The Adjudication Process in Clinical Events Committees

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3rd Annual DIA Clinical Forum - Nice 2009

Taking Decisions on Events

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Clinical Events

• Clinical trials can be driven by clinical events

• Many clinical events lack standard or commonly accepted definitions or are subject to interpretation

Clinical Event: examples

• Hospitalization for PAH-non elective with predefined criteria (including IV prostanoid, Tx and BAS)

• New *** due to *** as either the primary or relevant contributing cause
The Adjudication Process

- An event reported at a site is reviewed by a set of experts (CEC)
- The assessment done the set of experts is used for statistical analyses

Clinical Event Committee

Central Event Committee

Critical Event Committee

CENTRALIZED

ON-LINE
Why Central Review?

- **Accuracy** in Event detection: high level of expertise needed
- **Independency**: avoid bias in finding out events
- **Homogeneity**: centralized committee

Why an online system?

- **Time** to confirm an event as a study endpoint is a key factor
- **Amount of data** involved in the decision process
- Data can **change** during the adjudication process before file closure
- Users may need **interactive tools** (generate Charts, view Radiology / CT images with zoom / measure / contrast features)
Online Adjudications System in Actelion

- 2001: Enable (>1600 Patients)
- 2005: Compass II (ongoing)
- 2008: Conscious II (ongoing)
- 2008: Seraphin (ongoing)
- 2009: Conscious III (under development)
- 2009: Restora (planned)

What is the difference between the implementations?

- The roles involved
- The process
- The link with External Sources
- Interactive tools
Patients data handled by the system

1. CRF “Key data” (e.g.: Primary cause of death, Neurological worsening onset date, …)
2. Case Report Summary (CRS) or Patient Profile listing all patient data (including external)
3. External (non-CRF) documents (e.g.: ECG, Death Certificate, Hospital Discharge Summary, …)

A real example

CONSCIOUS – 2
Aneurismal Subarachnoid Hemorrhage
Roles (inside Sponsor)

- **Coordinator**: Actelion responsible for patient cases submission to the CEC, document organization and upload.

- **BatchProcess**: Automatic jobs loading data, preparing CRS, detecting changes.

Roles (outside Sponsor)

- **Primary Reviewer**: The CEC member who makes the primary review of a subject case and completes a CEC Form.

- **Consensus Reviewer**: The CEC member who leads the consensus meeting and completes the Consensus Form.
Roles (outside Sponsor)

- **Adjudicator**: The one who decides when no unanimity could be reached during a consensus meeting and completes the Adjudication Form.
- **Chairman**: Is responsible to indicate whether changes occurring after the subject case was submitted should trigger a re-review of the case.

Process Workflow

1. Batch Jobs detecting cases
2. The Coordinator submits ready cases to a trio of Reviewers
3. Dr. A Reviews submitted patient cases
4. Decision Dr.A
5. More Data Needed
6. Batch Jobs detecting changes
3. Dr. B Reviews submitted patient cases
4. Decision Dr.B
3. Dr. C Reviews submitted patient cases
4. Decision Dr.C
5. More Data Needed
6. Batch Jobs detecting changes
4. Decision Dr.A

Identical decision?

Yes

4. Decision Dr.B

No

4. Decision Dr.C

7. Results stored on DB

Yes

8. Consensus Meeting

No

9. Adjudicator

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21 October 2009

The Control Panel
# Key Variables Section

## In case of Submission

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## In case of Re-Submission

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View Images Section  Example

Graphics Section  Example
Two-Levels EDC

1st: Many Data Sources – One Way data flow

2nd: On line System fed with data from Level 1 – Two Ways data flow

Conclusion

Online Adjudication System is critical tool to:

- Reduce the time to confirm an event as a study endpoint
- Handle the huge quantity of data involved in the decision process
- Handle the change of data during the process
- Ensure Accuracy, Independency, Homogeneity