Near-term opportunities to leverage RWE for regulatory use

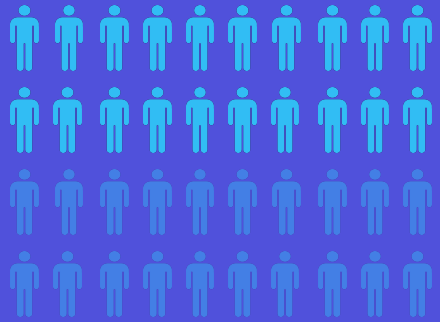
Lynn Howie, MD
Medical Director, Flatiron Health

October 27, 2021

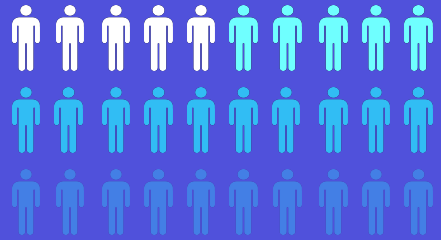
flatiron | Research x

Our need to understand cancer is only growing…

Pre 1990's
Cancer was a histological and anatomical diagnosis with systemic therapy (chemotherapy) as our main option



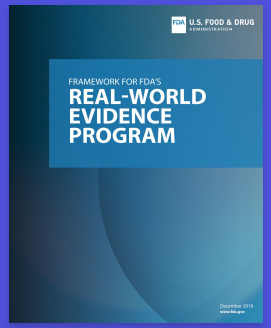
1990s
Targeted therapies such as monoclonal antibodies and tyrosine kinase inhibitors increased biological understanding of cancers



Today
Cell therapy, immunotherapy, pan-tumor therapy and more, treats patients of different genomic make up in a personalized manner

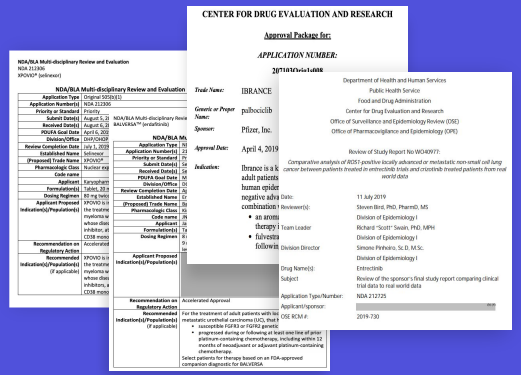
flatiron

Our understanding of the role of RWE use has come a long way in a short amount of time



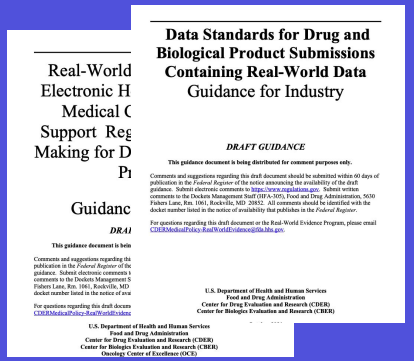
FDA RWE Framework

December 2018



Actionable Regulator Feedback

In Process



RWD/RWE Guidances

In Process

flatiron

Flatiron's experience shapes our perspective on regulatory RWE

Supported **12** briefing packages & **7** information requests

Participated in **7** health authority meetings[†]

Flatiron RWE used in **14** submissions*

Since 2019, we've received regulator input/feedback on 22 unique RWE project opportunities with more than a dozen life science partners

flatiron

[†]Includes formal and informal meetings and written response only

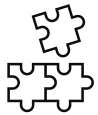
*Inclusive of submissions where Flatiron has provided direct regulatory support.

FDA has signaled specific circumstances in which RWD can complement traditional evidence

Significant unmet need, limited available therapies

Rare cohorts of interest, making randomized trials infeasible

Expected **large effect size** from preliminary data (e.g., from clinical trials)



Existing body of evidence around safety / efficacy of a drug in related population(s)

"In limited instances, FDA has accepted RWE to support drug product approvals… often when using a parallel assignment control arm is **unethical or not feasible and usually when the effect size is expected to be large**, based on preliminary data."

—

FDA's framework for RWE program

flatiron

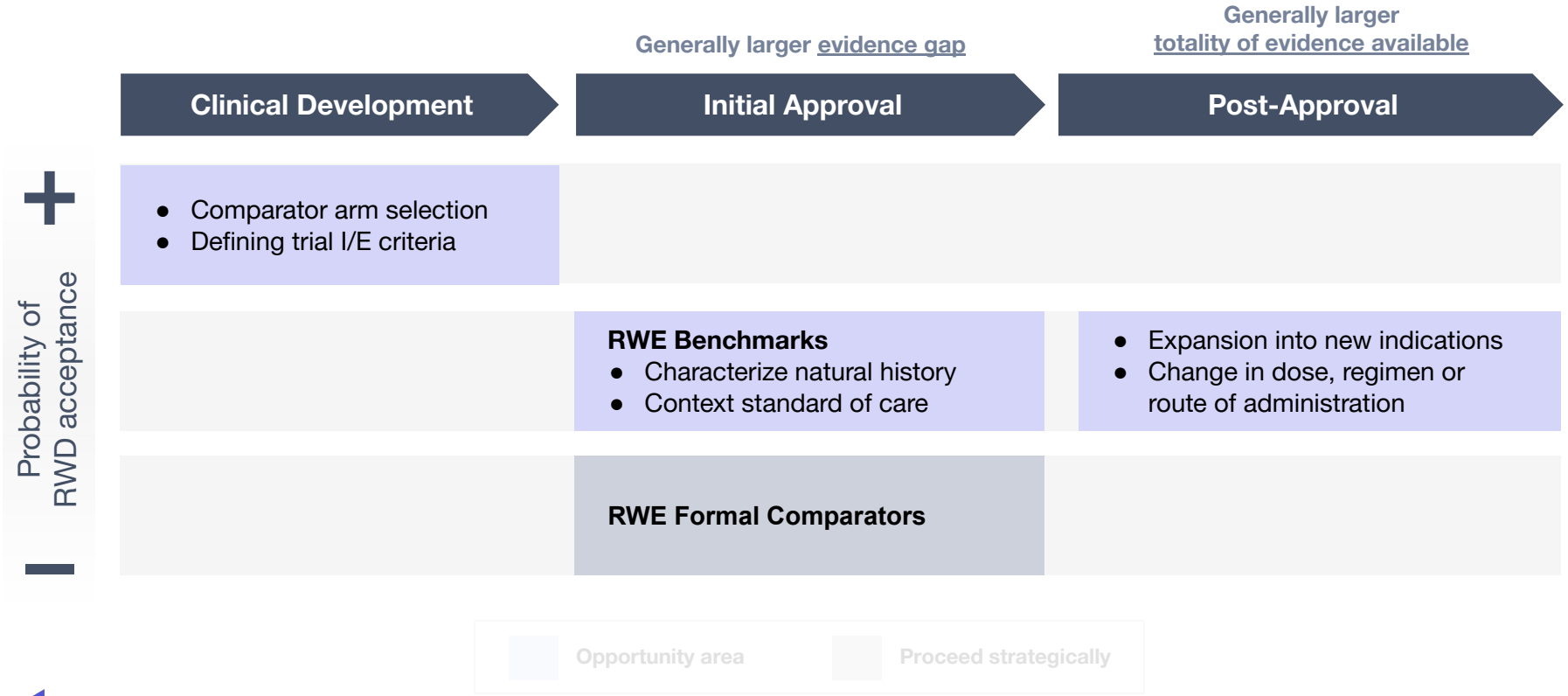
- Duke Margolis Whitepaper: Determining Real-World Data's Fitness for Use and the Role of Reliability
- Framework for FDA's Real-world evidence program

Regulatory feedback has highlighted common limitations of RWE that are critical to consider for a given use case

Key Examples

Endpoint definition and measurement	Lack of a) standardized definition of real-world efficacy outcome endpoints and/or b) characterizing concordance between real world and clinical trial measures of efficacy
RWD missingness	RWD are subject to different types of missingness (e.g., ECOG available at index), which may impact outcomes and conclusions
Cohort comparability	• Clinical trial eligibility criteria may not be available in RWD for real-world cohort selection resulting in non-equivalent populations impacting outcome comparisons and conclusions • Unmeasured confounders currently blocks time-to-event real-world endpoints

Near term opportunities for regulatory RWE



flatiron