Beth Israel Deaconess Medical Center

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Current State of Endpoint Adjudication in Device Trials

Academic View

CSRC/MDEpiNet Device Adjudication
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Event Adjudication in Cardiac Device Trials

- **Large, global trials with long-term follow-up**
- **Multiple clinical endpoints for assessment of device and disease-related impact on mortality and morbidity.**
- **Trials are almost always unblinded to investigators and patients.**
- **Event adjudication essential**
  - Consistent event reporting across sites and regions
  - Limit bias in investigator and patient reporting
  - Complete and accurate ascertainment of all endpoints

Event Adjudication in Cardiac Device Trials

"All events were adjudicated by an independent CEC"

What does it mean?

- Accurate and consistent reporting with limited bias
  - CEC members were qualified experts and independent of scientific or financial conflicts
  - CEC worked without sponsor or investigator influence
  - Definitions were standardized and pre-specified
- Complete ascertainment of endpoints
  - Robust event identification method
  - Data compliance and missing data management

What works well today?

- Mature CEC processes
  - Experienced managing groups (AROs)
  - FDA, investigators, and trial sponsors agree on importance of an independent CEC
  - Data collection and trial operations generally allow for dynamic, real-time adjudication
- Standardized endpoint definitions
  - In most cases general agreement on endpoints of interest
  - Wide acceptance of proposed standardized definitions for clinical CV endpoints (MI, TLR, ST, bleeding, stroke)

What can be done better?

Complete Reporting of Events

- Endpoint triggers based on CRF data responses and source
- Site monitoring (percentage, frequency)
- Missing data reports for endpoint trigger data elements including CEC procedures for adjudicating events when data mising

Standardize CEC Qualifications

- Recognized experts within the appropriate clinical specialty
- Knowledge of clinical trial and CEC operations
- Lack of standardization across CECs

What can be done better?

Quality Assurance

- Intra- and Inter-observer variability
- Frequency of returned adjudications by sponsor
- Frequency of changed adjudications
- Consistency of results between CECs and Processes
  - Panel experience and expertise
  - Parallel versus consensus meetings – single specialty versus multidisciplinary endpoints

What can be done better?

- Independence of Operations
  - Minimize contact between sponsor/investigators and CEC
  - Management of CEC by third party
    - Identify events and issue CEC data requests
    - Contracts and Payments
    - Communication with other trial operational groups
- Lower costs

What can be done better?

Future Direction:

Study Populations Beyond Standard Clinical Trials

Large Simple Trials

Large Observational Studies

- Novel processes (eg. algorithms versus case by case)
- Full study adjudication versus sample

Goals – Short-Term

Standardize CEC Processes

- Minimum membership requirements
- Level of independence from sponsors and investigators
- Recommendations for CEC manual of operations
- Robust event identification
- Management of missing endpoint data
- Reconciliation of investigator reports and adjudication

Goals – Long-Term

Identify Adjudication Process for Large Simple Trials and Registries

- Is adjudication required?
- Is adjudication requirement specific to endpoint type?
- Are adjudication algorithms acceptable/better than other event report methods (investigator report, administrative data)?
- Does adjudication of a sample improve quality of evet reporting for overall study?