# Registry-Based IDEs
## *FDA View*

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# Potential Advantages of an IDE Embedded in an Ongoing Registry

Efficiencies of data capture

- Studies completed faster
- Studies completed at lower cost

# Study Site Efficiencies
## *(Non-IDE Regulation-Related Benefits)*

- Data already being collected per routine
  - Sites already experienced in data collection
  - Familiar with use of electronic medical records
- IRB is familiar with the Registry's objectives and patient protection elements
- The patients are there!

# Site and Investigator Selection

- Identify sites with high rates of complete and accurate IDE-level data collection
- Identify investigators with appropriate training and experience with regard to;
  - Patient treatment and care
  - Compliance with an investigator agreement and adherence to the clinical study protocol

Some sites/operators which excel in clinical **care** may not be the same as those which excel in clinical **research**

# Study Execution and Scientific Validity Must Be Up to IDE Standards

# The 9A's of an IDE

- 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

# Monitoring

What's necessary?

# What is Clinical Study Monitoring?

- Methods used to oversee the conduct of, and reporting of data from, clinical investigations
- Focus on the processes that are critical to:
  - Protect human subjects
  - Maintain study data integrity
- Intended to identify and correct practices that could result in inadequate patient protection and/or poor data quality

# What Needs to be Monitored in an IDE?

- Data critical to the reliability of the study findings
  - Data that support primary and secondary endpoints
- Data critical to subject safety
  - Subject eligibility criteria
  - SAEs and UADEs, deaths, and withdrawals
- Processes critical to ethical treatment and subject safety
  - Obtaining informed consent
  - Providing appropriate medical consultation in the event of specified clinical or laboratory findings
- Processes critical to data integrity
  - Referring specified events for adjudication

# Data Capture Monitoring

- Validity of event rates depends on:
  - Methods of potential event identification
  - Intensity of surveillance efforts
  - Completeness of data collection
  - Criteria for validating events
  - Quality control

**Review monitoring program with FDA**

# CEC Adjudication

Is it always needed?

Can claims data suffice for identifying reportable events?

# Adjudication in Device Studies

- Enhances validity of study outcomes
  - More consistent event assessments
  - Increased accuracy of event rates
- Reduces bias
  - Particularly important for device trials
    - Rarely double-blind and sometimes not even single-blind
    - Greater frequency of pivotal trials that utilize historical controls or are single arm studies
      - Adjudication committee unblinded to treatment assignment

**Uniform event definitions particularly important**

# Special Considerations for Device Study Adjudication: *Mechanistic Insights*

- Allows for a more complete assessment of factors contributing to adverse events or benefits
- Can address the relatedness of an event to the device or procedure
  - Typically more relevant to device vs. to drug studies
    - Device, procedure/operator, or patient/anatomic-related factors
  - Causality may reflect on the safety or effectiveness of the device (and impact regulatory decisions), and assigning causality isn't always obvious

# Depth of Adjudication

There is a relationship between how clearly an event can be defined and how much adjudication is needed.

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**What questions need to addressed in the study?**

**Death or cardiovascular death**
**Any coronary revascularization or ischemia-driver TLR**
**Any MI or MI due to stent thrombosis**

# Depth of Adjudication

## Status of the technology should be considered

| Novel Device | "Me - Too" Investigational Device | Approved Device with New Intended Use |
|---|---|---|
| • Novel use<br>• Well-understood use | • Novel use<br>• Well-understood use | • Novel use<br>• Well-understood use |

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**From the unknown unknowns to the known knowns**

# SAFE PCI STEMI for Seniors IDE Study

Post-market study

- –Well understood clinical context
- –Mature technologies
  - Well understood device performance attributes
- –New indication for use for approved devices

# Claims Data vs. Traditional Adjudication

- Claims data can provide a means to identify potential events post-procedure and, subject to validation, help establish event rates.
- Claims data would not be sufficient to:
  - Investigate device failure modes
  - Provide timely completion of root cause analyses
- Claims lack adequate detail for some important interventional cardiology IDE study endpoints.

# Parting Thoughts

- Use of registries to facilitate IDE studies requires cooperation among stakeholders and industry's willingness to give up complete control of their study.
- Monitoring and adjudication remain important challenges.