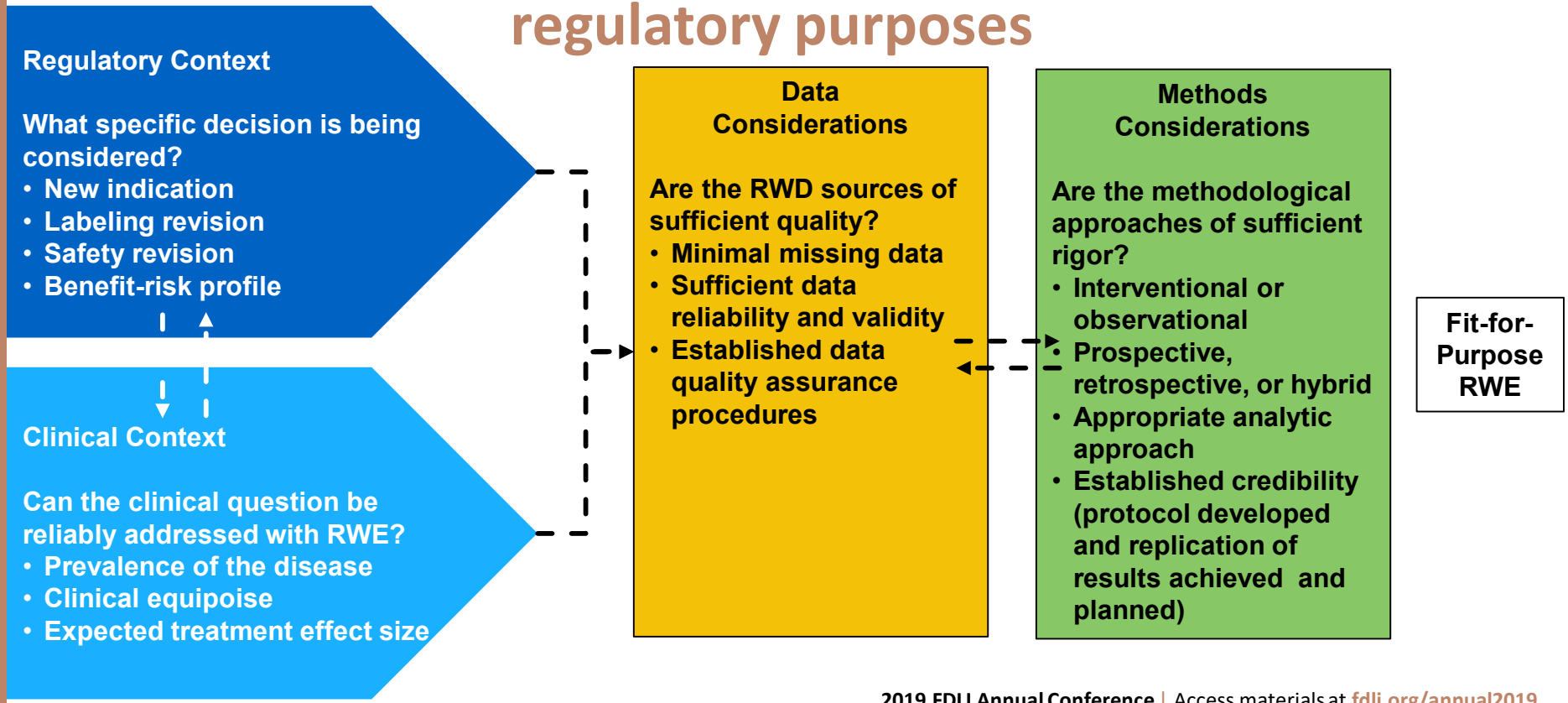
Leveraging RWE to obtain new product approval for blinatumomab



Gokbujet et al. Blood Cancer Journal, 2016; Kantarjian et al. NEJM, 2017

Complete remission (and median overall survival) in the historical comparator group was confirmed by the blinatumomab phase 3 clinical trial standard of care (SOC) arm

Success of a RWE use case will depend upon scientific credibility of the study design and if data are fit for regulatory purposes



Reference: Duke-Margolis Center for Health Policy White Paper. A Framework for Regulatory Use of Real-world Evidence 13 September 2017

Although importance of RWE is appreciated by industry, barriers to its use to inform regulatory decisions remain

- **Knowledge, awareness and certainty**
  - Lack of understanding of observational research methodology
  - Mistrust of data captured outside of RCTs
  - Regulatory guidance for use of RWE evolving
- **Talent and capabilities**
  - Product development organizations have been optimized to deliver RCTs
  - Lack of experience across organizations on impactful use of RWE
- **Systems and processes**
  - Lack of 'fit for purpose' processes for observational research
  - Organizational structures must facilitate effective interaction between individuals with RWE expertise and team leaders (decision makers)

The visible support of senior leaders across the health care ecosystem will facilitate and de-risk appropriate use of RWE

To advance these efforts, collaboration and transparency are critical

Academic, industry, and regulatory scientists