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(Thursday 9:59pm) 15 June 2000

Memorandum

To: Center for Clinical Trials faculty and staff

Fr: Curt Meinert

Re: Organization good practice policies and procedures (GPPP)

Definitions

advocacy representation construct *n* - [**multicenter studies**] A **representation construct** based on **advocacy**, eg, one where **membership** on the **steering committee** includes persons **external** to the **study** chosen to advocate a position or to represent an interest. rt: **center representation construct**, **discipline representation construct**, **PI representation construct**

center *n* - [ME *centre*, fr MF, fr L *centrum*, fr Gk *kentron* sharp point, center of a circle, fr *kentein*, to prick; akin to OHG *hantag* pointed] [general] 1. The middle **point** or part, as in a **distribution**. 2. A point or focus around which things are organized. 3. The focus of attention or interest. 4. core 5. The source or focus of an influence, action, or force. 6. **study center** (defn 4) 7. A place, such as a **study clinic**, where **study candidates** and study **enrollees** are seen for evaluation and **treatment** in a trial; **study center** (defn 1). syn: **site** ***Usage note***: In **multicenter trials**, often used in the sense of defn 7 to the exclusion of associated **resource centers**, as in the statement *the trial has 8 centers*, when in fact it has 12 centers, 8 of which are clinics and the other 4 of which are **resource centers**. Avoid such usage because of lack of precision and insensitivities to those in the resource centers of such trials. See **study center**, **investigator**, and **principal investigator** for added comments. Avoid by reserving the term, **center**, for uses in the collective sense of that term; use **study clinic** or some other appropriate term, such as **field site** or **data collection site**, in references to the subset of centers responsible for **data collection**.

center representation construct *n* - [**multicenter studies**] A **representation construct** based on **center**, eg, one where **membership** on the **steering committee** is by center or one where voting in the study is by center. rt: **advocacy representation construct**, **discipline representation construct**, **PI representation construct**

democratic governance *n* - A form of **government** in which power is vested in the citizenry and exercised directly, or through a system of representation involving periodic elections; rule by majority. [**multicenter trials**] Governance by the **research group** or by a body elected by the research group; governance in which membership of the research group is empowered to vote on key design and conduct issues. rt: **monarchic governance**, **oligarchic governance**

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discipline representation construct *n* - [**multicenter studies**] A **representation construct** based on **discipline**, eg, one where **membership** on the **steering committee** is apportioned by discipline or one where voting in the **study** is by discipline. rt: **advocacy representation construct**, **center representation construct**, **PI representation construct**

executive committee (EC) *n* - [**multicenter trials**] A **committee** within the structure of some studies, especially **multicenter studies**, responsible for direction of the day-to-day affairs of the study. One of the **key committees** in the organizational structure of a **multicenter trial**. Usually consists of the **officers of the study** and perhaps others selected from the **steering committee** and typically headed by the **chair** or **vice-chair** of the steering committee and reporting to that committee. rt: **steering committee** ***Usage note***: Sometimes used interchangeably with steering committee (not recommended). The term, **executive committee**, should be reserved for settings in which it is part of or subservient to a larger committee or body. In settings where there is only one leadership committee, use steering committee.

key committee *n* - [**trials**] A **committee** essential to the operation of a trial; generally any of the following: **steering committee**, **executive committee**, **advisory-review committee**, **treatment effects monitoring committee**, and **advisory-review and treatment effects monitoring committee** in **multicenter trials**. syn: major committee

monarchic governance *n* - A form of **governance** with absolute sovereignty vested in a single person. [**multicenter trials**] Governance by a single person, eg, the **study principal investigator** or **study chair**. rt: **democratic governance**, **oligarchic governance**

officers of the study *n* - The set of persons holding elected or designated **offices** in a **study**; in **multicenter trials** generally the **study chair** and **vice-chair** and the heads or **directors** of **key centers**, such as the **data center**, **data coordinating center**, or **coordinating center**, and **project office**. rt: **executive committee**

oligarchic governance *n* - A form of **governance** with power vested in a few. [**multicenter trials**] Governance by a **committee** composed of heads of **study centers**. rt: **democratic governance**, **monarchic governance**

organizational structure *n* - The **structure** of an **organization**, in the case of **multicenter trials**, usually one involving a series of **committees** as represented in the definition of **key committee**.

PI representation construct *n* - [**multicenter studies**] A **representation construct** based on PI-ship, especially one where **membership** on the **steering committee** is limited to PIs (defn 3 or 5) or one where voting is by PI. rt: **advocacy representation construct**, **center representation construct**, **discipline representation construct**

principal investigator (PI) *n* - [**research**] 1. The person having responsibility for conduct of the research proposed in a **grant application** submitted to the **National Institutes of Health**; such a person in any **funding application** submitted to the NIH, whether for **grant** or **contract** funding; such a person named on any **funding proposal**, regardless of funding source. 2. The person in charge of a **research project**; the lead scientist on a **research project**. 3. The head of a **center** in a **multicenter study**. 4. The **chair** of a **multicenter study**. 5. The head of a **clinical center** in a **multicenter trial** rt: **co-principal investigator** ***Usage note***: The term serves both as an administrative (defn 1) and leadership label (defn 2). It is a mistake to assume that an administrative role translates automatically into to a leadership role, though often the person named in the sense of defn 1 is the same person named or implied in the sense of defn 2 in the case of most investigator-initiated **single-center** research projects. Avoid use of the term, or its abbreviation, PI, as a leadership label in any single-center setting where more than one person is being referenced. Avoid in the sense of defn 2 in settings having multiple "principal investigators"; use **center director** and **chair of study** to designate positions of leadership in **multicenter** settings. Avoid uses in the sense of defn 5 since those uses carry subtle connotations that those heading **resource centers** are not as "principal" to the overall effort as their clinical counterparts. See also usage notes for **co-principal investigator**, **investigator**, and **center**.

resource center *n* - Any **center** providing supply, support, or expertise in a differentiated structure; in **multicenter trials** usually any of the following: **data center**, **data coordinating center**, **treatment coordinating center**, **coordinating center**, **central laboratory**, **reading center**, **quality control center**, **project office**, and **procurement and distribution center**.

representation construct *n* - [**multicenter studies**] Any of various **constructs** used for **representation** on the key governing bodies of a multicenter study or **study network**; includes **advocacy representation construct**, **center representation construct**, **discipline representation construct**, and **PI representation construct**.

research group *n* - The entire set of personnel involved in the conduct of a **research project** such as a **study**; in **multicenter trials** includes **center directors** and support staff, representatives from the **sponsoring agency**, and **study committee** members. syn: investigative team, **investigative group**, **study group** (not a recommended syn, see usage note for **study group**), **study staff**

steering committee (SC) *n* - A **committee** of an organization responsible for directing or guiding the activities of that organization. In **multicenter trials**, the committee responsible for conduct of the **trial** and to which other **study committees** report. Usually headed by the **study chair** and consisting of persons designated or elected to represent **study centers**, disciplines, or activities. One of the **key committees** in **multicenter** structures. rt: **executive committee** ***Usage note***: Sometimes used interchangeably with **executive committee**; not recommended (see **executive committee** for comment).

study center *n* - [**trials**] 1. **data collection site**; **study clinic** 2. **Data collection** or **data generation site**. 3. The **center** (defn 3 or 4) from which activities are directed; **coordinating center**; **project office**. 4. An operational unit in the structure of a **study**, especially a **multicenter** structure, separate and distinct from other such units in the structure, responsible for performing specified functions in one or more stages of the study; eg, a **clinical center** or **resource center**. ***Usage note***: Avoid usage in the sense of defn 1 in **multicenter trials** for reasons stated in the usage note for **center**. Restrict usage as a collective term to uses in the sense of defn 4; use an appropriately modified term when the reference is to a specific subset of centers. For example, use **study clinic** or simply **clinic** when referring to the subset of centers responsible for enrolling and treating **study patients**.

study position *n* - 1. **study officer** (eg, **study chair**, **study vice-chair**, **coordinating center director**, **project officer**) 2. A **position** or post designated or held in a **study center**, eg, **clinic director**, **clinic coordinator**.

study principal investigator *n* - The scientific or administrative head of a **study**; **study chair** ***Usage note***: See **principal investigator**.

treatment effects monitoring committee (TEMC) *n* - [**trials**] A standing **committee** in the structure of **single** or **multicenter trials** responsible for the periodic review of accumulated **data** for evidence of **adverse** or **beneficial treatment effects** during the **trial** and for making recommendations for modification of a **study treatment**, including termination, when appropriate. One of the **key committees** in the organizational structure of a multicenter trial. Usually constituted such that voting privileges are restricted to members not directly involved in the execution of the trial and not associated with participating **centers** or **sponsors** of the trial. Others, such as **officers of the study** or other key **study investigators**, if included as members, serve without vote. Voting members are appointed by the **sponsor** (defn 2) or **research group**, often with the advice and consent of the other party. The committee reports to the appointing authority and usually to the other party via the appointing authority or directly. syn (not recommended): **data monitoring committee**, **data and safety monitoring committee**, ethical committee, **ethics committee**, **safety monitoring committee** rt: **advisory-review and treatment effects monitoring committee**, **external treatment effects monitoring committee**, **internal treatment effects monitoring committee** ***Usage note***: The committee may be variously named. One of the more common synonyms is **data monitoring committee**. Though acceptable, it is not recommended because of its nondescript nature and possible confusion with other types of monitoring. Also common is the name **safety monitoring committee**; not recommended because of the implied emphasis on **safety**. The committee may have a compound name when the treatment monitoring function is vested in a committee having other broad responsibilities, eg, **advisory-review and treatment effects monitoring committee** or **data and safety monitoring committee** (not recommended).

P&P 1: Regard the design of the organizational structure as an essential element of design; create and formalize before the trial starts; allow sufficient time for deliberation of the pros and cons of different organizational structures and for "buy-in" by study investigators before formal acceptance.

P&P 2: Designate key committees and their interrelationships.

Comment

The likely minimum set of key committees in multicenter trials is steering committee, executive committee, and treatment effects monitoring committee.

P&P 3: Prepare and maintain specification sheets for key committees; include the following:

- Official name
- Charge
- Period of operation
- Type (ad hoc or standing)
- Appointing body
- Membership
- Term of membership
- Disclosure requirements re conflicts of interest
- Chair; vice-chair
- Secretary; rapporteur
- Meeting frequency and mode
- Quorum specifications
- Voting rules and procedures
- Method of filling vacancies
- Reporting procedure

P&P 4: In creating key committees and officer positions, strive for balance of power; avoid undue concentration of power in officers or in steering committee or in one institution or center.

P&P 5: Create structures providing for due process in addressing proposals to:

- Change enrollment criteria
- Change treatment or data collection protocol
- Stop or modify a study treatment
- Dismiss a study center because of inadequate performance
- Investigate a clinic because of suspicion of fraud

P&P 6: Be parsimonious in creating committees.

Comment

Committees create their own overhead, to say nothing of "trouble" if they are in search of a charge.

P&P 7: Define center to include resource centers; develop and maintain a list of study centers.

Comment

Center is usually a key building block in the organizational structure of multicenter trials. List clinics and resource centers. Designate centers qualifying for membership in center-based organizational structures; generally, clinics, coordinating center, and other key resource centers, exclusive of service centers.

P&P 8: Designate and list study officers and key study postions.

P&P 9: Prepare and maintain a specification sheet for officers and key study postions; indicate the following:

- Nature of office or position (ex officio, appointed, or elected; if appointed, appointing body or person; if elected, electing body)
- Name or title
- Duties and authority
- Term, when elected or appointed
- Disclosure requirements re conflicts of interest
- Membership or representation on key study committees

P&P 10: Delineate nature and limits of sponsor rights and prerogatives in regard to:

- Approval of the study protocol prior to the start of the trial
- Review of TEMC recommendations prior to transmission to study investigators
- Review of study publications prior to submission for publication
- Review of ancillary studies prior to implementation
- Review of protocol changes prior to implementation
- Addition or dismissal of centers from the trial
- Termination of the trial

P&P 11: Delineate, in writing, steps involved in receiving and acting upon recommendations coming from the TEMC; cover the following:

- Who in the TEMC is responsible for communicating a recommendation
- When is a recommendation regarded as transmitted
- The routing of the recommendation from the TEMC to study investigators (if not direct from the TEMC, indicate how it gets to study investigators and limits on sojourn times en route to study investigators)
- How and when a recommendation is presented to study investigators
- When and how investigators vote on whether to accept or reject a recommendation from the TEMC
- When a recommendation is considered to be accepted or rejected by study investigators
- When a recommendation for change is communicated to IRBs
- When and how treatment is to be stopped based on a recommendation from the TEMC

P&P 12: Strive for an organizational structure designed to maintain "arms length" separation from study sponsors.

Comment

The interests, duties, and responsibilities of sponsors, whether public or private, are different than the interests, duties, and responsibilities of study investigators. Arms length separation reduces the likelihood of confusion as to division of duties and responsibilities and of undue influence of sponsors in regard to conduct of the trial or in the analysis and publication of study results.

P&P 13: Strive for a structure in which the coordinating center is:

- Organizationally, operationally, and physically independent of the study sponsor
- Organizationally, operationally, and physically independent of study centers
- Funded via the same mode as other centers; ie, by grant if all other centers are so funded or by contract if all other centers are so funded
- At parity with other centers in standing

P&P 14: Assess adequacy of the organizational structure created by answering the following questions; regard variations in answers by study leaders as evidence of inadequate structure or lack of clarity in specifications:

- What person or body within the structure has final say on whether to modify entry criteria during the course of the trial?
- How do recommendations from the TEMC to stop or modify a treatment reach study investigators?
- Where do recommendations to separate a clinic from the trial come from and who implements them?
- What person or body has final say as to whether or not to accept a TEMC recommendation to stop a treatment?
- What person or body has the final say regarding content and conclusions in study manuscripts?

Comment

The organizational structure has "holes" if key study personnel are not able to answer the questions or if the answers they give differ; discuss areas of uncertainty or disagreement; revise as necessary.

P&P 15: Document details of organizational structure and related operating procedures in the study handbook or in written bylaws.

P&P 16: In creating subcommittees:

- Delineate and separate functions (to avoid overlap of function and "jurisdictional" disputes)
- Specify attendance requirements (attendance clauses are useful in purging committees of inactive members)

- Specify period of commission; create with sunset provision (sunset provisions are useful in keeping the books clear of defunct committees)

P&P 17: Delineate disclosure requirements and procedures for protecting against conflicts of interest in the investigatorship; see *Conflict of interest disclosure and redress good practice policies and procedures (GPPP)*.

P&P 18: Create and maintain a study credit roster; when creating consider the following:

- Who establishes policy regarding credit listings? Recommendation: Study officers, executive committee, or steering committee
- Who gets listed in credits? Recommendation: Study personnel by centers, study officers, study committees and memberships, sponsors, contributors of materials or supplies
- Who is the custodian of the list? Recommendation: office of study chair or coordinating center
- How will listings be checked for accuracy; for completeness? Recommendation: Require the custodian to circulate, at periodic intervals, to solicit updates from individual centers; require a "sign-off" by center directors prior to use of list in study manuscripts; supplement sign-off process with central review to ensure uniformity of listing procedures across clinics
- Degrees of persons listed? Recommendation: Limit to advanced degrees of relevance; expect task to be difficult and tedious and likely to be error prone without concerted effort to ensure accuracy; expect list to need periodic updating
- Time coverage of listing: Snapshot or cumulative? Recommendation: Maintain to be cumulative (ie, to include dates and times of comings and goings in regard to centers, investigators, and committee members); reduce to snapshot only when appropriate, eg, for inclusion in funding renewal; use cumulative in mainline publications
- Format of listing: Abridged or unabridged? Recommendation: Maintain as unabridged; trim as needed for secondary publications
- List submitted with study publications? Recommendation: Submit full unabridged listing in relation to primary and mainline publications; produce abridged listing for secondary and ancillary publications