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Current State of Endpoint Adjudication in Device Trials

Academic View

CSRC/MDEpiNet Device Adjudication
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Donald E. Cutlip, MD
Harvard Clinical Research Institute
Smith Center for Outcomes Research in Cardiology
Beth Israel Deaconess Medical Center
Professor of Medicine
Harvard Medical School

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



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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



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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)



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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 missing

Standardize CEC Qualifications

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



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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



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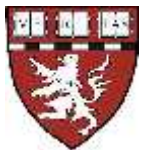
What can be done better?

- 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



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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



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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



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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 event reporting for overall study?



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