FDA U.S. FOOD & DRUG ADMINISTRATION

Real-World Evidence (RWE): Context for Supporting Regulatory Decisions

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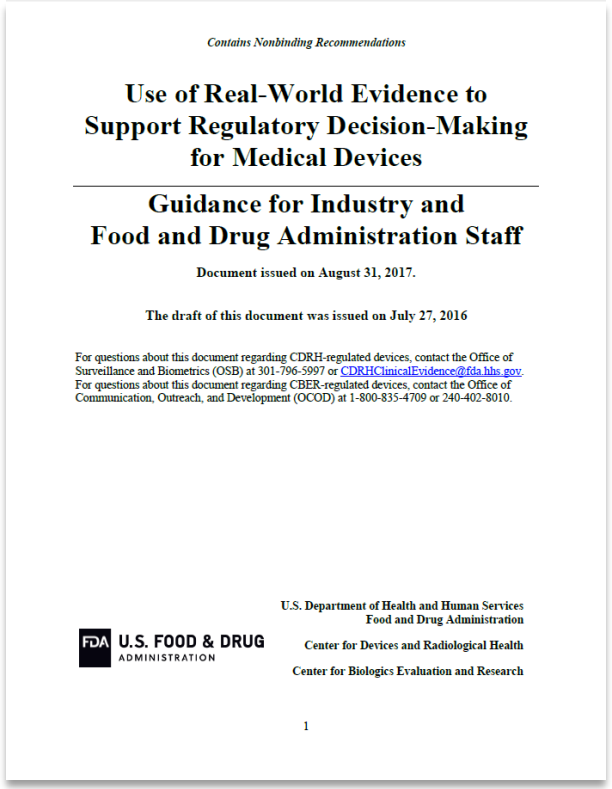
Food and Drug Administration (FDA)

SHIELDx *Systematic Harmonization and Interoperability Enhancement for Lab Data*

Context for RWE Guidance

- FDA Reauthorization Act (*FDARA) including MDUFA IV commitment to use of real-world evidence to support device pre/postmarket decisions*
- National Evaluation System for health Technology (NEST)
- *CDRH Strategic Priorities*
- *Guidance issued to clarify how RWE may be used to support regulatory decisions*



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.

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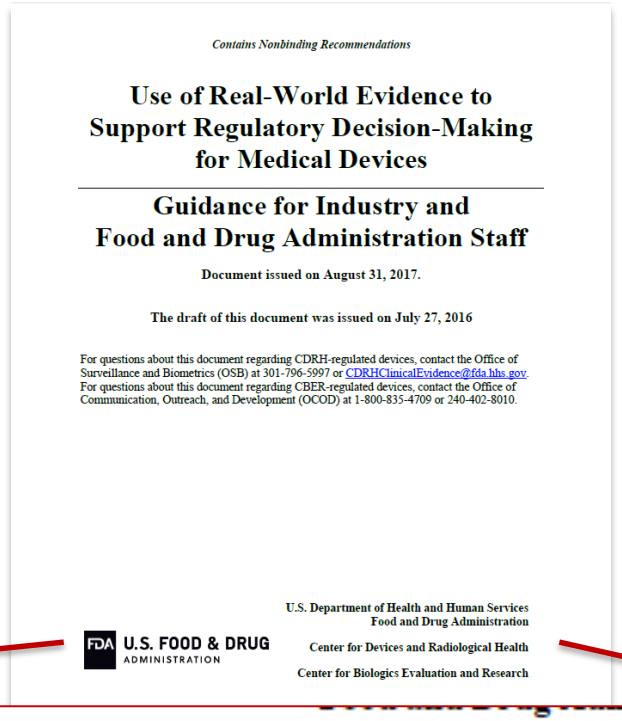

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Turning Data into Evidence

Real-World Data (RWD)

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

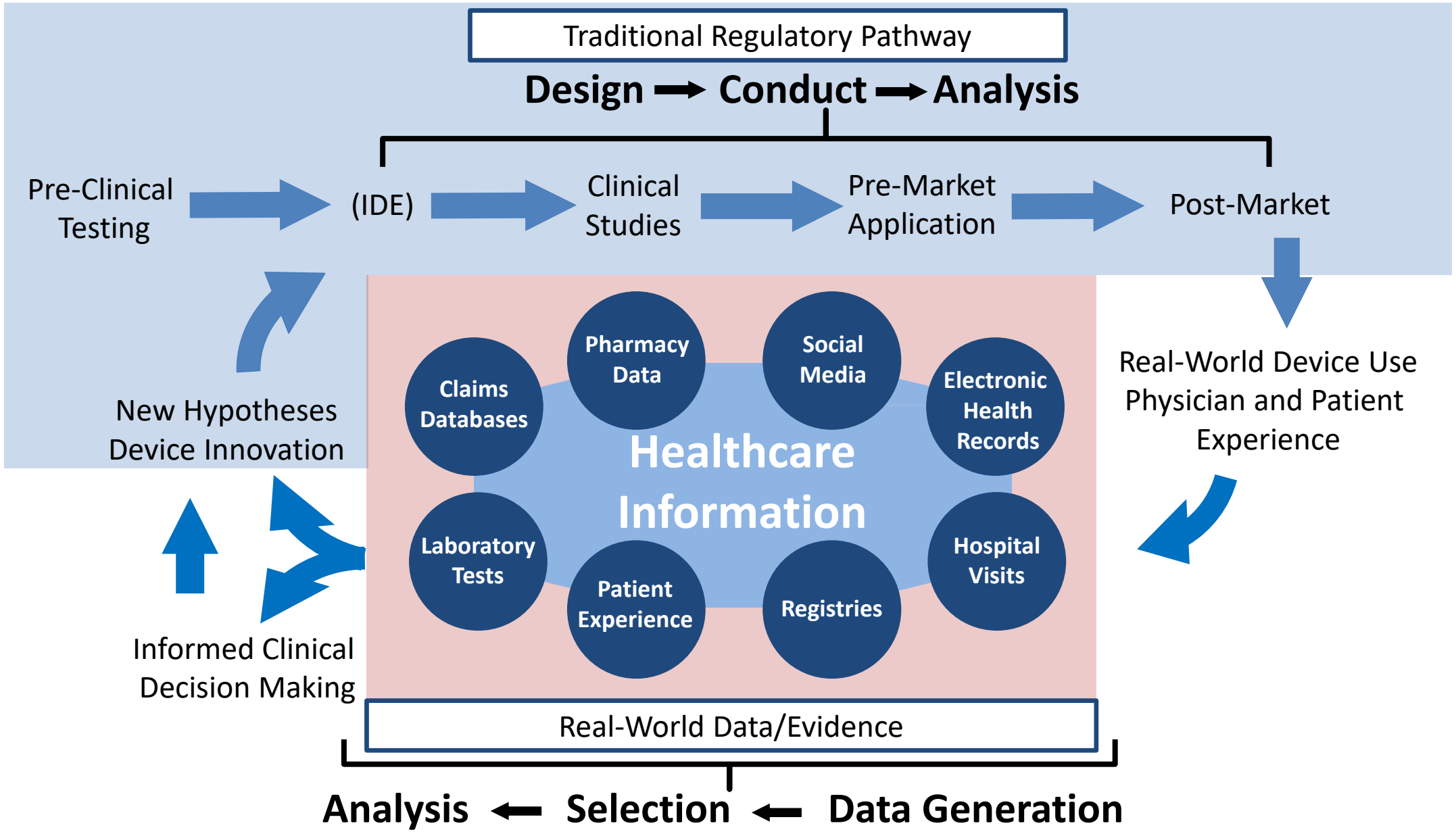
Real-World Evidence (RWE)

"Clinical evidence regarding the usage and potential benefits or risks of a medical product derived from analysis of RWD"

Guidance Addresses issues related processes of:

- Generation and collection of RWD
- Analysis of RWD
- When results might be considered valid scientific evidence

Traditional and Real-World Evidence



Traditional

Evidence

FDA

Pre-Clinical Testing → (IDE) → ysis → Post-Market

Real-World Device Use
Physician and Patient Experience

RWE must be understood and reliable to be useful

Informed Clinical Decision Making

Analysis ← ration

DATA QUALITY NEEDED!

Valid Scientific Evidence

- 21CFR 860.7(c)(1)
  - Although the manufacturer may submit any form of evidence to the Food and Drug Administration in an attempt to substantiate the safety and effectiveness of a device, the agency relies upon only valid scientific evidence to determine whether there is reasonable assurance that the device is safe and effective.

What is Acceptable?

- 21 CFR 860.7(c)(2)

  Valid scientific evidence is evidence from
  - Well-controlled investigations,
  - Partially controlled studies,
  - Studies and objective trials without matched controls,
  - Well-documented case histories conducted by qualified experts,
  - Reports of significant human experience with a marketed device from which it can fairly and responsibly be concluded by qualified experts that there is reasonable assurance of the safety and effectiveness of a device under its conditions of use.

What is Not Acceptable?

- 21 CFR 860.7(c)(2) continued

  …Isolated case reports, random experience, reports lacking sufficient details to permit scientific evaluation, and unsubstantiated opinions are not regarded as valid scientific evidence to show safety or effectiveness. Such information may be considered, however, in identifying a device the safety and effectiveness of which is questionable.

Data Quality

‘Fit for Purpose’

Data must be complete, consistent, accurate, and *contain all critical data elements needed* to evaluate a medical device and its claims.

Relevant & Reliable

Benefit

Risk

Safety

…probable *benefits to health* from use of the device *outweigh any probable risks*

[21 CFR 860.7(d)(1)]

Effectiveness

…use of the device in the *target population* will provide *clinically significant results*

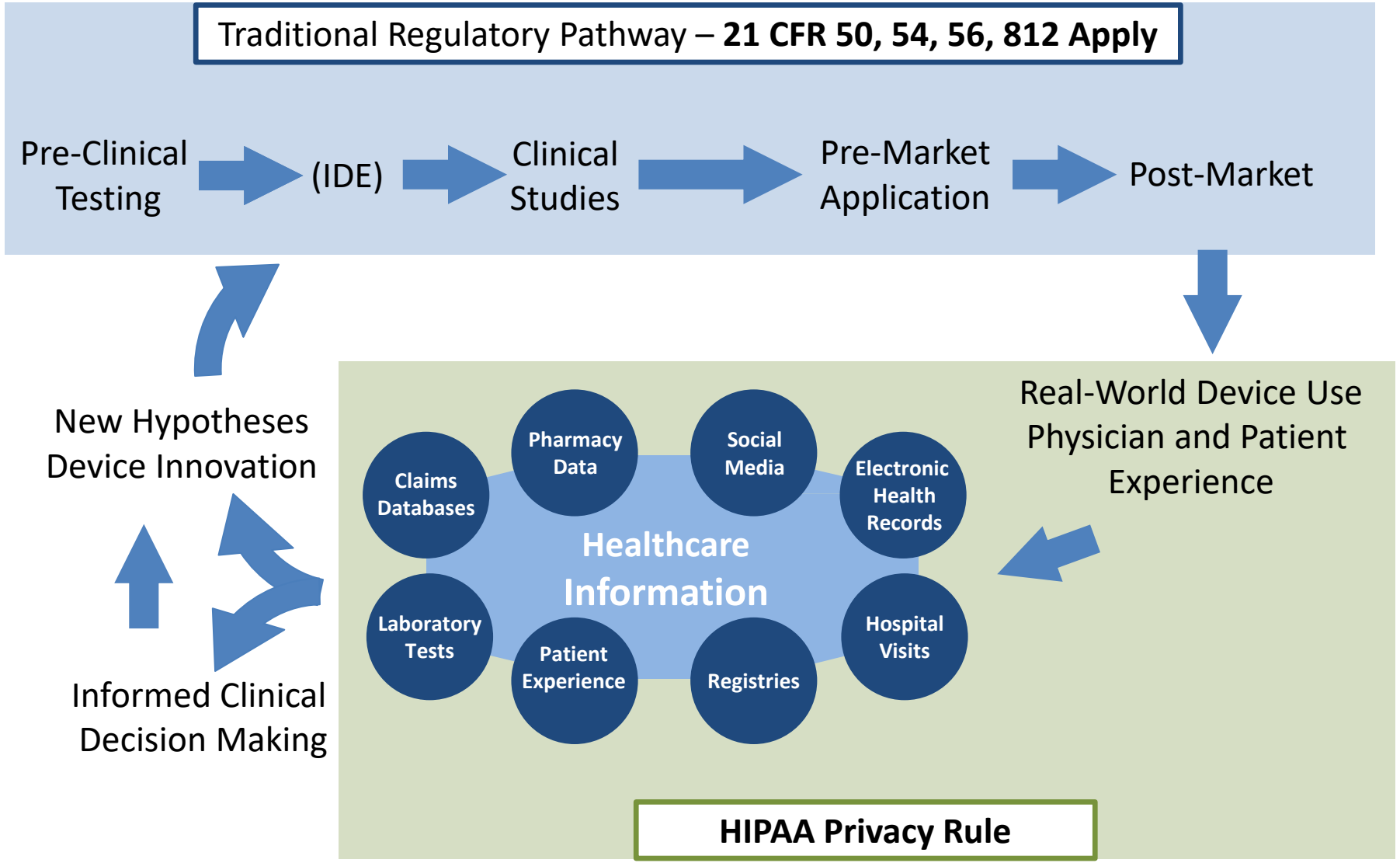
[21 CFR 860.7(e)(1)]

Patient Protections

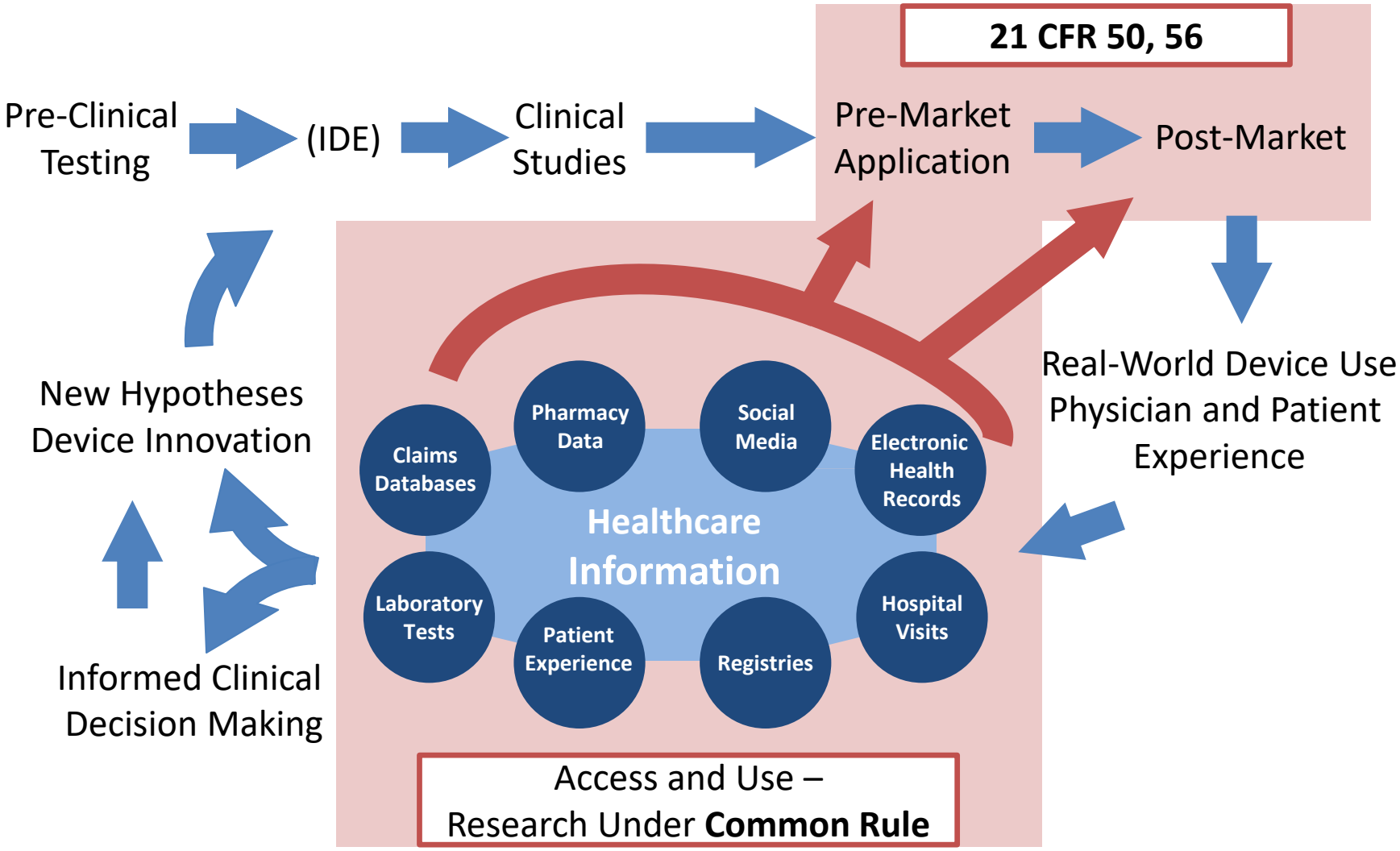
- 21 CFR 812 Investigational Device Exemptions
- 21 CFR 50 Protection of Human Subjects (Informed Consent)
- 21 CFR 54 Financial Disclosure of Investigators
- 21 CFR 56 Institutional Review Boards (IRBs)
- 45 CFR 46 “Common Rule”
- Health Insurance Portability and Accountability Act (HIPAA)
- Other federal and local regulations

- RWE Guidance does not address all issues related to patient protection - focus is on the IDE process.

Patient Protections



Research on Information



RWE Example Case Studies

#	Device (Submission)	Data Source	Used	Action
1	Wearable (PMA/S)	*Wearable Device & Patient Reports*	Modification of claims from adjunctive to non-adjunctive to use diagnostic for treatment decisions	Indication Expansion
2	Computer assisted triage software (De Novo)	*Literature*	Peer reviewed literature Meta-analysis.	New Indications
3	Sequencing assay (510(k))	*Public NGS database*	Publicly-maintained database support clinical validity of the test in lieu of clinical trials	Indication Expansion
4	Screening assay (De Novo)	*State lab & surveillance databases*	Pivotal clinical trial was embedded in routine clinical practice (under an IDE) in lieu of a traditional pivotal trial.	New Indications
5	Implantable Cardioverter-Defibrillator (PAS)	*Multiple RWD data sources*	Monitor multiple aspects of real-world device safety and performance using data collected in routine care.	Condition of Approval

Case Example: Leveraging a RWD Database to Enable Pre-Market Claims

FDA cleared two 510(k)s for sequencing assays for variant/variant combinations associated with cystic fibrosis using a public next-generation sequencing (NGS) database.

Traditional Studies: Full clinical trials/summary of information available in peer-reviewed literature to provide evidence of the test's clinical validity.

https://www.accessdata.fda.gov/cdrh_docs/reviews/K124006.pdf
https://www.accessdata.fda.gov/cdrh_docs/reviews/K132750.pdf
https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm509837.pdf

Case Example: Leveraging a RWD Database to Enable Pre-Market Claims

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~~**Traditional Studies**: Full clinical trials/summary of information available in peer-reviewed literature to provide evidence of the test's clinical validity.~~

Study Using Public Database – An established publicly-maintained database hosted by the academic institution was used to support clinical validity of the test in lieu of clinical trials.

- Database used as a source of valid scientific evidence to establish which variants/ variant combinations were causal for the target disease.
- Additional relevant patient information, e.g. sweat chloride, lung function, pancreatic status, and *Pseudomonas* infection rate, associated with each variant/variant combination were included in the evaluation.

https://www.accessdata.fda.gov/cdrh_docs/reviews/K124006.pdf
https://www.accessdata.fda.gov/cdrh_docs/reviews/K132750.pdf
https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm509837.pdf

Need RWE help for medical devices?

CDRHClinicalEvidence@fda.hhs.gov

There are Public-Private Partnerships (PPP) in FDA to enable access to high-quality RWE.

GET INVOLVED – LEARN MORE

Michael.Waters@fda.hhs.gov

THANK YOU!


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