Pre- and Post-market Use and Current Considerations of Real-World Evidence for Regulatory Use

Misti Malone, PhD
US FDA / CDRH

December 11, 2019

FDA's Perspectives on RWE

- FDA recognizes the wealth of data available from routine clinical experience
- RWE plays a roll in ongoing efforts to balance premarket and postmarket data collection
- RWE may help to streamline the regulatory approval process while generating robust and meaningful evidence to support the safety and effectiveness of devices

Real-World Data (RWD)

- Data relating to a patient health status and/or delivery of healthcare routinely collection from a variety of sources

Advantages of RWE

Potential benefits of RWD sources include:

- Understanding device performance in real-world environment to inform benefit-risk
- Collection of outcomes not always feasible in traditional trials
  - performance in diverse patient populations and subgroups
  - long-term outcomes
  - larger datasets to assess rare but important events
- Opportunities to partner w/patients in new ways (e.g., patient reported outcomes, mobile medical apps, wearable devices, user experience)
- Reduced time/cost to answer important questions

Data Quality

'Fit for Purpose'

Data should be assessed for completeness, consistency, accuracy, and whether it contains all critical data elements needed to evaluate a medical device and its claims.

Relevance & Reliability

Effectiveness

Is there reasonable assurance, based on valid scientific evidence that the use of the device in the target population will provide *clinically significant results? [860.7(e)(1)]*

Benefit

Risk

Safety

Are there reasonable assurances, based on valid scientific evidence that probable benefits to health from use of the device *outweigh any probable risks? [860.7(d)(1)]*

Some (Not Exhaustive) Data Quality Pitfalls

Relevance

- Duration of Follow-Up Not Comparable
- Event Definitions Don't Match Exactly
- Patient Population Not Directly Comparable
- Standard of Care Used Not Comparable

Reliability

- No Assurance that All-Comers Captured
- No Auditing Process
- Follow-up Incomplete
- RWD Source Not Representative of All Treatment Sites

U.S. Food and Drug Administration
Protecting and Promoting Public Health

www.fda.gov

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

Current Considerations on Real-World Evidence Use in FDA Regulatory Submissions

Examples and decision making from the Center for Devices and Radiological Health's Peripheral Interventional Devices Branch.

BY ELENI WHATLEY AND MISTI MALONE

October 2017

CLINICAL TRIALS **TRANSFORMATION** INITIATIVE

Developing & driving adoption of practices that will increase the quality and efficiency of clinical trials

CTTI Recommendations:

Use of Real-World Data to Plan Eligibility Criteria and Enhance Recruitment

October 2019

SPEED: A New Initiative in Real-World PAD Evidence Evaluation

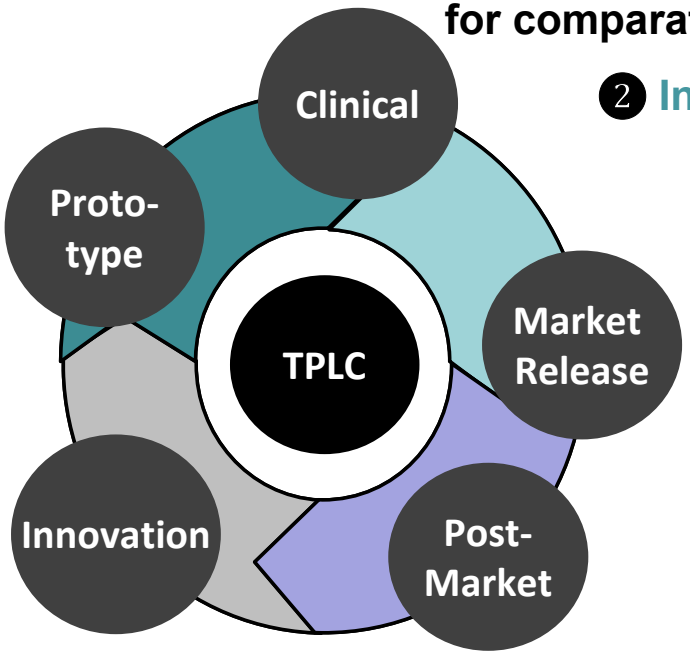
An overview of the FDA's new multistakeholder project to support real-world evidence evaluation for devices aimed at treating peripheral artery disease.

BY MISTI MALONE, PHD

November 2018

EXAMPLES

Potential Usages of RWE for TPLC



1. Hypothesis Generation (e.g. treatment effect estimation for comparative studies)
2. Inform prospective trial design
3. RWE as a control arm for a clinical trial
4. Real-world data source as a platform to support a clinical trial (data collection / randomization)

---

5. Data collection framework for post-market condition-of-approval studies
6. Adverse event reporting
7. Generate evidence to support indication expansions and future innovation

OCVD and NESTcc

https://nestcc.org/demonstration-projects/

Registry Assessment of Peripheral Interventional Devices (RAPID)

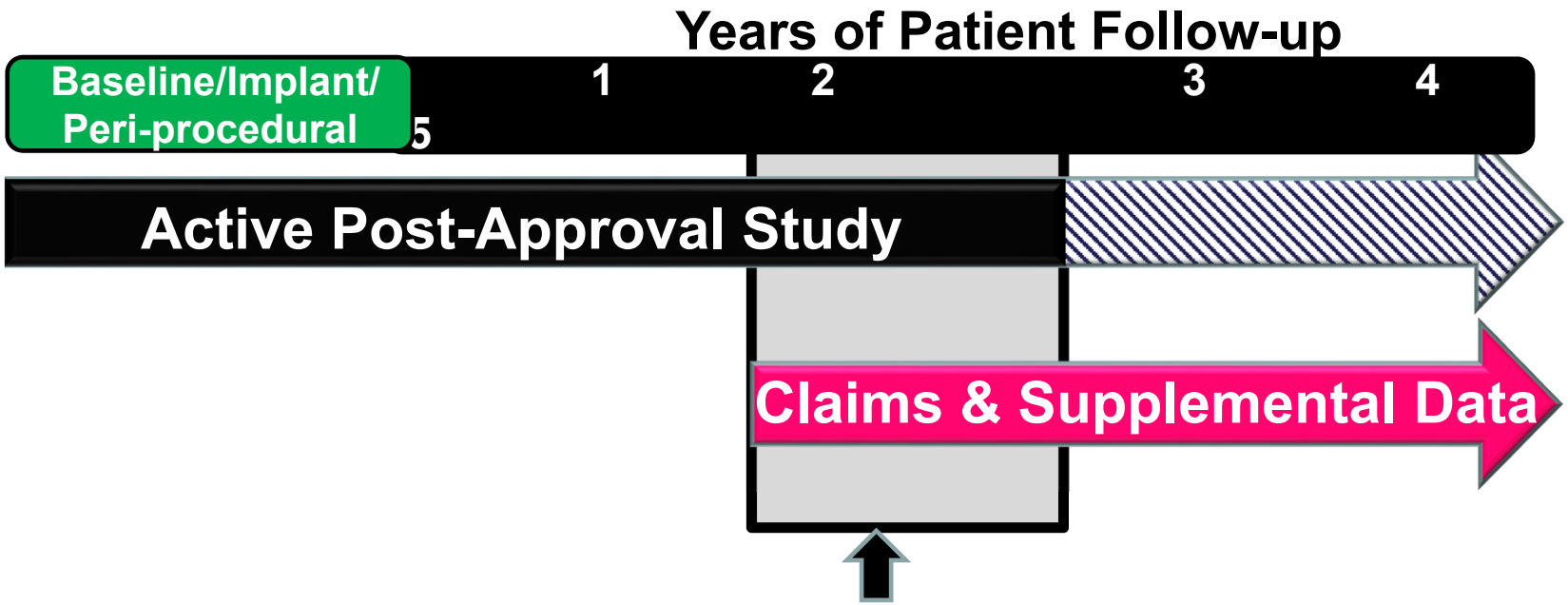
- Public-private partnership to advance a TPLC approach for the evaluation of PAD devices
- Multi-stakeholder collaboration of clinicians, medical professional societies, regulators, device manufacturers, and clinical research organizations
- Use of RWE in the peripheral vascular space offers an opportunity to overcome challenges due to:
  - Disease heterogeneity
  - Variability in comorbidities
  - Numerous device types in treatment strategies
  - Lack of consensus among medical specialties on the best treatment strategy for a given patient population

EP Passion

ElectroPhysiology Predictable And SuStainable Implementation of National registries

- **Aim**: Develop a sustainable mechanism to collect performance data across the Total Product Life Cycle for new and substantially modified implanted electrophysiology devices and transition away from the traditional post-approval study

Proof of Concept



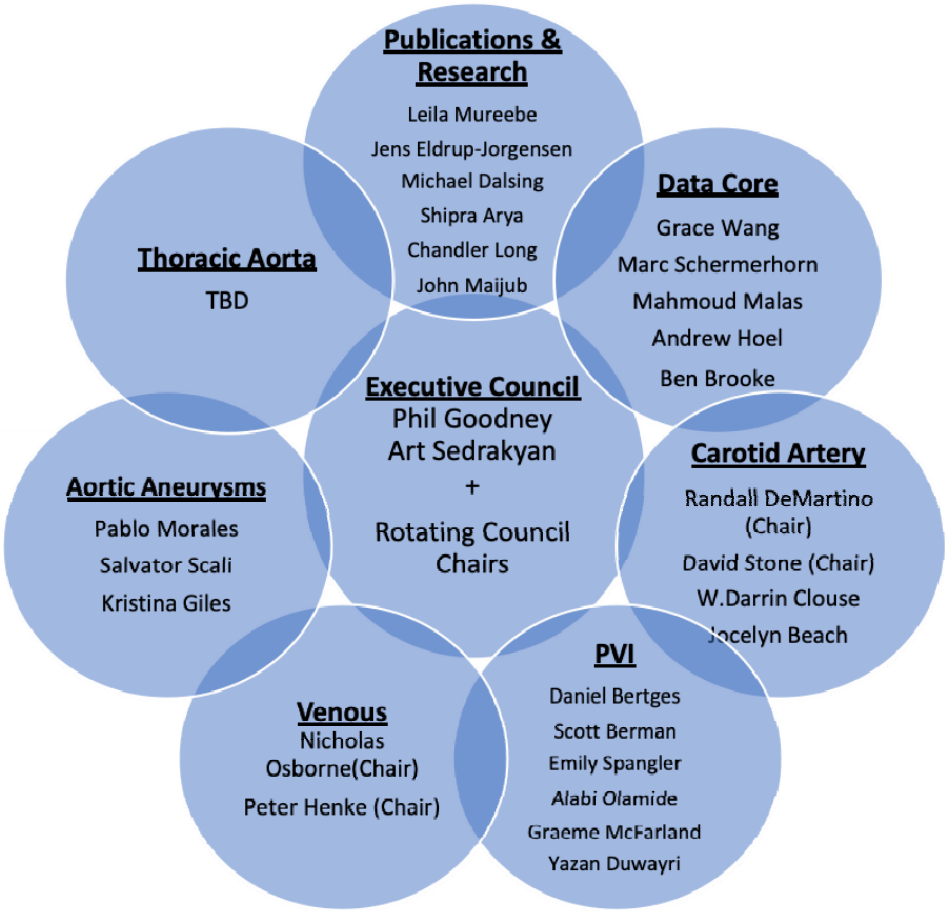
Demographic Comparison
Event Rate Comparison Year 2-3
1:1 Matching

VISION CRN

Vascular **I**mplant **S**urveillance & **I**nterventional **O**utcomes **N**etwork

- Partnership with VQI to enrich data through linkages with claims to measure safety and effectiveness of vascular devices to evaluate
  - the impact of provider characteristics on device outcomes
  - health disparities related to device use and outcomes;
  - the impact of medical practice guidelines and healthcare policies.

VISION CRN


Publications & Research
Leila Mureebe
Jens Eldrup-Jorgensen
Michael Dalsing
Shipra Arya
Chandler Long
John Maijub
Thoracic Aorta
TBD
Data Core
Grace Wang
Marc Schermerhorn
Mahmoud Malas
Andrew Hoel
Ben Brooke
Executive Council
Phil Goodney
Art Sedrakyan
+
Rotating Council Chairs
Aortic Aneurysms
Pablo Morales
Salvator Scali
Kristina Giles
Carotid Artery
Randall DeMartino (Chair)
David Stone (Chair)
W.Darrin Clouse
Jocelyn Beach
Venous
Nicholas Osborne(Chair)
Peter Henke (Chair)
PVI
Daniel Bertges
Scott Berman
Emily Spangler
Alabi Olamide
Graeme McFarland
Yazan Duwayri

In Conclusion

- Supporting evidence generation with high quality RWD generating RWE across the TPLC produces timely access to safe and effective medical devices.
- FDA is here to help and facilitate engagement
- High quality device/patient Registries are strategically positioned to further enhance the care of patients
  - A multi-stakeholder community (e.g., different medical specialties, drugs and device manufacturers, patients)
  - A platform capable of embedding clinical trials, RWD generating RWE to support regulatory and payor decisions, refine medical practice, and patient/caregiver care.

Future Directions

- Collaboration is key
- Support data capture, collection and analyses through:
  - Global harmonization of clinical definitions
  - Generate clinically-meaningful minimum core datasets, lean CRFs
  - Automate data input (e.g., UDI)
  - Improve interoperability