



The Adjudication Process in Clinical Events Committees

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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**



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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**



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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 Committe

Central Event Committe

Critical Event Committe



The Adjudication Process

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



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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)



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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)



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What is the difference between the implementations?

- The **roles** involved
- The **process**
- The link with **External Sources**
- Interactive **tools**



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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, ...)



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A real example

CONSCIOUS – 2

Aneurismal Subarachnoid Hemorrhage



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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.



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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.



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Roles (outside Sponsor)

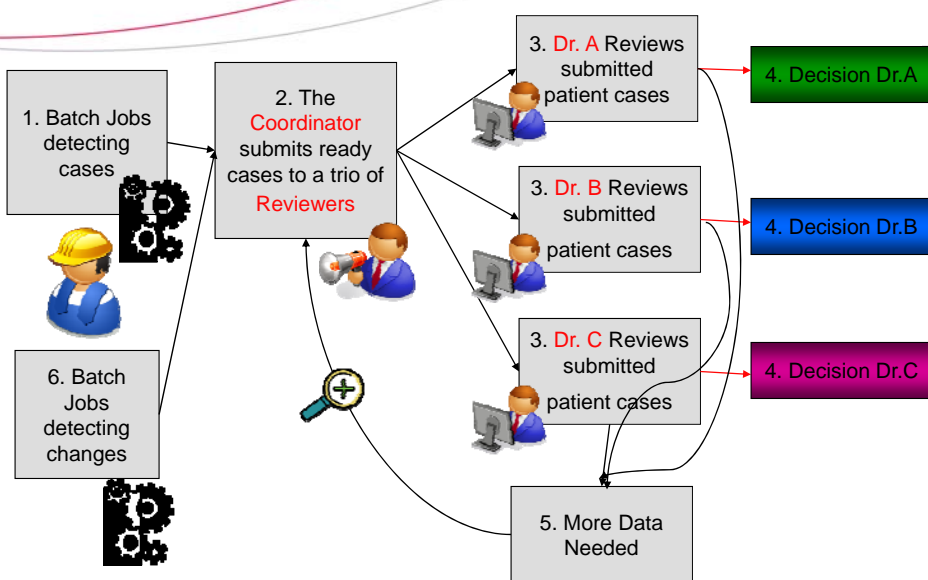
- **Adjudicator:** The one who decides when **no unanimity** could be reached during a consensus meeting and completes the Adjudication Form
- **Chairman:** Is responsible to indicate whether **changes** occurring after the subject case was submitted should trigger a re-review of the case.



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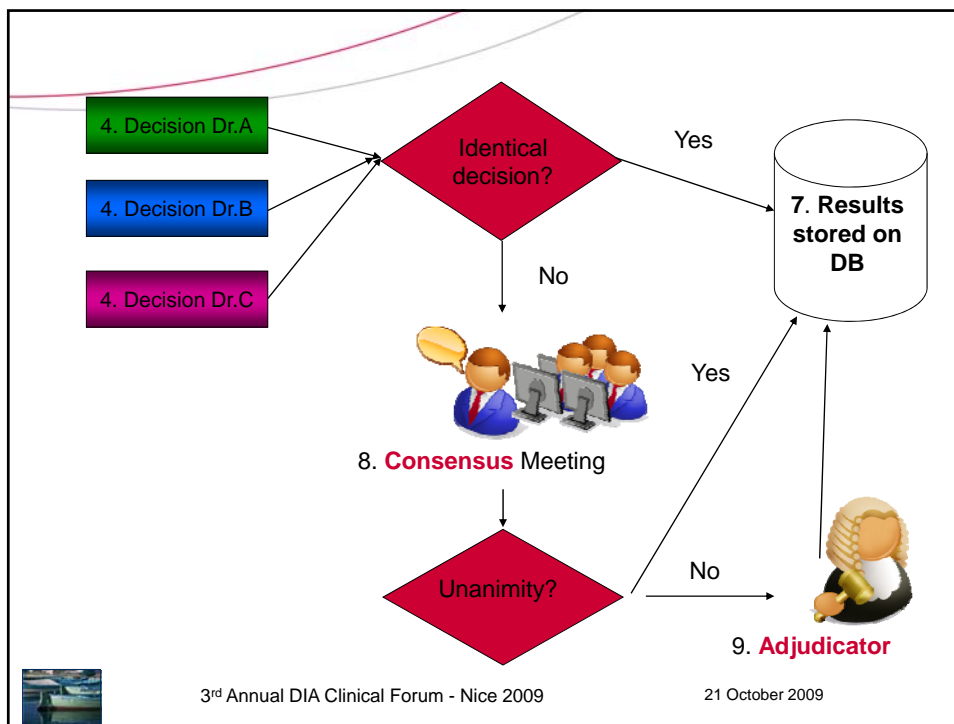
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Process Workflow



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The Control Panel

Actelion CADP - Microsoft Internet Explorer

CEC support system
Conscious II

Cases List
Current Roles: Coordinator

Changed Only Submission status: All Review status: All

Site: All Patient: All Data Quality: Best data

Site	Patient	Case date	Doc	Crs	Key	Img	Gra	Submission status	Review status	Last submission date	Details
10100		14DEC07	●	●	●	●	●	Re-submitted due to data changes	To be discussed/Adjudicated	08/MAY/08 16:43:45	
10101		16DEC07	●	●	●	●	●	Submitted	To be discussed/Adjudicated	23/MAY/08 11:14:23	
10104		28DEC07	●	●	●	●	●				
10102		29DEC07	●	●	●	●	●				
11348	UNK		●	●	●	●	●				
10111		09JAN08	●	●	●	●	●	Submitted	To be discussed/Adjudicated	08/MAY/08 15:08:53	
10460		15JAN08	●	●	●	●	●	Re-submitted due to data changes	Pending	08/MAY/08 16:59:56	
10464		17JAN08	●	●	●	●	●	Re-submitted due to data changes	To be discussed/Adjudicated	27/MAY/08 10:29:32	
10109		27JAN08	●	●	●	●	●				
10105		29JAN08	●	●	●	●	●	Re-submitted after request for more data	To be discussed/Adjudicated	08/MAY/08 16:38:36	

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CRS Section - Compare

Date	Collection	SD	TD	Total input (ml)	Total output (ml)	Calculated Fluid Balance (ml)
03/13/07				37.0		37.0
04/13/07				36.5		36.5
03/13/07						
03/14/07						
03/15/07						
03/16/07						
03/17/07						
03/18/07						
03/19/07						
03/20/07						
03/21/07						
03/22/07						
03/23/07						
03/24/07						
03/25/07						
03/26/07						
03/27/07						
03/28/07						
03/29/07						
03/30/07						
03/31/07						
04/01/07						
04/02/07						
04/03/07						
04/04/07						
04/05/07						
04/06/07						
04/07/07						
04/08/07						
04/09/07						
04/10/07						
04/11/07						
04/12/07						
04/13/07						
04/14/07						

Subject number: 10587
 Randomization number: 5037
 Date of Anesthesia capture: 19FEB08
 Study Day (SD): 0
 Day/Time of study initiation: 21FEB08 22:15 TD: 1
 Day/Time of study stop: 14:00 TD: 14

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Key Variables Section

In case of Submission

View Key Variables			
INITIAL HOSPITALIZATION			
Category	Description	Submission Value	
Hospitalization	Date Of Admission	15DEC07	
NEUROLOGICAL WORSENING			
Category	Description	Submission Value	
Neurological Worsening	Onset Date	24DEC07	
Neurological Worsening Primary Cause	Cerebral Infaction Due To Vasospasm	X	
RESCUE THERAPY			
Category	Description	Submission Value	
Type Of Rescue Therapy	In Vasopressor Therapy	X	

In case of Re-Submission

View Key Variables					
INITIAL HOSPITALIZATION					
Category	Description	Submission Value	Change	Latest Adjudication	
Initial Hospitalization	Date Of Admission	15DEC07	●	15DEC07	
NEUROLOGICAL WORSENING					
Category	Description	Submission Value	Change	Latest Adjudication	
Worsening Neurological	Onset Date	24DEC07	●	15DEC07	
Worsening Neurological	Pc Cerebral Infaction Due To Vasospasm	X	●	X	
RESCUE THERAPY					
Category	Description	Submission Value	Change	Latest Adjudication	
Type Res...	pressor Therapy	X	●		



View Images Section Example

W1301-10101 - Intelrad PACS - ActelonCR - IntelViewer

File Print View Tools Utilities Patient Help

Study Members:

Subject Member C

Case date:

Date of film edit:

View Documents

View CRIS

View Key Variable

View Images

View Graphics

View CRF Form

Comments:

Neurological Verdana

2009-10-11 11:11

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Graphics Section Example

CEC support system Graphics Form

Current Roles: Coordinator

Subject Number/CRF Number: 10100

Case date: 14DEC07

Graphic Set: Labs AEs Pressure

BRONCHOSPA

240

207

154

101

48

5

Days after

Legend:

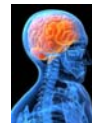
- AE
- SBP
- HR
- WBC
- CVP caltZO *
- Na

At Zoom

Graphic Pack

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**



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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**



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Questions



West Ham United's Carlton Cole fouls Arsenal's Alexandre Song Billong, resulting in a red card - Sonntag 26. Oktober 2008, 19:04 Uhr



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