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

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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)]

**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)]
<table>
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<tr>
<th>Relevance</th>
<th>Reliability</th>
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<tr>
<td>• Duration of Follow-Up Not Comparable</td>
<td>• No Assurance that All-Comers Captured</td>
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<td>• Event Definitions Don’t Match Exactly</td>
<td>• No Auditing Process</td>
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<tr>
<td>• Patient Population Not Directly Comparable</td>
<td>• Follow-up Incomplete</td>
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<td>• Standard of Care Used Not Comparable</td>
<td>• RWD Source Not Representative of All Treatment Sites</td>
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Some (Not Exhaustive) Data Quality Pitfalls
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

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

NESTcc has identified and selected vascular implant devices and developed evidence throughout the medical device lifecycle, including:

- Develop, verify, and operationalize methods or evidence for service-oriented outcomes
- Demonstrate scalability across healthcare systems, including public and private sectors
- Demonstrate impact on patients by stimulating innovation and innovation launch
- Inform NEST's strategy as it builds out critical functions and partnerships

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

Years of Patient Follow-up

Baseline/Implant/Peri-procedural

Active Post-Approval Study

Claims & Supplemental Data

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

Vascular Implant Surveillance & Interventional Outcomes Network

- 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.
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