The Clinical Events Committee: Purpose and Function

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Clinical Events Committee

The Clinical Events Committee (CEC) is responsible for:

- Development of specific criteria used to categorize clinical events and clinical endpoints.

Clinical Events Committee (cont'd)

- Review and adjudication of all clinical events which comprise the primary endpoints of the clinical trial.
- Review and adjudication of all clinical events for which the minimum data required for internal CRO adjudication are unavailable.

Clinical Events Committee (cont'd)

- Review all deaths which occur throughout the duration of the trial.

Membership of the CEC

- The members of the CEC are usually drawn from the local physician community and should have experience in clinical trial events adjudication.
- The number of members required for a meeting is variable (at least 3 members preferably 5-7).

Membership of the CEC (cont'd)

- At least one member should have special expertise related to the trials being reviewed at the meeting (e.g. for stent trials, an interventional cardiologist should be present).

Identification of Events

The process of identification of events for CEC review is multi-tiered:

- All events which comprise the primary endpoints of the trial are reviewed by the CEC (e.g., in stent trials, the events which require review are death, myocardial infarction, emergent CABG, abrupt or sub-abrupt closure, repeat revascularizations and vascular complications).

Identification of Events (cont'd)

- Other events may require CEC adjudication (i.e., events with insufficient data available or for which there are contradictory data).

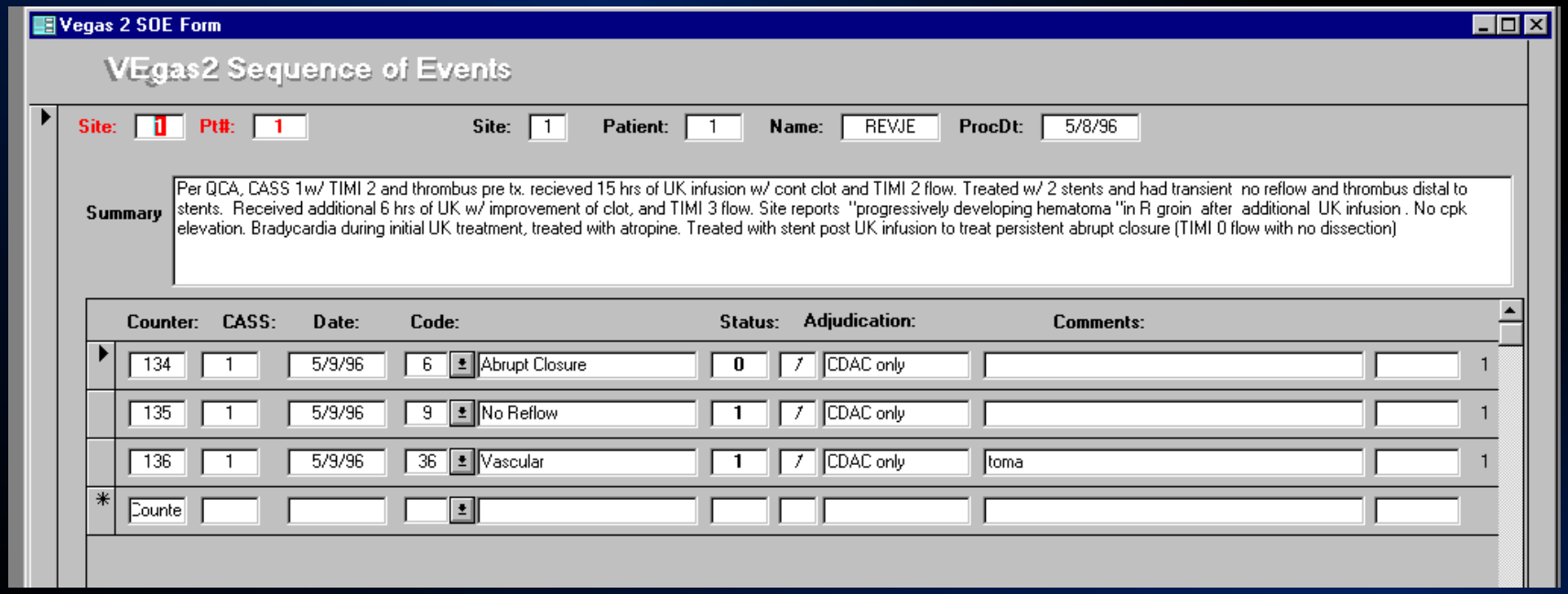
Identification of Events (cont'd)

- Questions are identified on the case report forms which enables capture of all potential events.
- A listing of event codes is developed for the nurses and physicians to utilize while coding and adjudicating events.

Identification of Events (cont'd)

- IS support programs queries which are run against database to identify patients with potential events.
- Nurses review patient records, code events, and prepare narrative summaries for internal CRO physician and CEC review.

Identification of Events (cont'd)



Identification of Events (cont'd)

- Internal CRO physicians review the events to determine if they did or did not occur.
- Once events are internally adjudicated by CRO physicians, they are brought before the CEC for review.

Preparation of Information for CEC Adjudication

- IS programs queries to identify patients with events to be reviewed by the CEC.
- A document containing the narrative summaries of the identified patients is prepared for the CEC meeting.
- This document ultimately serves as the minutes of the CEC meeting.

Preparation of Information for CEC Adjudication (cont'd)

- Care is taken to ensure that narratives are blinded to treatment assignment and to any information which may give away the treatment assignment.
- Multiple trials are usually included in the CEC document.

Preparation of Information for CEC Adjudication (cont'd)

Site	Pt	Complication to adjudicate	# days since procedure	Status
AA	Agree	B	Non Cardiac Death	120

The patient is a 62 year-old woman with no significant cardiac history who presented with CCS Class III angina. On 10/31/95 she underwent an uncomplicated index procedure in which the 1st diagonal branch was treated with the assigned device. There was a QCA reported final 28% residual stenosis. There were no complications post-procedure and she was discharged on 11/1/95. She had several hospital admissions for cancer and subsequently died of cervical cancer in August of 1996. No autopsy was performed.

CEC Adjudication Procedure

- At the start of each meeting, the rules and definitions for the events being adjudicated are reviewed.
- The narrative summaries are presented one at a time and a vote is taken to classify each event in question.

CEC Adjudication Procedure (cont'd)

- Each event is determined as having occurred, not occurred, or lacking sufficient information for adjudication (i.e. missing Core Laboratory data).
- All efforts are made to acquire additional information and the event is submitted for re-review.

CEC Adjudication Procedure (cont'd)

- If additional information is not forthcoming, the CEC shall adjudicate the event with the information available.
- All decisions of the CEC should be unanimous.

CEC Adjudication Procedure (cont'd)

- In the event of disagreement amongst CEC members, a vote is taken and the resolution determined by majority vote Any member of the CEC who is an investigator in a study being reviewed is excused for adjudicating events.

CEC Adjudication Procedure (cont'd)

- The decisions of the CEC are not divulged while the trial is in progress but are available for review at the conclusion of the study.

Summary

- The Clinical Events Committee plays an integral, unbiased role in the determination of occurrence of adverse events.