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

Interaction interfaces

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Curtis L Meinert, PhD

The Johns Hopkins University
Bloomberg School of Public Health
Department of Epidemiology
Baltimore Maryland

Interaction interfaces

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Interconnected bodies

- **Investigators**
- **Sponsor**
- **FDA**
- **TEMC**
- **IRBs**
- **Patients**

\CTTalk\Parties

Investigator bodies

- **PIs (center directors)**
- **Study officers**
- **Steering committee**
- **Research group**

\CTTalk\Investor

Sponsor

sponsor *n* **- [LL, fr L, guarantor, surety, fr *sponsus*, pp of *spondēre* to promise] 1. A person or agency responsible for funding a project. 2. The person or agency named in an Investigational New Drug Application or New Drug Application (usually a drug company but not always, eg, as with an INDA submitted by a representative of the research group). 3. A firm or business establishment marketing a product or service.**

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Facts regarding sponsors

- **A sponsor is a sponsor**
- **All sponsors have "conflicts of interests"**
- **Interests of sponsor are different than the interests of investigators**
- **All parties best served by arms length separation of and from sponsor**

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Interaction interfaces

Rules re sponsor interface

- Provide sponsor position (nonvoting) on TEMC
- Standing of sponsor on TEMC should be at parity with other study representatives
- Provide sponsor with right of review (but not right of approval) of key study publications
- Establish TEMC reporting procedure to include sponsor; avoid structures in which TEMC reports via sponsor

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IRB good practice procedures

- IRB hierarchy; parent IRB for submissions and approvals
- Prototype consents
- Review of IRB approved consents to ensure proper content and language
- Zero tolerance policy for protocol overrides
- Designated conduit for transmission of AEs to IRBs
- Protocol for informing IRBs of TEMC mtgs and recommendations for change

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IRB interface re treatment effects monitoring

- Specify for IRBs: Nature and extent of treatment effects monitoring; persons responsible for monitoring (voting and nonvoting members); frequency of monitoring looks; linkage of monitoring body to investigators; reporting procedure for IRBs
- Construct prototype consent to indicate nature and extent of monitoring, whether monitoring is masked (and reason for masking), and how recommendations for change re monitoring will be communicated to investigators

- Establish protocol for reporting results of TEMC to IRBs (Note: It is important, when establishing protocol, to determine what constitutes a mtg of the TEMC); suggested reporting procedure:
  - Report from CC direct to parent IRB; report within 60 days of mtg but not less than 30 days of mtg
  - Report to center directors for transmission to respective IRBs
  - Report should indicate time of mtg, persons in attendance (voting and nonvoting), narrative list of categories of data reviewed, and recommendations (without indication of whether unanimous)

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Sponsor-investigator tension re TEMC

- **Who appoints the TEMC?**
- **To whom does it report?**
- **What does it look at?**
- **How often does it look?**
- **How do recommendations get to investigators?**
- **Who is the final authority re recommendations?**

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Nüremberg Code

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 (Item 8)

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Proposition

Constructs involving watertight separation of the monitoring body from study investigators violate basic ethical codes underlying research on human beings because such separations are tantamount to requiring investigators to assign an alienable duty, namely the duty to preserve and protect those studied from harm, to a party having no direct responsibility for such protection and not accountable to any IRB

That linkage is threatened or severed when the TEMC is devoid of study investigators or when commissioned to report to the study sponsor

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TEMC-investigator linkage assurances

Appointment: Via SC; if by sponsor with the advise and consent of the SC
Membership: Comprised to include study representatives (voting or nonvoting)
Deliberations and votes: In the presence of study representatives
Reporting: Direct to study chair or simultaneous to study chair and sponsor

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Interaction interfaces

Investigator interface

- **Recommendation for change communicated by study chair or director of CC**
- **Mtg (face-to-face or conference phone) of SC to discuss and debate recommendation**
- **Formal vote by SC**
- **Mtg of research group to receive recommendation and result of SC vote**
- **Formal action taken by research group re recommendation**

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Patients re monitoring

- **Consent should indicate nature and extent of monitoring**
- **Patients should be informed of a results based change even if change does not affect a given patient**

In regard to treatment or trial stops

- **Should be informed of stop before results are published or summarized in press**
- **Should be notified as to whether assigned to treatment being stopped**
- **Patients on treatment being stopped because of harm should be seen at study clinic to discuss treatment options**
- **If trial is being stopped because of benefit, persons not on treatment producing beneficial result should be offered beneficial treatment (when possible)**
- **Letters and mailings should come from clinics of record**

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Notifications of action

- **Investigators**
- **Patients**
- **IRBs**
- **Sponsor**
- **Announce results on financial wire service if action involves proprietary product of publicly traded stock company**
- **FDA**
- **Institution officials and public relations departments**

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