Cardiac Safety Research Consortium

CSRC and MDEpiNet Thinktank Meeting: "The Role of Endpoint Adjudication in Medical Device Clinical Trials"

ACC Heart House
Friday, March 11, 2016
8:00am-4:00pm
Meeting Agenda

8:00am-9:50am Session I: Tailoring best practices for the evaluation of endpoints in clinical device trials.

1) Introductory Remarks:
   William Maisel, MD, MPH (FDA) (10min)
   Danica Marinac-Dabic MD, PhD (FDA) (10min)
2) Introduction: Current State of Endpoint Adjudication in Device Trials
   a) What are rationales for clinical trial adjudication; i.e. why and when is it appropriate or desired to adjudicate an endpoint.
      1. Regulatory View- **Andrew Farb, MD** (FDA) (10min)
      2. Industry View **Thomas Christen, MD** (Boston Scientific) (10min)
      3. Academic View- **Donald Cutlip, MD** (Harvard University) (10min)

1) What are the key components of the adjudication process including study endpoints and CEC elements (committee membership, charter, voting, QA, interactions with other clinical study committees, and independence from study sponsors/funders) **Jonathan Seltzer, MD, MBA** (ACI Clinical) (10min)
2) How do the following study elements add bias or variability to the adjudication of endpoints in device clinical trials? What types of trial designs and clinical study operational factors help to minimize bias/variation? Are there other aspects of device trials which might contribute to or reduce endpoint variability? **George Dangas , MD** (Mt Sanai Medical Center)(10min)
   a) Study Blinding Challenges
   b) Variability in Operator Expertise and Operator Learning Curve Issues.
   c) Gathering the Necessary Data for Adjudication
   d) Role of Core Labs
   e) Sham/Mock Intervention

Standardized Endpoint Definitions. **Karen Hicks, MD** (FDA) (10min)

Panel Discussion: All Speakers
*Lead Discussant: **Pascal Vranckx, MD** (Cardialysis)*

What features of device trials would assist in the adjudication of endpoints? When do we need adjudication to determine if an event occurred? When do we need adjudication to ascertain device-related causality? Is adjudication helpful in determining the impact the operator expertise or technique on outcomes?

Break-9:50am-10:00am

10:00am-12:10 pm Session II- Practical Issues in the adjudication of events in device trials: Case studies which highlight the issues involved with adjudicating event occurrence, causality, blinding, operator variability, committee composition, endpoint definitions, gathering endpoint data, and clinical study operational issues.

1. Therapeutic Device Trials (e.g., Companion CHF) **Peter Carson, MD** (Washington, D.C. VA Medical Center)(10min)
2. Implantable Diagnostic Device (e.g., Chronicle, CardioMems)- **Alan Miller, MD** (Health Science Center) (10min)
3. Diagnostic Devices (e.g. Troponin, other biomarkers) **Jim Januzzi, MD** (Massachusetts General Hospital)(10min)
4. Drug-Device Combination Products (e.g., Bio absorbable Drug-Eluting Stents) – **Ted Heise**, **PhD, RAC** (Cook Medical)(10min)
5. FDA Perspective **Bram Zuckerman, MD** (FDA)(10min)

Panel Discussion: All Speakers & Rochelle Fink, MD, JD (FDA)
*Lead Discussant: **Wojciech Zareba, MD, PhD** (University of Rochester Medical Center)*

What practical issues should influence our thinking about adjudication? Are there critical clinical study issues in which adjudication is *required*? Are there issues in which adjudication is practically impossible? Do these issues differ among clinical studies of stents, valves, diagnostics, pacers, and non-implantable devices used for procedures (e.g. ablation)?

Working Lunch 12:10pm-12:40pm

12:40pm- 3:00 pm Session III: The Role of Adjudication in Efforts to Streamline the Process of Making Beneficial Devices Available to the Public: Regulatory and Reimbursement Issues

1) Post Market approval: Safety/Efficacy Data collection to support development and expanded labelling: The role of Big-Data in assessing post-marketing safety and effectiveness outcomes: What types of post-market data is susceptible to bias in reporting? Is it likely that adjudication would reduce this bias? How reliable are

claims data or other large patient care databases to determine event rates without independent adjudication?

a) Claims based data**- Matthew Brennan, MD,MPH** (Duke University) (10min)
b) Registry (e.g. TAVR) **Mitchell Krucoff, MD** (Duke University) (10min)
c) Big-Data (e.g. EMR data, data consolidators) **Jo Carol Hiatt, MD, MBA** (Kaiser Permanente) (10min)
d) Industry Perspective/Emerging data sources (e.g. PCORI, patient reported outcomes data) **Richard Kuntz, MD** (Medtronic)(10min)

Panel Discussion: All Speakers
*Lead Discussant: **Mitch Krucoff, MD** (Duke University)*

What types of post marketing events require adjudication? What are the characteristics of types of devices that might require adjudication? What are the key factors that provide for practical endpoint adjudication in the post-market setting? Does the statistical power of databases obviate the need for adjudication? If not, what are potential strategies for adjudication? Can databases be used to identify potential events (reducing the burdens and costs associated with on-site study monitoring), which can then be independently adjudicated by a CEC? Can database strategies replace registries?

2) Efficient use of premarket data sets to meet both FDA-CMS requirements:

a) Engagement with CMS and FDA: What is it and what is its current status in device trials? When can we use clinical study data to support both CMS and FDA requirements? When would endpoint adjudication be helpful?
    1. Industry View**— Bradley Horst** (Boston Scientific)(10min)
    2. Regulatory View- **Murray Sheldon, MD** (FDA)(10min)
b) CDRH's Expedited Access PMA (EAP) Program. What is it? Since the focus is to speed approval of devices meeting unmet medical need with less pre-market data than typically required for a PMA but with enriched post-market data collection, what is the role of adjudication in these situations to satisfy FDA data requirements post-market? What is the role of adjudication in these situations to satisfy coverage with evidence development (CED) for CMS? Is there a difference in adjudicating safety vs. effectiveness? In what cases could the additional effort needed for endpoint adjudication reduce the length or breadth of post-market follow-up?
    1. CMS View- **Daniel Canos** (10min)
    2. Industry View—**Wendel Smith, MD** (Edwards Life Science) (10min)

3:00pm-3:30pm Summary and Next Steps