# Key Messages and Themes from the September 13th FDA/Duke-Margolis Workshop: Generating Fit-for-Purpose Evidence

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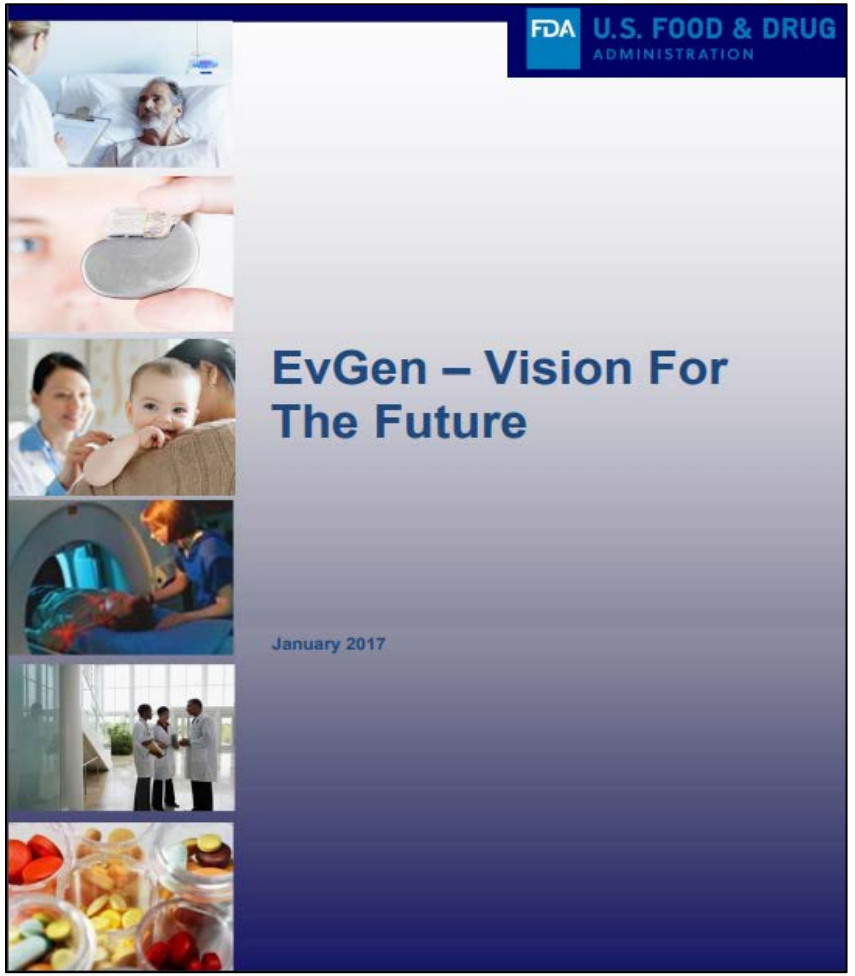
# FDA has identified a set of goals for contributing to a learning health care system

- Leverage previously isolated data systems in a way that ensures available information collected during healthcare-related activities (e.g., medical research, medical product development, clinical care) enhance:
  - Patient care
  - The body of clinical evidence
  - Healthcare delivery
  - Policy decisions
- Develop a learning health care system by combining insights, expertise, and technologies from across the spectrum of federal and private health sectors



# Recent legislation directs FDA to explore further uses of RWE within the regulatory framework

## Prescription Drug User Fee Act VI

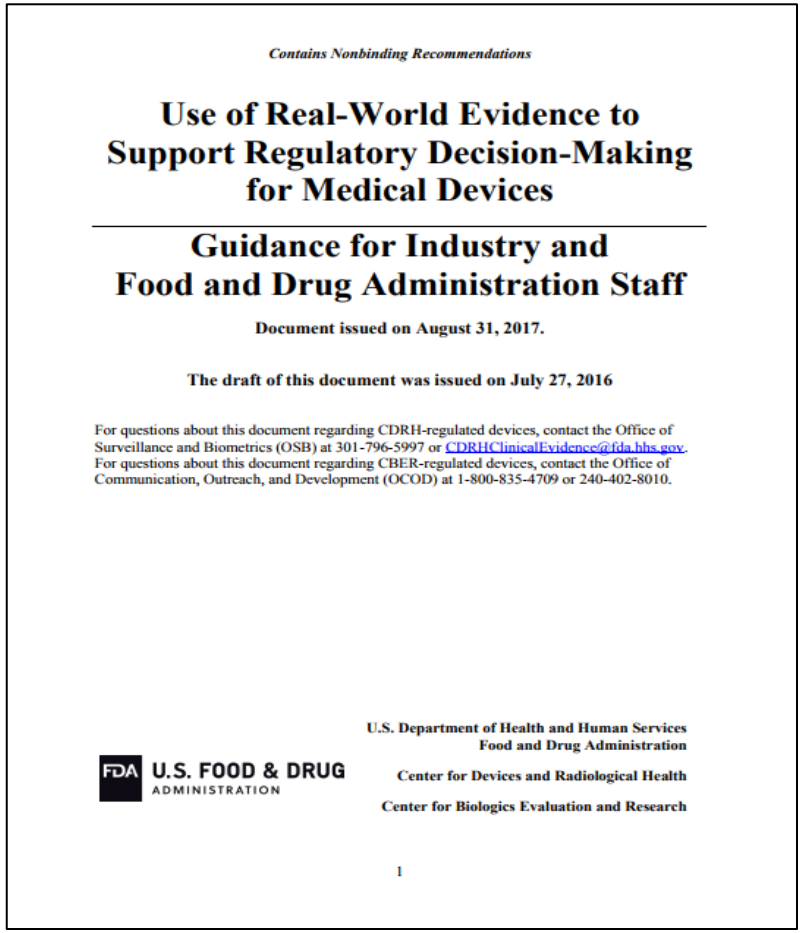
- Requires FDA to enhance use of RWE for use in regulatory decision-making
- FDA must:
  - Hold a public workshop with key stakeholders (e.g., patients, industry, academia) by the end of 2018
  - Initiate (or fund) activities (e.g., pilot studies or methodology development projects) aimed at addressing key concerns and considerations in the use of RWE by the end of 2019
  - Issue draft guidance by the end of 2021

## 21st Century Cures Act

- Requires FDA to establish a program to evaluate the potential use of RWE to:
  - Help support the approval of new indications for an approved drug
  - Help support or satisfy post approval study requirements
- FDA must issue:
  - A draft framework for this program by the end of 2018
  - Draft guidance by the end of 2021

# FDA has finalized guidance on using RWE for Medical Device Regulatory Decisions

- Released in August 2017
- Describes the characteristics and sources of RWD and RWE that may be sufficient for use in regulatory decision-making related to medical devices
- Preceding draft guidance was released In July 2016:
  - Provided insight into how the agency plans to evaluate RWD for various regulatory decisions and
  - Clarified when an Investigational Device Exemption (IDE) may be needed to prospectively collect and use RWD for the purposes of determining the safety and effectiveness of a device



*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. Department of Health and Human Services
Food and Drug Administration

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Center for Devices and Radiological Health

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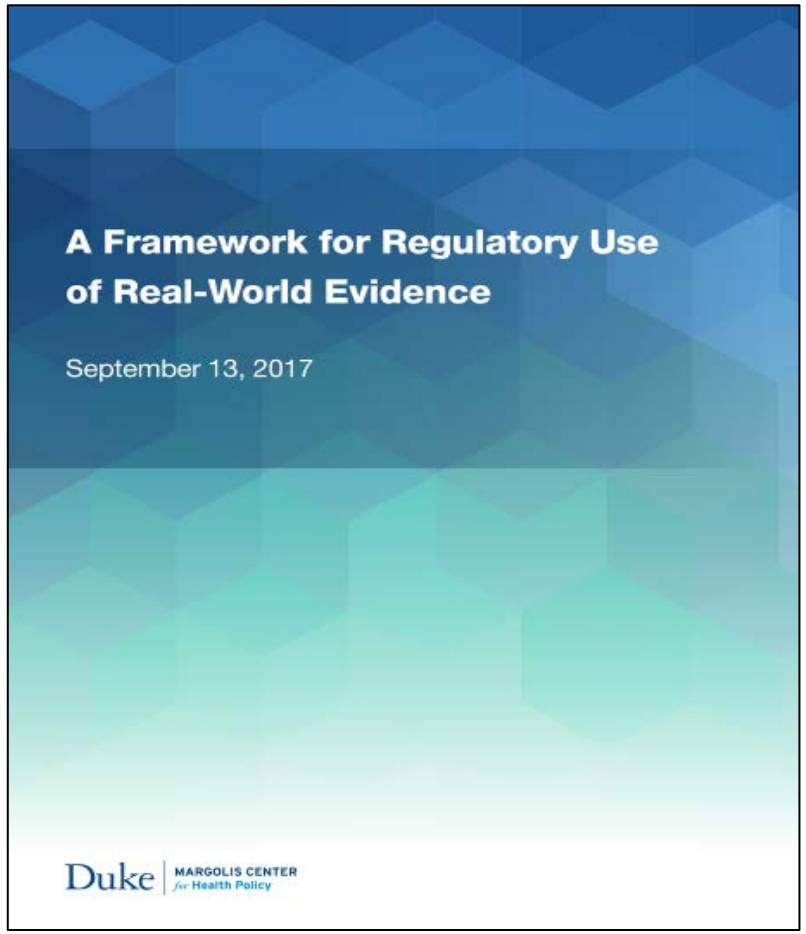
# FDA and Duke-Margolis have pursued early work on regulatory acceptability of RWE

- Joint FDA-Duke cooperative agreement
- Work to date has included:
  - Formation of an RWE working group in summer 2015
  - Expert workshop: Incorporating Evidence from Clinical Experience in Regulatory Decision-Making: A Pragmatic Approach to Randomization in the Clinical Setting – January 15, 2016
  - Public workshop: Enhancing the Application of Real-World Evidence in Regulatory Decision-Making – March 3-4, 2016
  - Public workshop: A Framework for Regulatory Use of Real-World Evidence – September 13, 2017
  - White paper: A Framework for Regulatory Use of Real-World Evidence

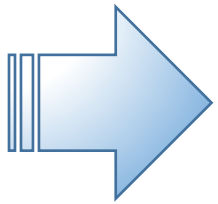
# Duke-Margolis paper on regulatory use of RWE

- Released in September 2017
- Proposes a framework of considerations to guide sponsors and FDA in RWE discussions, and puts forward near term steps on priority issues
- Intends to help clearly establish the current RWD/RWE landscape and the potential process that stakeholders should go through when assessing RWE approaches for regulatory use
- Seeking comments and input on framework and potential activities
- Synthesized comments and additional worked case examples will be released later this fall



# Stakeholders need clarity on key terms

- **Real world data (RWD)** is 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 evidence derived from RWD through the application of research methods.
- For regulatory applications, RWE can further be defined as clinical evidence regarding the use and potential benefits or risks of a medical product derived from analysis of RWD.

*How we define RWD/RWE has follow-on implications for discussing how to develop and use both within stakeholder decision making processes*

# Fit-for-purpose RWE for regulatory use

## Regulatory Context

The intended regulatory use will dictate how RWE is produced and evaluated:

- Postmarket Monitoring Commitments and Requirements
- Label Changes
- Pivotal Study for approval of new drug or biologic

## Clinical Context

Variations in patient characteristics and care will impact type of RWE required:

- Rare vs. common condition
- Chronic vs. acute episodes of care
- One-time vs. multiple doses of treatment
- Specific treatment vs. regimen which changes overtime

## Data Development

Ability to collect reliable, credible and timely data on patient outcomes varies by:

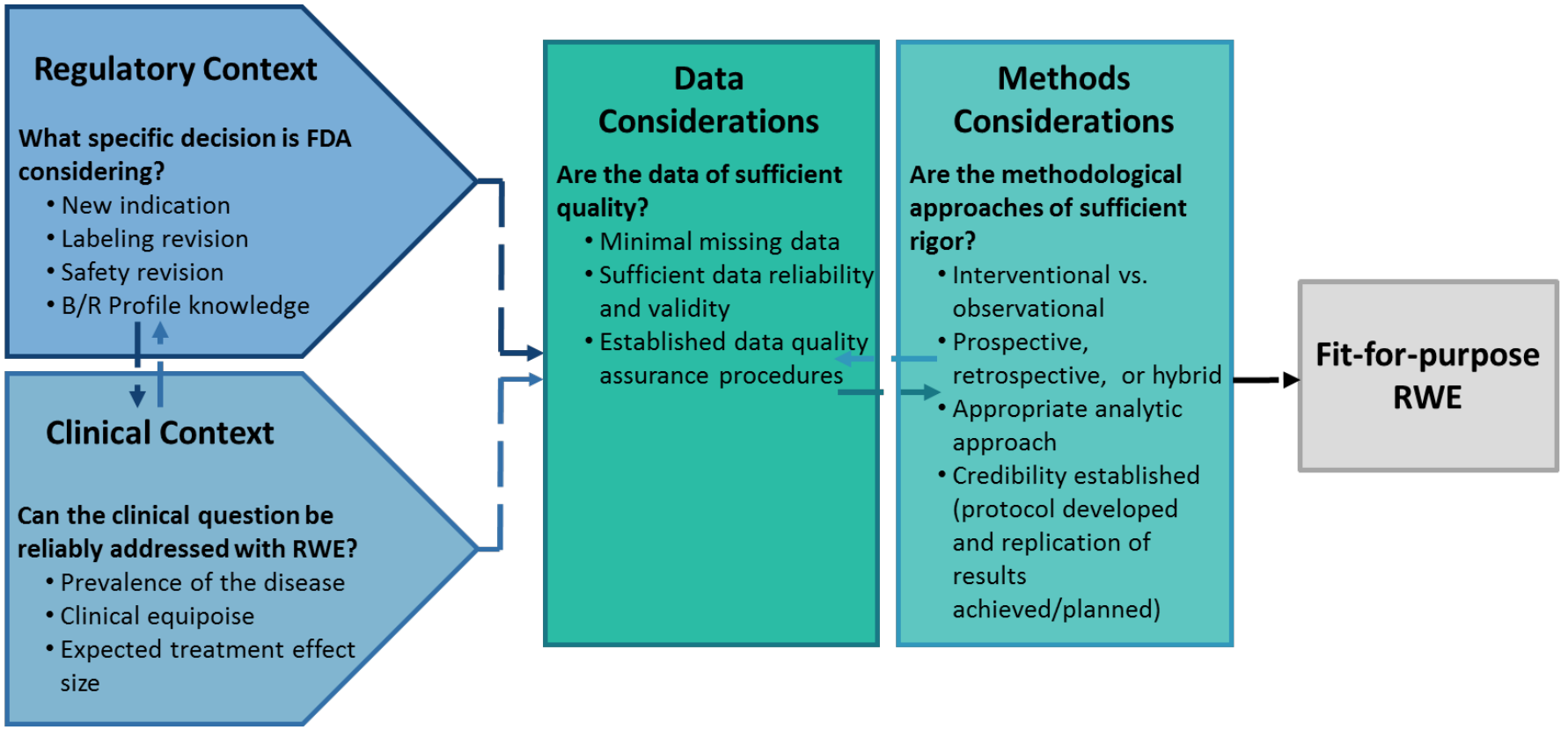
- Provider types and settings
- Benefits coverage
- Adequacy of clinical documentation of relevant information
- Individual patient actions to seek care

## Design Methods

Researchers may chose design elements to build studies that meet their regulatory goals:

- Treatment assignment (interventional vs. observational designs)
- Prospective vs retrospective designs
- Choice of analytic tools
- Reproducibility

# Considerations for Generating RWE Fit for Regulatory Purposes




*Matching data sources and methods to answer specific clinical and regulatory questions will dictate vary inappropriate g applicability of RWE for different regulatory use cases*

# September 13 Workshop: Data Highlights

- Eliminating the barrier between research and care for purposeful collection
- Incorporating good provenance and traceability of data sources improves the credibility of RWD
- Integrating the patient perspective into RWD collection and evidence generation
- Prioritizing data governance and stewardship to support data sharing activities
- Utilizing innovative data platforms (e.g. IBM's Block Chain Platform) which can enable more secure aggregation of patient data from a wide-array of sources such as EHRs, claims and billing, devices, patient-generated information, etc

# September 13 Workshop: Methods Highlights

- Developing quality evidence requires robust primary data sources, use of appropriate analytic methods, good procedural practices and the ability to reproduce the study design with different data sources
- Promoting analytic plans that are transparent and specified in advance
- Establishing methods for a totality of the evidence approach across the drug development and post-market continuum
- Linking RWD such as claims can support the identification of key safety outcomes
- Ascertaining appropriate endpoints in real-world settings is still a challenge
- Emphasizing methods development for observational designs over randomized designs may be a near term priority

# Regulatory acceptability will have a synergistic effect on infrastructure and other uses for RWE

- Many other areas where better, more robust evidence from the clinical setting will improve health and health care:
  - Providers and payers are moving toward alternative payment and reimbursement models focused on value over volume
  - Improved evidence on real-world outcomes helps support clinical decision support tools and revised clinical practice guidelines
  - Clear pathways for including patient-generated health data into product labeling and regulatory decision-making will continue to make patients more engaged partners in data generation and their own treatment plans

# Further steps are needed to accelerate RWE development and use

- Policy goals of expanded RWE in a learning health care system will require significant private leadership and investment
  - More efficient approaches for reliable RWE development needed
  - All stakeholders can contribute to the development of reusable infrastructure for developing reliable fit-for-purpose data and robust methods
- To sustain investment, stakeholders need to demonstrate that RWE can support important decisions
  - Practical uses of RWE are still limited
  - Consensus best practices and acceptable uses need further development
- NASEM, Duke-Margolis, and other collaborative stakeholder efforts can advance these goals