Use Experience of Real World Evidence in the Actual Review

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Clinical Evidence Generation

Current Paradigm

Patients
- Evidence Based Decisions:
  - Personalized Risks vs. benefits of alternative therapies
  - Informed decisions regarding preferences
  - Innovation – Devices and device therapies for unmet needs

Clinicians
- Evidence Based Medicine:
  - Informed Clinical Decision-Making
  - Appropriate Use Criteria (AUC)
  - Professional Society Practice Guidelines (PG’s)
- Timely introduction of new therapies

Regulators
- Safety and Effectiveness
- Benefit > Risk
- Least Burdensome
- Total Product Life Cycle (TPLC) Assessments:
  - Surveillance & PAS
  - Pre-Post-Market balance
  - Dynamic labeling

Payers
- Reasonable and Necessary
- Comparative Effectiveness
- QoL effects
- Cost Effectiveness
- Coverage

Appropriate, Timely and Generalizable Evidence For Informed Decisions
Clinical Evidence Generation

*Current Paradigm*

- Protocol development and complexity
- Site recruitment, contracting, & monitoring
- Patient enrollment and retention

Slow Time to Market

Inefficiency and High Costs

Increasingly becoming the primary source for clinical evidence generation:

Industry goals may not always align with clinical needs
Regulatory Considerations for Using Real-World Evidence

• Data source, relevance, reliability, quality, completeness, bias
• Demonstrate reasonable assurance of safety & effectiveness

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When is Use of Real-World Evidence Appropriate

• Expansions of Indications
  – Increased indicated lesion length for the Zilver DES and Lutonix DCB
  – Expanded lesion type to include in-stent restenosis for In.Pact Admiral DCB and Lutonix DCB

• Post-approval surveillance
  – Evaluate longer term outcomes
  – Evaluate outcomes in US patients
Pathway for Success

• Pre-Submission to discuss a prospective analysis plan
  – Identify analysis type (e.g., propensity matching)
  – Identify confounders/covariates, appropriate endpoints
  – Determine methods to reduce bias
    → Build confidence in the SAP

• Follow the plan

• Submit supplement
Thank you!