Experience and Considerations for Using RWE

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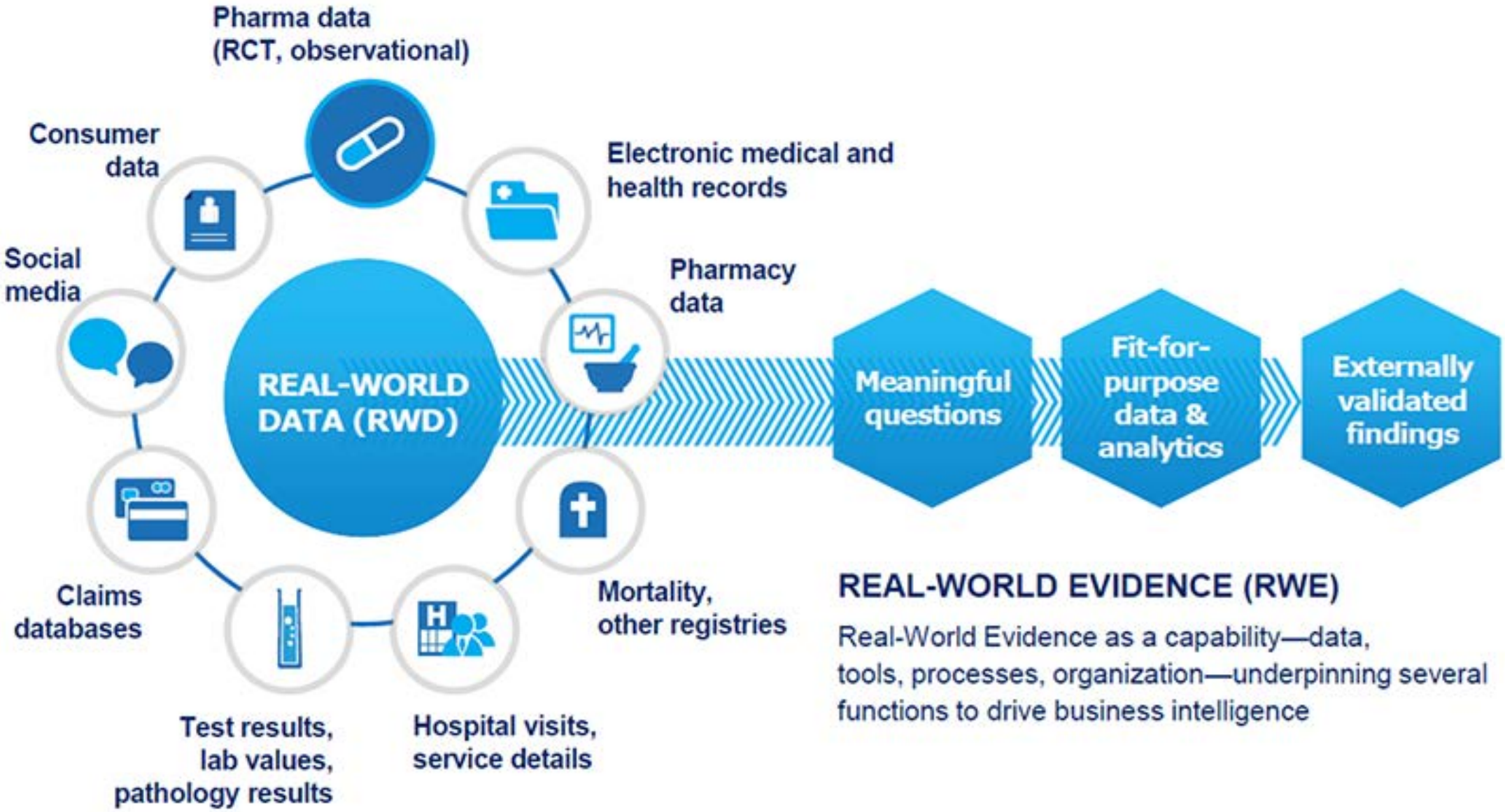
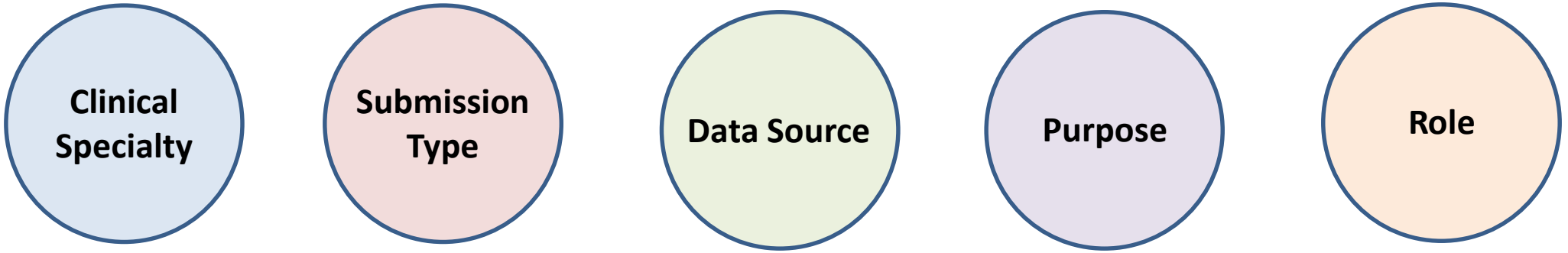


REAL-WORLD EVIDENCE (RWE)

Real-World Evidence as a capability—data, tools, processes, organization—underpinning several functions to drive business intelligence

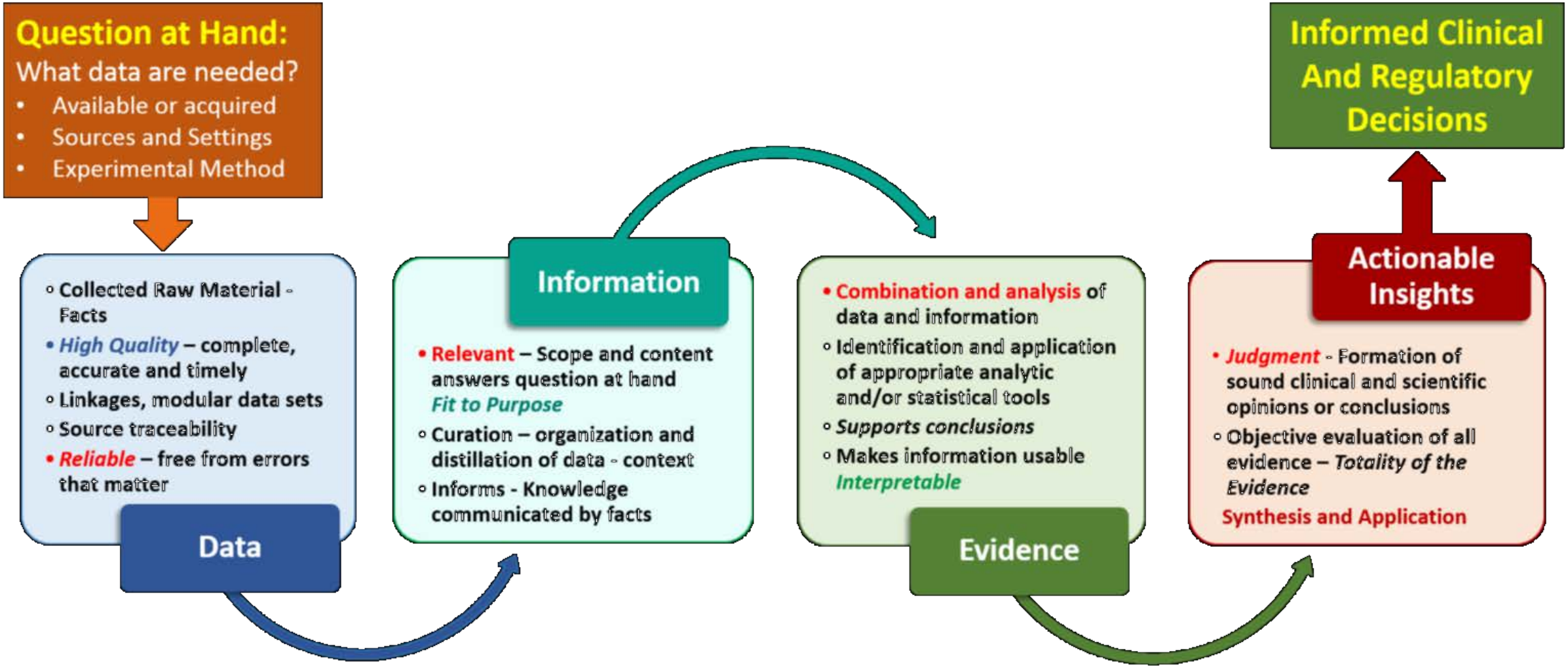
RWE Successes

In March 2021, CDRH published 90 Examples of RWE used in medical device regulatory submissions.



Clinical Specialty	Submission Type	Data Source	Purpose	Role
Cardiovascular Diagnostics General Hospital Neurological Ophthalmic Orthopedics Surgical	510(k) De Novo PMA HDE	Medical Records or Charts Claims Registry S-I Studies Literature	New Marketing Submissions Indication Expansion Postmarket Study Signal Detection	Primary Supplementary Partnering Find patients

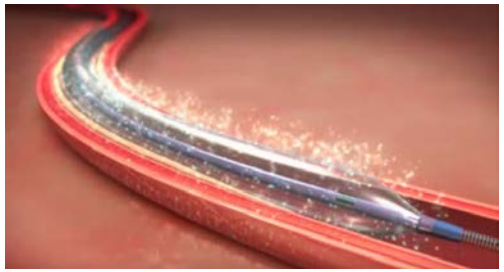
NESTcc Data Quality Framework



The 9A's of an FDA IDE Trial

- Agreement to participate - informed consent
- Avoidance of selection bias
- Accountability of study subjects - minimize subject withdrawals/lost to follow-up
- Accumulation of data - capture relevant events and minimize missing information
- Accuracy of data collection and recording
- Analysis of data using pre-specified event definitions, endpoints, a SAP, and core labs (when needed)
- Access to data (e.g., investigators, industry, FDA, CMS)
- Auditing & monitoring of study data and study progress
- Adjudication of events

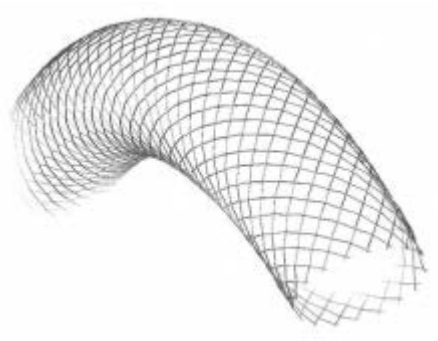
Peripheral Vascular Examples



- Premarket indications expansion to include in-stent restenosis and/or long-lesions
  - Global sponsor registry as test matched with VQI control
  - Global single arm study and Japanese postmarket surveillance in real-world populations
- Postmarket studies
  - Both sponsors utilized the VQI registry to meet postmarket study requirements with data capture in real-world patients

Peripheral Vascular Examples

Venous Wallstent



- Premarket indications expansion to include treatment in the iliofemoral veins for treatment of symptomatic venous outflow obstruction
- Data Sources:
  1) US and OUS systematic literature review (2000-2019)
  2) Retrospective analysis of single center medical records
- Safety Endpoint: Major adverse events through 30-days and throughout follow-up
- Effectiveness Endpoint: 12-month Primary patency with various definitions

Peripheral Vascular Examples

Phillips CavaClear IVC Filter Removal Laser Sheath

- First of a kind indications for the first laser-based device for removal of IVC filters
- Data Source: Retrospective analysis of RWD of 265 subjects at 7 sites, evaluating procedure success rate and device-related complications
- De Novo granted December 21, 2021

Plan early and be flexible because RWD can be messy

Role of RWE:
- Primary
- Supplementary (to get over the bar)
- Partnering (e.g., as control, prior, or otherwise combined with traditional clinical study data)

Statistical Methods:
- Pre-specified flexible SAP
- Methodology (eg, matching)
- Accounting for confounders and biases
- Handling missing data

Data Source:
- Patient Population
- Elements and definitions
- Outcomes
- Duration

Other considerations:
- Quality measures
- Multiple sources and linkages
- Other data (eg, imaging)

Thank you!