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**The Johns Hopkins Center for Clinical Trials  
Monitoring treatment effectiveness and safety in  
clinical trials  
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*Baltimore  
School of Nursing Auditorium*

**Selection of committee members:  
Competency vs objectivity**

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## **Selection of committee members: Competency vs objectivity**

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## **Treatment effects monitoring**

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In trials, the act of or an instance of reviewing accumulated outcome data by treatment group to determine if the trial should continue unaltered.

**treatment effects monitoring committee (TEMC)** *n* - [trials] A standing committee in the structure of trials responsible for the periodic review of accumulated data for evidence of adverse or beneficial treatment effects and for making recommendations for modification of a the trial based on accumulating data.  
syn: data monitoring committee, data and safety monitoring committee, safety monitoring committee

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## **Assertions**

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1. Treatment effects monitoring is an inalienable duty of study investigators
2. Requirements for competency in monitoring must supersede requirements for objectivity
3. That requirement is violated when the monitoring is comprised to exclude study representatives having intimate familiarity with details of the study protocol and study data
4. Monitoring bodies devoid of study investigators and commissioned to report to sponsors constitute violations of fundamental ethical codes underlying research on human beings

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## **Objective/competent**

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**objective** *n* - Uninfluenced by emotion, surmise, personal prejudice, or bias; not subjective.

**competent** *adj* - Having the requisite skills, abilities, and qualities sufficient to allow one to perform up to some standard or level

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## Selection of committee members: Competency vs objectivity

### Objectivity vs competency: Nuremberg Code

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*Item 2: The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature*

*Item 8: The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment*

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### The principle of competence

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A principle in medical ethics asserting that the care and treatment offered to research subjects must be consistent with accepted standards of care and treatment and that such care and treatment must be offered and applied in a competent fashion by people having the requisite skills, expertise, information, knowledge, and wherewithal necessary to ensure competence

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### Objectivity vs competency in trials

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- Need for competency supersedes need for objectivity (eg, in regard to conduct, one cannot mask treatments if doing so carries more than minimal risk for subjects)
- Most objectivity constructs have potential for reducing competency
- The tendency, in regard to monitoring, is to impose objectivity constructs assuming no effect on competency

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## **Selection of committee members: Competency vs objectivity**

### **On why objectivity takes precedence over competency in monitoring**

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Because

- Sponsors and the FDA value objectivity over competency
  - Decision making re monitoring is believed to be largely a statistical question
  - Investigators marginalization and disenfranchising re monitoring
  - IRBs don't get it
  - No presumed downside
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### **Monitoring objectivity constructs**

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- P-value-based pre-ordained stopping rules
  - "Look" restrictions; re number of "looks" allowed and on what can be "looked" at
  - Masked analysts
  - Firewall separation in the coordinating center to keep the CC Director and other key CC personnel from seeing interim results; especially when person is seated on the study steering committee
  - TEMC masked
  - TEMC voting members not associated with the trial
  - TEMC study representatives limited to those not having treatment responsibilities in the trial
  - TEMC votes and deliberations in closed executive sessions
  - TEMC members appointed by sponsor
  - TEMC commissioned to report to sponsor
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### **Requirements for competent monitoring**

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- Timeliness
  - Completeness of data
  - Accuracy
  - Independence
  - Unmasked
  - Unconstrained by construct
  - Medical, scientific, and analytic competence
  - Detailed knowledge of study protocol and procedures
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## **Selection of committee members: Competency vs objectivity**

### **Dogma re monitoring**

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- Isolated from study investigators
- Pre-ordained # looks (to protect p-values) and stopping rule
- Masked reports
- Firewall separations

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### **Meinert's "ideal" monitoring body**

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**Size: 10 (5 voting and 5 nonvoting)**

**Standing: Nonvoters at parity with voters except when voting**

**Voting members (no study affiliation):**

Expertise in disease and treatments being evaluated (at least 2 such people)

Biostatistician/trialist

Safety expert

Medical ethicist or theologian

**Nonvoting members (study affiliated)**

Study chair and vice chair

Director and deputy director of CC

Sponsor project officer

Treater

**Meeting**

**Mode: Face-to-face; conference telephone in emergency**

**Frequency: At least twice a year**

**Reports**

- Prepared by CC; distributed at least 7 days prior to meeting
- Unmasked
- Bound and page numbered

**Deliberations and votes: Open (ie, no executive sessions for voting members only re recommendations)**

**Reporting: To the chair of the steering committee**

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## Selection of committee members: Competency vs objectivity

### Multicenter trials profile

	Disease/organ	CC	Type	Trt	Sponsor	Status
ADAPT	Alzheimer	JHU	Pri	Drug	NIH-NIA	Ongoing
CBET	Cancer	JHU	Pri	Drug	NIH-NCI	Ongoing
COMBINE	Alcoholism	UNC	Trt	Drug/Counsel	NIH-NIAAA	Ongoing
CAMP	Asthma	JHU	Trt	Drug	NIH-NHLBI	1999
GCCRT	AIDS	JHU	Trt	Drug	NIH-NEI	2000
LODO	Asthma	JHU	Trt	Drug	ALA	2003
NETT	Emphysema	JHU	Trt	Surg/med	NIH-NHLBI	2003
OCTAVE	BP	BMS	Trt	Drug	BMS	2000
WGET	Vascular	JHU	Trt	Drug	NIH-NIAMS	2003

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### TEMC profiles

	Members			CC firewall	Director CC	Study chair	Project officer
	Vote	w/o vote	Tot				
ADAPT	5	2	7	N	Y	N	Y
CBET	5	6	11	N	Y	Y	Y
COMBINE	4	1	5	N	Y	N	Y
CAMP	10	-	10	N	Y	N	Y
GCCRT	7	3	10	N	Y	Y	Y
LODO	5	-	5	N	Y	N	Y
NETT	11	-	11	N	Y	N	Y
OCTAVE	5	1	6	Y	N	N	N
WGET	5	2	7	N	Y	Y	Y

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## Selection of committee members: Competency vs objectivity

### TEMC profile

	Appointing authority	Masked	Votes	Reporting route
ADAPT	SC	N	Open	SC
CBET	SC	N	Open	SC
COMBINE	SC	Self	Open	SC
CAMP	NHLBI	Y	Closed	Sponsor
GCCRT	NEI	N	Open	Sponsor
LODO	SC	Y	Open	Sponsor
NETT	NHLBI	N	Closed	Sponsor
OCTAVE	BMS	N	Closed	Sponsor
WGET	NIAMS	Y	Closed	Sponsor

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## Selection of committee members: Competency vs objectivity

### Selected references

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### Acknowledgements

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Slide set on: [TrialsMeinertsWay.Com](http://TrialsMeinertsWay.Com)

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