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U N I V E R S I T Y

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(Tuesday 8:58am) 30 January 2001

Memorandum

To: Center for Clinical Trials faculty and staff

Fr: Curt Meinert

Re: Training, certification, quality control, and quality assurance good practice policies and procedures (GPPP)

Definitions

audit *n* - [ME fr L *auditus* act of hearing, fr *auditus*, pp] 1. A systematic **examination** or review of an **organization**, activity, or procedure. 2. A careful step by step review of some method or process. 3. **record audit** rt: **desk audit**, **off-site audit**, **on-site audit**, **record audit**, **audit for cause**, **audit not for cause** ***Usage note***: Subject to varying usage; accompany with sufficient detail to make sense of usage clear. Take care to distinguish usages having legal implications from those devoid of such meanings, such as audits done primarily as a part of **quality assurance** processes. See also **record audit**.

audit, **audited**, **auditing**, **audits** *v* - To examine, verify, or correct. ***Usage note***: Not to be used interchangeably with **monitor** *v*. As a rule, **audit** *v*, implies a more detached and passive process than is the case with **monitor** *v*; see note for that entry. See also notes for **record audit** and **record monitor**.

audit for cause *n* - An **audit** performed because of known or suspected aberrancies. rt: **audit not for cause**

audit not for cause *n* - A routine **audit** performed in the normal course of activities in the absence of known or suspected aberrancies. rt: **audit for cause**

audit trail *n* - The sequence of transactions linking two **events** or actions. In **data processing**, the sequence of transactions linking **data** in a finished **dataset** to those recorded in **source documents**, such as **data collection forms** or **medical records**.

certification *n* - 1. The act or process of **certifying**. 2. The state of being certified. In the case of **trials**, a process for clearing a **center** or personnel for participation. In regard to a center, a process intended to ensure that it has the requisite facilities, equipment, staffing, approvals, and that it meets specified standards; may involve onsite inspections. In regard to personnel, typically a process involving study specific training and evidence of proficiency in regard to performing key procedures and activities related to **data collection**.

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circuit rider *n* - One who travels a **circuit**. In the setting of **multicenter trials**, typically a person from the **sponsoring agency**, or **coordinating center** responsible for visiting participating **clinical centers** on a regular basis to **monitor**, **audit**, and trouble-shoot. rt: **clinical research associate**, **study clinic monitor**

performance monitoring *n* - The act of or an instance of reviewing **performance** of an ongoing activity to determine if corrective action is necessary. syn (not recommended): **data monitoring**, **safety monitoring**, **data and safety monitoring** rt: **administrative review**, **efficacy monitoring**, **multiple looks**, **safety monitoring**, **treatment effects monitoring**

performance monitoring *v* - 1. **Monitoring** (defn 2) of **performance** of some activity (or set of activities) at periodic time points over the course of the activity to determine whether the activity should be allowed to continue unaltered; in the context of **trials**, such monitoring as summarized in a **performance monitoring report**; such monitoring as part of ongoing **quality assurance**; in the context of **multicenter trials**, monitoring relating to the performance of the various **centers** in the trials. 2. **performance review** (defn 1) rt: **administrative review**, **treatment effects monitoring** ***Usage note***: Not to be confused with forms of monitoring involving evaluations of **treatment results** as in **treatment effects monitoring**, **safety monitoring**, or **efficacy monitoring**. Note also that defns 1 and 2 have different operational meanings and should not be used interchangeably. Use **performance monitoring** when the interim review is part of a planned ongoing process; use **performance review** when it is not. See also note for **administrative review**.

performance monitoring committee *n* - 1. A **committee** charged with **performance monitoring**. 2. A committee that reviews **performance monitoring reports** and takes or recommends appropriate corrective actions when indicated to deal with identified performance problems. rt: **treatment effects and performance monitoring committee**

performance monitoring report *n* - A **report** summarizing **performance** of a **center** or centers and used for **performance monitoring**. In the case of **multicenter trials**, typically prepared by the **data coordinating center** and reviewed by the full **research group**, **steering committee**, or some other body or **committee** having responsibility for performance monitoring. rt: **treatment effects monitoring report**

performance review *n* - [**trials**] 1. An **ad hoc interim review** (defn 2) of **performance** of activities or functions to determine whether the trial should be stopped or allowed to continue unaltered; eg, one done to determine whether the **rate** of **enrollment** is **adequate** to justify continuation of the trial. 2. **performance monitoring** (defn 1) 3. **administrative review** (defn 1) ***Usage note***: Not to be confused with reviews involving **treatment results**. Note also that defns 1 and 3 have different operational meanings than defn 2. Use **performance monitoring** when the interim review is part of a planned ongoing process. See also note for **administrative review**.

performance standard *n* - A **standard** to which one or something is held, eg, in **multicenter trials**, one relating to **clinic enrollment** and used to determine whether a clinic should be placed on probation (**clinic probation**) or separated from the **trial**.

quality assurance (QA) *n* - 1. [broadly] Any method, procedure, process, or practice aimed at achieving, ensuring, or improving the **quality** or **reliability** of something; the aggregate of such methods, procedures, processes, or practices. 2. [**data collection**] Any method, procedure, process, or approach for collecting, processing, or analyzing **data** aimed at maintaining or improving their **reliability** or **validity**; includes any or all of the following activities: **pilot testing**, **pretesting**, **repeat reading**, replicate measurement, **data editing**, **double data entry**, **performance monitoring**, aspects of **data analysis** for **treatment effects monitoring**, **site visiting** (defn 1), and **record auditing**; the aggregate of such methods, procedures, processes, or approaches. 3. A procedure or practice intended to reduce or eliminate the chance of **error**; the aggregate of such procedures or practices. rt: **adherence**, **compliance**, **quality control** ***Usage note***: The terms **quality assurance** and **quality control** have similar meanings and are used interchangeably. Use **quality control** (defn 1) in contexts where the reference is to a process or procedure having a statistical component. Use **quality assurance** in regard to the aggregate of procedures used to ensure quality.

quality control (QC) *n* - 1. An aggregate of sampling and testing procedures based on statistical theory and **analysis** designed to ensure adequate **quality** in relation to a finished product. 2. A procedure or practice aimed at reduction or elimination of defective parts or **errors**; in relation to collection, transcription, or entry of **data**, a procedure or practice intended to eliminate or reduce the chance of error; the aggregate of such procedures or practices. rt: **adherence**, **compliance**, **quality assurance** ***Usage note***: See **quality assurance**.

quality control center *n* - A **center** concerned with **quality control**. In the case of **multicenter trials**, usually a **resource center** with responsibility for monitoring the quality of various aspects of the **data collection** or **analysis** processes employed in the trial. ***Usage note***: Term not recommended except where there is a specific center with designated quality control functions over and above those normally assumed by the **data center**, **data coordinating center**, or **coordinating center**.

site visit *n* - 1. A **visit** to a proposed or functioning **study site** by personnel not associated with the site or its **parent institution**, mandated by a **study section**, **review group**, or **sponsoring agency**, and carried out for the purpose of assessing performance potential or actual performance in order to arrive at a recommendation for **funding** or continued funding of the site. 2. **study site visit** (defn 2) rt: **reverse study site visit**

P&P 1: Create and maintain a list of general control and assurance procedures practiced in trials, eg, as follows:

- Training and certification of study personnel
- Tested data collection forms
- Test or vanguard patients
- Pilot phase
- Phased start-up
- Certification site visits
- Regular site visits
- Site visits for cause
- Circuit riders
- Record auditing
- Performance monitoring
- Treatment effects monitoring
- Ongoing data analysis
- Independent replication of key data analyses
- Independent reprogramming of key analyses programs
- Replicate laboratory determinations
- Replicate readings
- Adjudicated readings
- Double data entry
- Intelligent data entry
- Ongoing data editing
- Independent replication of key counts in TEM reports used for a recommendation to stop or alter the trial
- Independent replication of key counts included in study publications
- Independent replication of results contained in study manuscripts

P&P 2: Choose the quality control and assurance procedures to be practiced from a menu of options, eg, as represented in P&P 1; rank choices in order of importance measured against objectives and needs of the trial; review ranking with study officers and steering committee; concentrate efforts on options ranked highest; fashion budget consistent with options selected.

Comment

The purpose in ranking is to cause investigators to be realistic given staffing and budget limitations.

P&P 3: Outline training and certification procedures to be employed during the design phase of the trial; specify classes of personnel to be certified and procedures for certification; submit to the SC for review and approval; review and revise periodically over the course of the trial.

P&P 4: Develop and maintain a system for issue of personnel Id numbers; develop so as to be able to track certification status of study personnel.

Comment

Best done in a spreadsheet format with space for entries to indicate the certifications held by a person and dates issued, and, where applicable, dates of de-certification (because of departures from the study or for other reasons).

P&P 5: Use personnel Id numbers to track whether procedures are done by personnel certified for performing those procedures.

Comment

Implementation of this P&P requires data collection forms with spaces for recording personnel Id numbers and spreadsheets to check the certification status of persons performing the indicated procedures.

P&P 6: Budget and plan for a meeting of all key study personnel for the purpose of training; conduct prior to initiation or within weeks of start of enrollment; repeat as needed over the course of the trial.

Comment

Investigators may have to battle for monies needed for such meetings if sponsors see them as "unnecessary".

P&P 7: List classes of personnel to be certified and procedures to employed in certification; submit to the SC for review and approval.

P&P 8: Design and administer procedures to ensure that study personnel are familiar with the basic design and operating principles of the trial.

Comment

A common way of accomplishing this requirement is by administration of a knowledge assessment test.

P&P 9: Discuss rules, regulations, norms, and standards underlying medical research with study personnel at meetings of the research group; cover the following:

- The Nüremberg Code and subsequent revisions
- Principles of medical ethics (beneficence, respect for persons, justice)
- Scientific misconduct (ORI definition, examples, consequences)
- Fraud, fabrication, falsification, and plagiarism (definitions, celebrated examples, consequences)
- Procedures practiced to ensure integrity
- Procedures practiced to detect fraudulent or falsified data
- Conflicts of interest (definitions, examples, procedures for disclosure, and mechanisms for dealing with conflicts)
- Insider trading (definition, SEC regulations, celebrated examples, avoidance mechanisms)

P&P 10: Set-up and maintain procedures to ensure flow of forms, as completed, to data entry, procedures to ensure timely data entry, and procedures for ensuring timely harvest of data keyed into dataset suitable for ongoing performance and treatment effects monitoring.

Comment

See *Forms design good practice policies and procedures*, *Data entry good practice policies and procedures*, and *Data processing good practice policies and procedures*.
