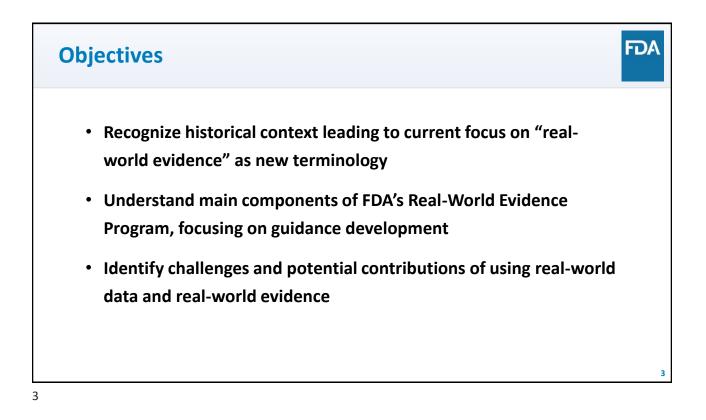
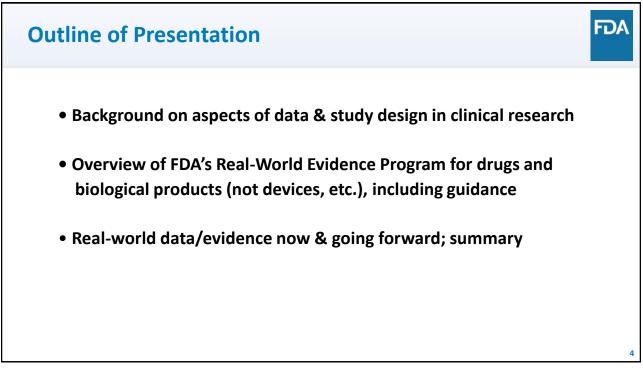
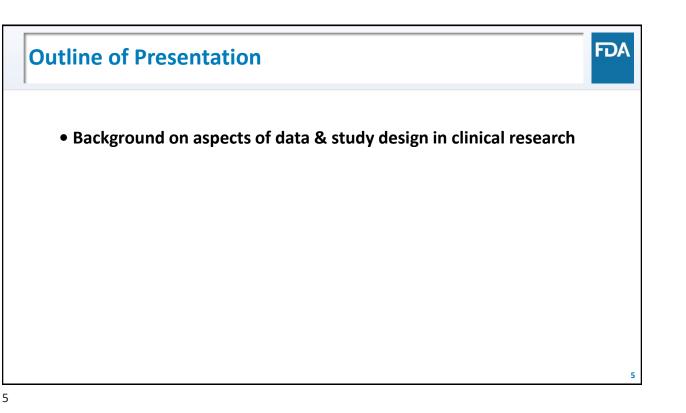


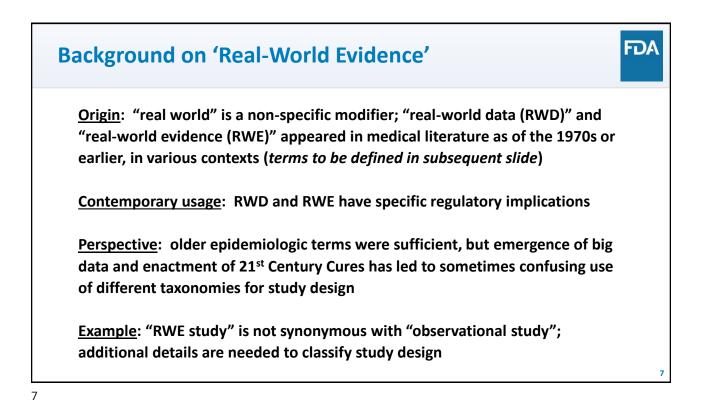
Disclaimer	FDA
 Views and opinions expressed are those of the presenter and should not be attributed to the Food and Drug Administration 	
 No conflicts of interest exist related to this presentation 	
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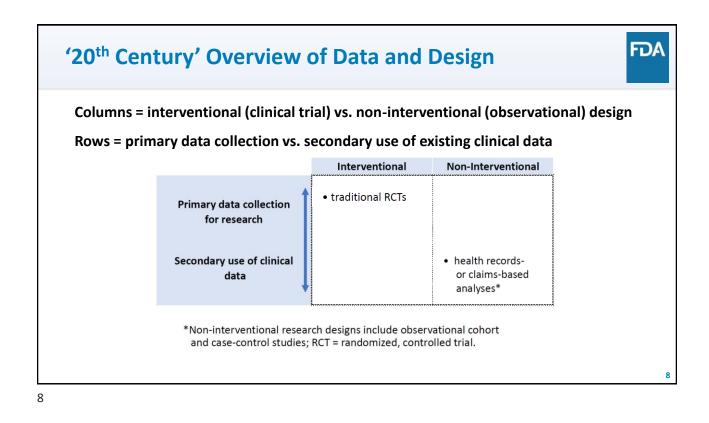


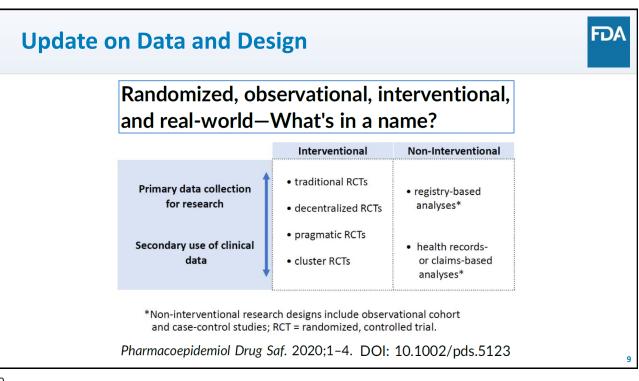




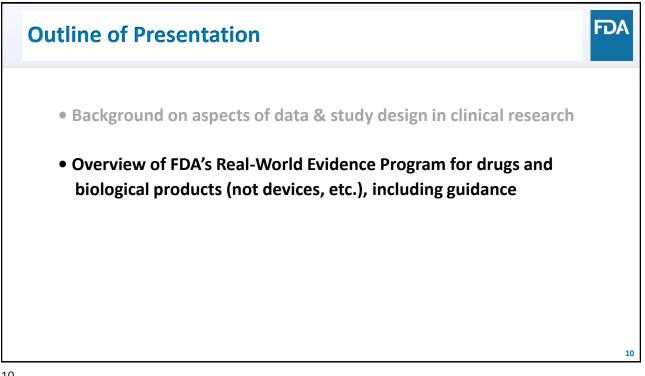
Background on 'Big Data' Image: Drigin: term appeared in computer science literature during 1990s, often referring to data too large to be stored in then-conventional storage systems Contemporary usage: Big Data represents "[...] shorthand for advancing trends in technology that open the door to a new approach to understanding the world and making decisions" (Lohr S, New York Times, 11 Feb 2012) Perspective: modern technology has increased quantity and forms of available data as well as the speed to merge and manipulate data, yet integration and analysis of large-scale data has always been integral to epidemiology

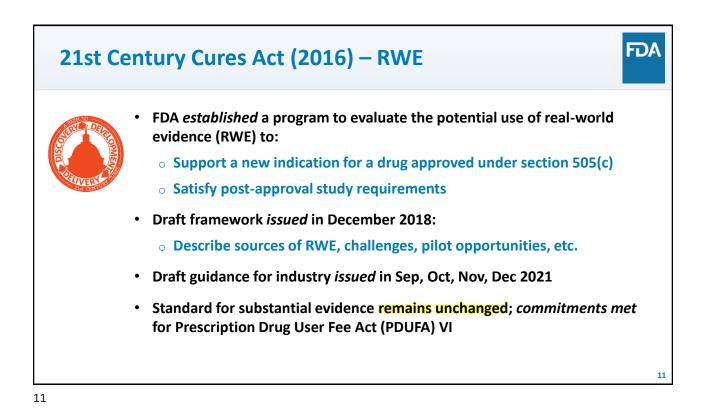


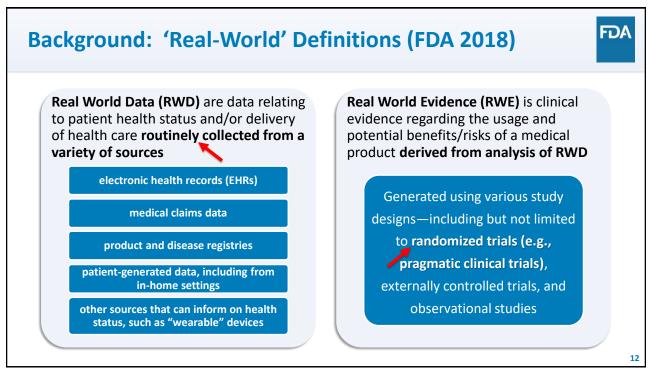


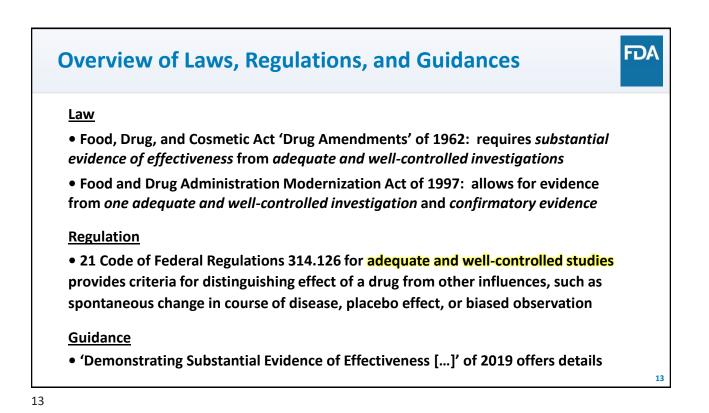


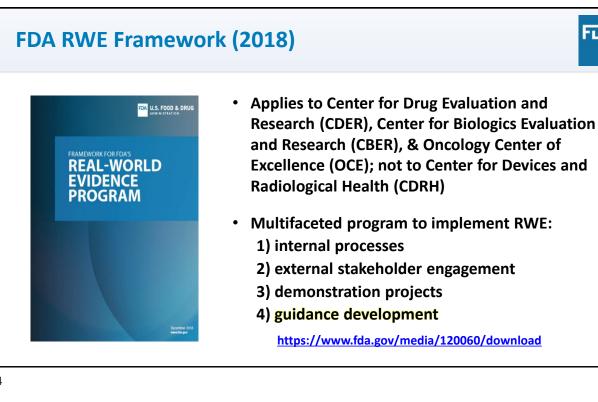


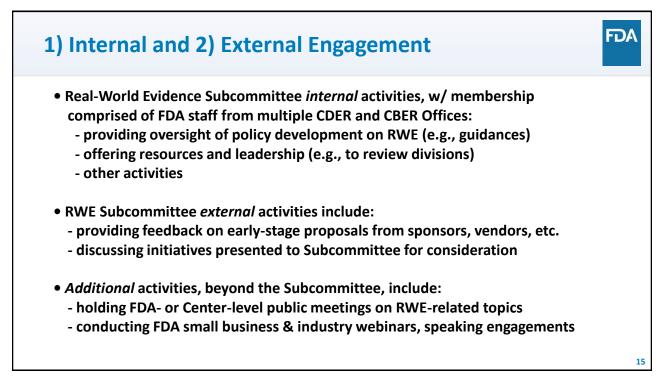


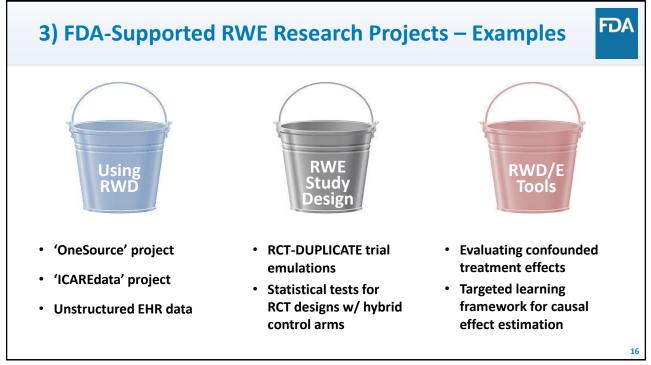


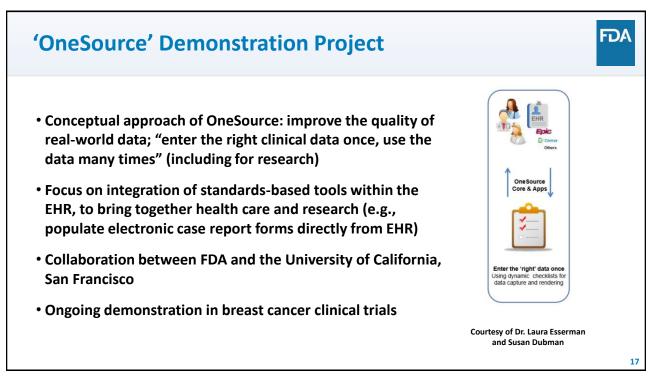








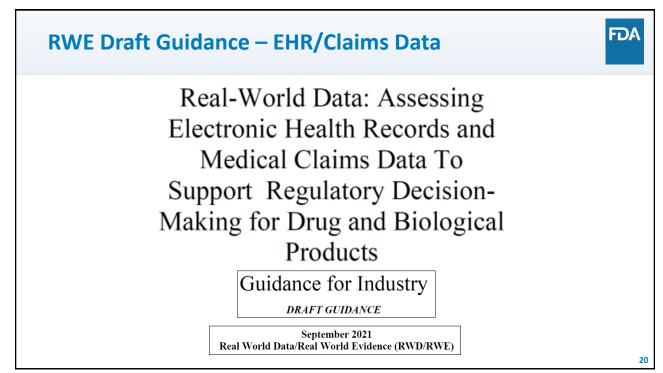


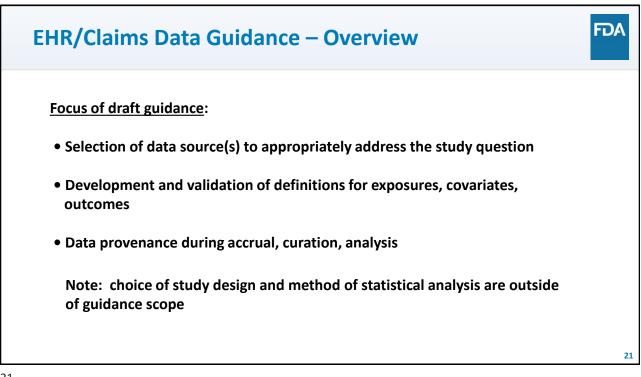


)1' A	wards	for RWD)/RWE	
Exp Re	gulatory De	use of Real-We ecision-Making	orld Data to Generate Real-World Evidence in (U01) Clinical Trials Optional RFA-FD-20-030 n=4 applications funded	
	Number	Applicant	Project Title	
1 U01F	D007213-01	Brigham and Women's Hospital	Enhancing evidence generation by linking RCTs to RWD	
1 U01F	D007206-01	Genentech-UNC	Applying novel statistical approaches to develop a decision framework for hybrid RCT designs, combining internal control arms with data from RWD sources	
1 U01F	D007172-01	Verantos, Inc.	Transforming RWE with Unstructured and Structured data to advance Tailored therapy (TRUST)	
1 U01F	D007220-01	Critical Path Institute	Advancing standards and methodologies to generate RWE from RWD through a neonatal pilot project	

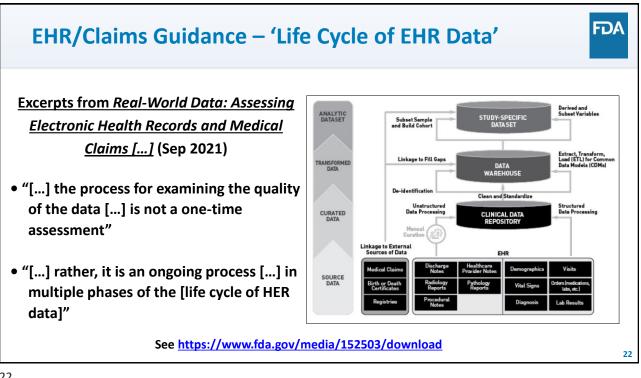


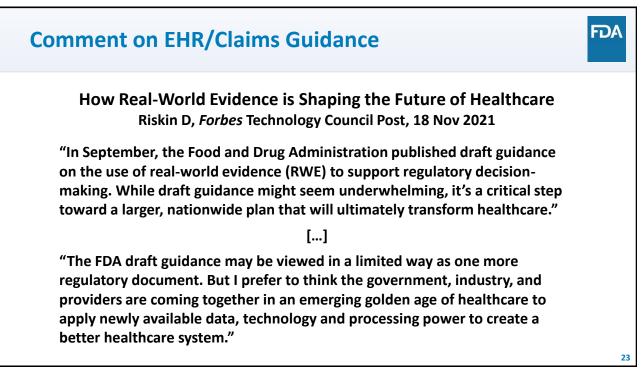


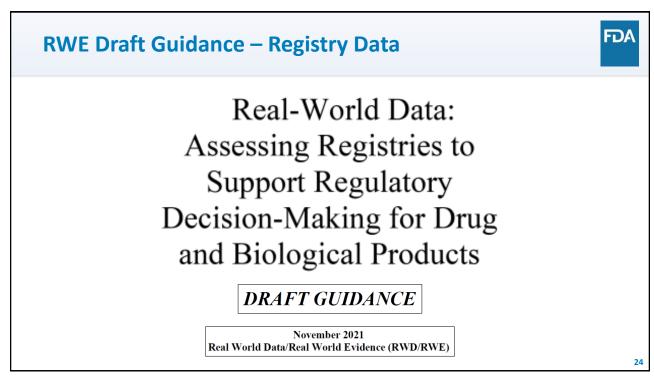




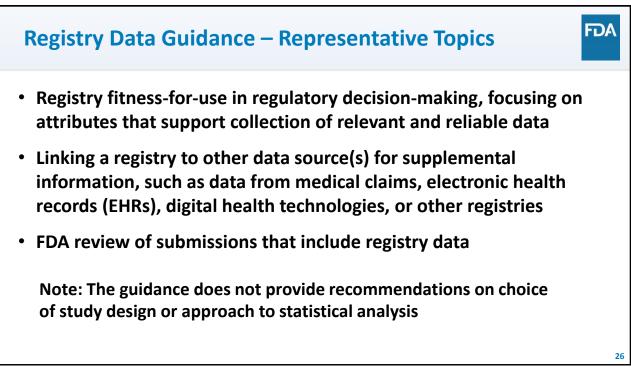


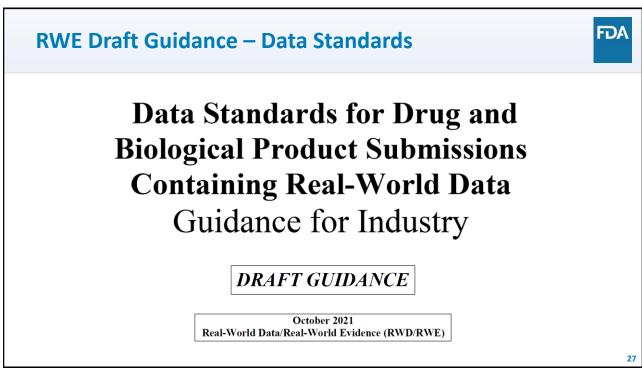


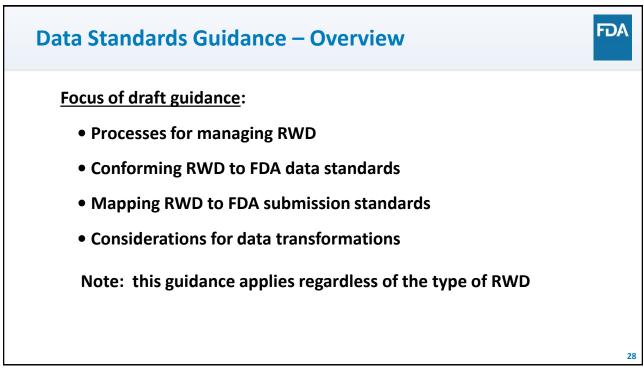


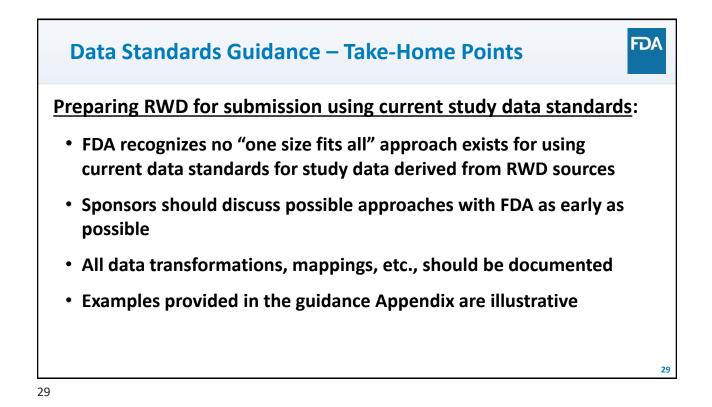


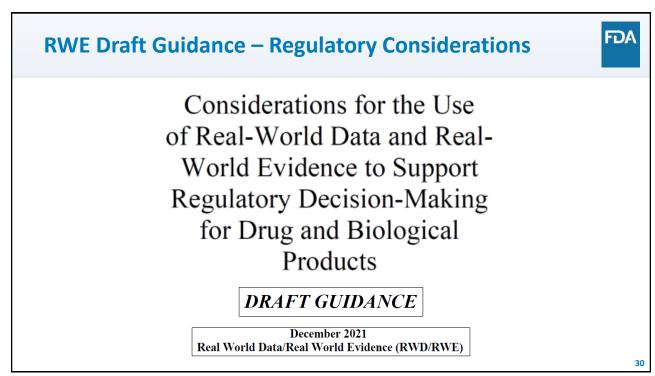
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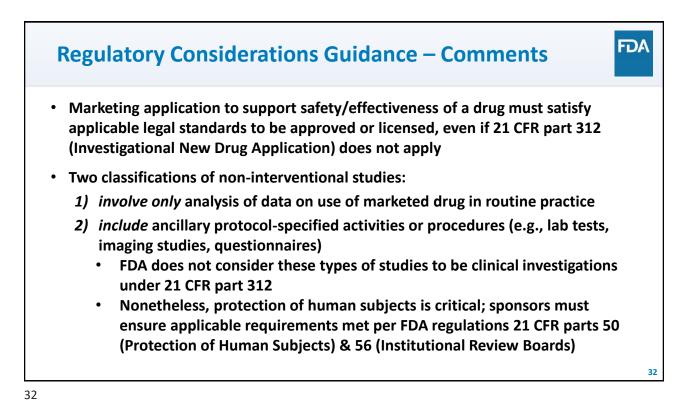




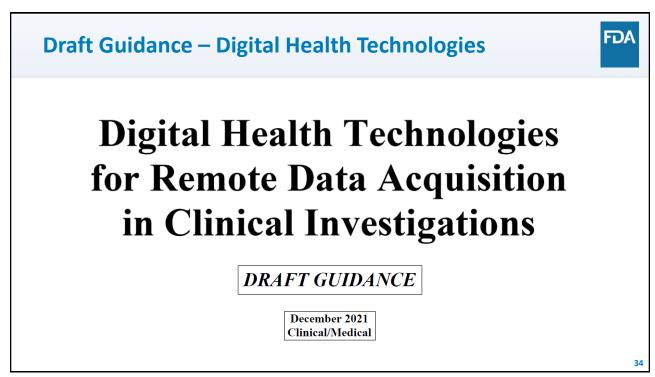


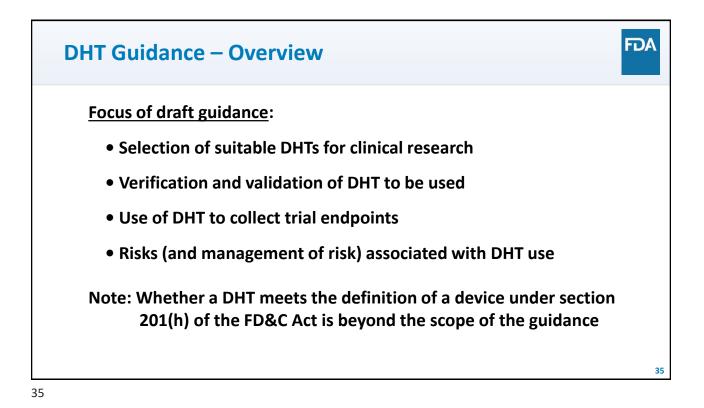


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	2	Transparency Regarding Data Collection and Analysis	
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		Safety Reporting	
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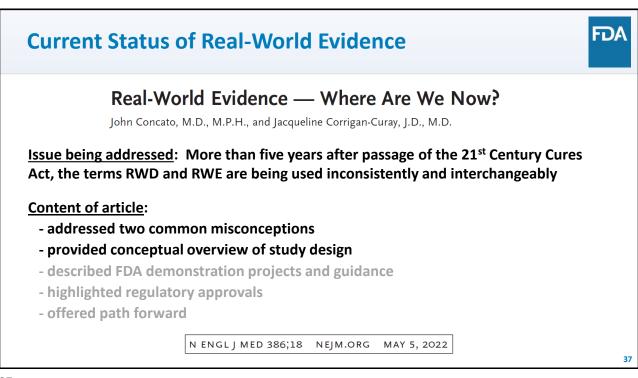


Торіс	Category	Status	Date
EHRs and claims data	Data considerations	published	Sep 2021
Data standards	Submission of data	published	Oct 2021
Registry data	Data considerations	published	Nov 2021
Regulatory considerations	Applicability of regulations	published	Dec 2021
Externally controlled trials	Design considerations	in development	-
RCTs in clinical practice settings	Design considerations	in development	_

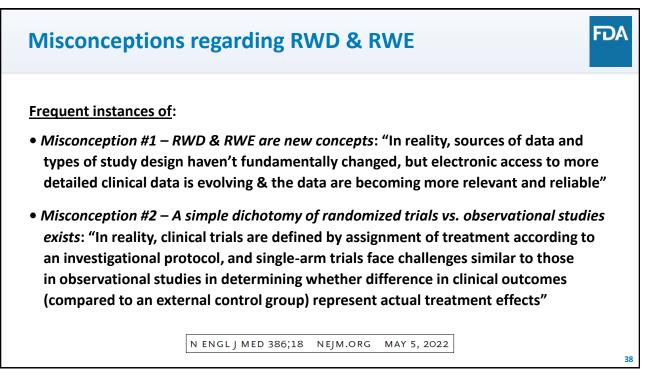








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	domized, ntional Study	Nonrandomized, Interventional Study	Nonrandomized, Noninterventional Study
Traditional randomized trial using RWD in planning	Trial in clinical practice settings, with pragmatic elements	Externally controlled trial	Observational study
RWD used to assess enrollment criteria and trial feasibility RWD used to support selection of trial sites	Selected outcomes identified using, e.g., health records data, claims data, or data from digital health technologies RCT conducted using, e.g., electronic case report forms for health records data or claims data	Single-group trial with external control group derived from RWD	Cohort study Case-control study Case-crossover study
	ļ	Generation of RWE	
	Increasing reliance on R	WD	

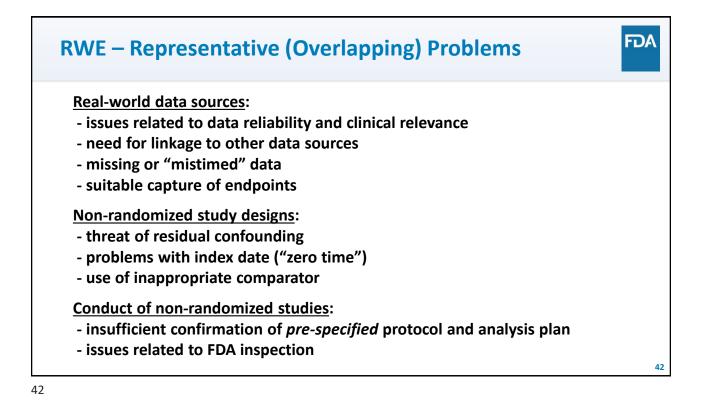
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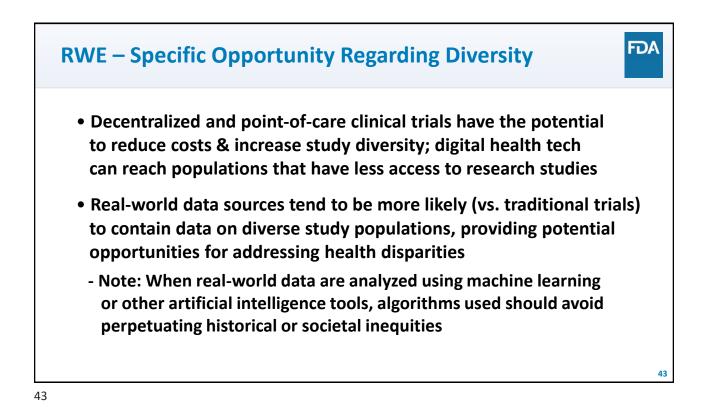
RWE Informs Effectiveness When Fit-for-Purpose

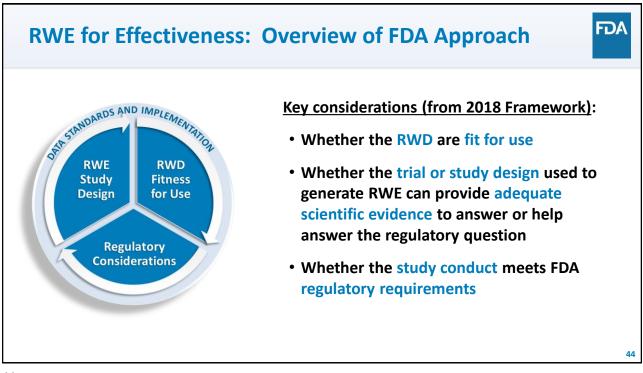
DRUG	INDICATION	APPROVED	DATA
Carbaglu (carglumic acid)	Treatment of NAGS deficiency	2010	Retrospective, non-random, unblinded case series of 23 patients compared to historical control group
Voraxaze (glucarpidase)	Treatment of MTX toxicity	2012	Approval based on open-label, NIH expanded access protocol
Blincyto (Blinatumomab)	Treatment of Acute Lymphoblastic Leukemia	2014	 Single-arm trial Reference group weighted analysis of patient level data on chart review of 694 patients at EU and US study sites
Vistogard (uridine triacetate)	Overdose of chemotherapy drugs 5-fluorouracil (5-FU)	2015	Two single-arm, open-label expanded access trial of 137 patients compared to case history control
L	ist not exhaustive		Bold = RWD

RWE Informs Effectiveness (cont'd)

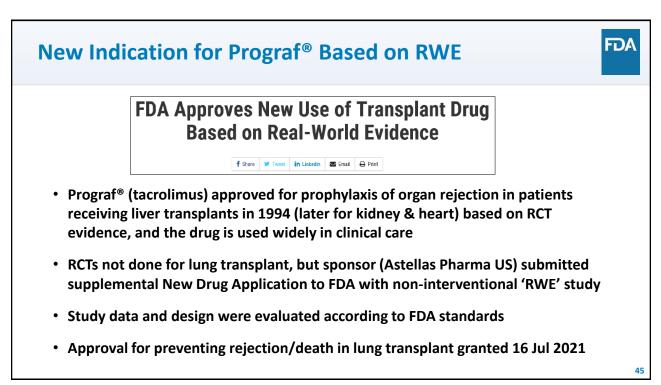
DRUG	INDICATION	APPROVED	DATA
Defitelio idefibrotide sodium)	Severe hepatic veno- occlusive disorder	2016	Two prospective clinical trials enrolling 179 patients and an expanded acce study with 351 patients
	Gastroenteropancreatic		Open-label clinical trial
L utathera Iutetium 177 dotate)	neuroendocrine tumours (GEP-NETs)	2017	 Analysis of a subset of 360 patients who participated in an investigator sponsored, open-label, single-arm, single institution study of 1214 patients that started as an expanded access program
Zostavax Zoster vaccine Live)	Prevention of herpes zoster (shingles) in persons 50 years of age and older	2018	Prospective, observational cohort study using electronic health records in Kaiser Permanente Northern California to characterize the duration of protection in persons 50 years of age and older
Zolgensma onasemnogene ubeparvovec-xioi)	Patients <2 years of age w/ spinal muscular atrophy and a specific mutation	2019	 Data from a single-arm trial compared to data in an external control group based on a natural history study
L	ist not exhaustive		Bold = RWD

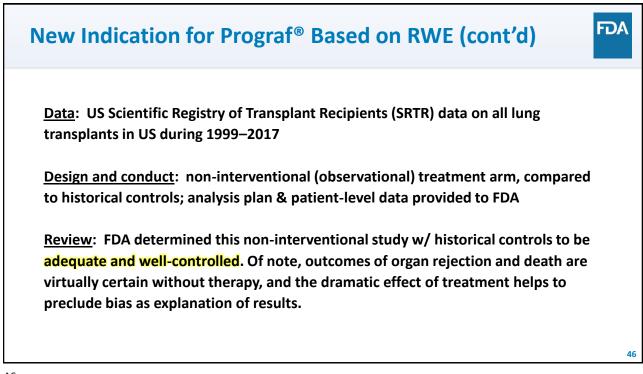


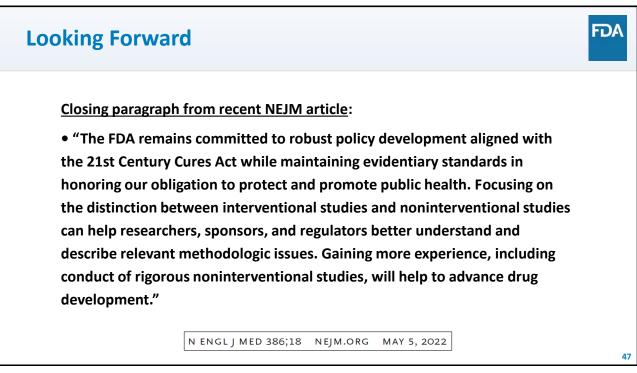




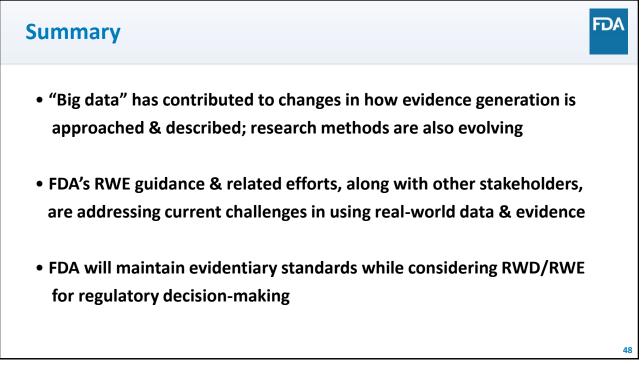
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