JOHNS HOPKINS
U N I V E R S I T Y

Center for Clinical Trials

Department of Biostatistics
Department of Epidemiology
Department of International Health

Department of Medicine
Department of Ophthalmology
Oncology Center

(Thursday 9:59pm) 15 June 2000

Memorandum

To: Center for Clinical Trials faculty and staff

Fr: Curt Meinert

Re: Enrollment good practice policies and procedures (GPPP)

definitions

baseline period *n* - [general] A **period** of **time** that is used to perform procedures needed to assess the suitability and eligibility of a **study candidate** for **enrollment** into a **study**, to collect required **baseline data**, and to carry out **consent processes**. [**trials**] 1. The period for a person or **treatment unit** defined by the start of the first **data collection visit** and ending with **assignment** to **treatment** or start of treatment. 2. Such a period ending with a **visit** or time point occurring shortly after **assignment** to **treatment** or the start of treatment. 3. A period of time during the course of treatment or **followup** of a person or treatment unit, usually marked by some **event**, process, or procedure, in which new **measurements** or **observations** are made to serve as a base for gauging subsequent change. 4. **enrollment period** rt: **treatment period**, **followup period**, **treatment and followup period**, **close-out period**, **baseline observation period**, **lead-in period**, **run-in period** ***Usage note***: Avoid in the sense of defn 2 without qualification (see note for **baseline** *adj*) and in the sense of defn 4. Provide qualifying detail for uses in the sense of defn 3. Traditionally, the point defining the end of the **baseline period** in trials is marked by the **treatment assignment** or initiation of **treatment**. The tendency to "stretch" the baseline period as in defn 2 arises from a desire to reduce missing **baseline data**. Clearly, the utility of an observation as a baseline, in the strict sense of usage, is diminished if there is any possibility of the observation being influenced by treatment or treatment assignment. Hence, the practice is not recommended, even if the time interval following treatment assignment or initiation of treatment is small and even if the likelihood of treatment having had an effect on the **variable** being observed within that interval is small. See also notes for **baseline** *adj* and for **baseline** *n*.

clinic start-up design *n* - **Start-up design** for recruitment and certification of **clinics**, for training and certification of clinic personnel, and for clearance of clinics to start **patient recruitment**. ant: **clinic close-out design** rt: **patient recruitment start-up design**

enrollment *n* - 1. The act of **enrolling** a person into a **research study**. 2. The state of having been **enrolled**. 3. **patient enrollment** ***Usage note***: Ambiguous when used in the absence of detail indicating the point at which enrollment occurs. Generally, in the case of **randomized trials**, that point is when **treatment assignment** is revealed to clinic personnel. A person is

considered to have been randomized at that moment in time and is, thereafter, counted to the **treatment group** indicated by the assignment, even if the person never receives the assigned treatment. Not to be confused with **registration**. See **patient enrollment** for additional comments.

enrollment goal *n* - The **goal** in relation to **enrollment**, such as that for a **trial** as set by a **sample size calculation** or other considerations; **patient enrollment goal**. syn: recruitment goal rt: **sample size calculation**, **enrollment quota** ***Usage note***: Not to be confused with **enrollment quota**.

enrollment quota *n* - 1. The number of individuals of a specified type to be **enrolled**; **patient enrollment quota**. 2. The proportionate share of a whole to be composed of a designated type or class of persons. syn: recruitment quota rt: **quota requirement**, **enrollment goal** ***Usage note***: Not to be confused with **enrollment goal**. **Enrollment goal** relates to the overall number to be enrolled in a recruitment effort; **enrollment quota** relates to the mix of people to be enrolled, as specified by **absolute numbers** or in relative terms. The imposition of quotas in trials should be done with caution since they make achieving a stated enrollment goal more difficult in that they limit the type of people who can be considered for enrollment after individual quotas have been met. For example, a trial having an enrollment goal of 100 and a quota of 50 males and 50 females means that only males or females can be considered for enrollment once the quota is met for the other gender group, thereby prolonging the time required to achieve the stated enrollment goal of 100. Quotas should not be imposed except where there is a need or desire to carry out **subgroup analyses** within subgroups defined by the quota and where there is a need or desire to perform **comparisons** within those subgroups at a specified level of **precision**.

followup period *n* - [**trials**] 1. The **period** of **time** from **enrollment** to termination of **followup** of a person or **treatment unit**. 2. The period of time in the course of a trial defined by the start of followup of the first observation unit **enrolled** and by the end of followup of the last unit enrolled; **followup stage**. rt: **baseline period**, **treatment period**, **treatment and followup period**, **close-out period**

patient recruitment start-up design *n* - **Start-up design** for **patient recruitment**; for the **trial** or for clinics within the trial. ant: **patient followup close-out design** rt: **clinic start-up design**

randomization *n* - 1. An act of assigning or ordering that is the result of a **random process** such as that represented by a sequence of numbers in a table of **random numbers** or a sequence of numbers produced by a **random number generator**, eg, the **assignment** of a **patient** to **treatment** using a **random process**. 2. The process of deriving an order or sequence of items, specimens, records, or the like using a **random process**. rt: **haphazardization**, **quasirandomization** ***Usage note***: Do not use as a characterization except in settings where there is an explicit or implied mathematical basis for supporting the usage, as discussed in usage

notes for **random** *adj*. Use other terms implying less rigor than implied by **randomization**, such as **haphazardization**, **quasirandomization**, or **chance**, when that basis is not present or evident.

registration *n* - 1. The act of **registering**, as in entering one's name and other pertinent information into a **register**. 2. **enrollment** 3. A **document** certifying an act of registering. 4. The granting of an **application** or **license**; in regard to a **new drug**, the approval of a **new drug application** by the **Food and Drug Administration**. ***Usage note***: Registration (defn 1) may or may not correspond to enrollment. Usually the act of registration (defn 1) is a necessary but not sufficient condition for enrollment. Hence, the two terms should not be used interchangeably. In the case of **trials**, registration typically takes place during the first contact with a person in relation to the **enrollment process**; signaled by the act of entering the person's name into a register or **log** or issuing an **identification number** for the person. The act of enrollment takes place when the **treatment assignment** is revealed or **treatment** is initiated and usually after **baseline** evaluations have been completed and **consent** has been obtained.

start-up design *n* - **Design** relating to **start-up** of an activity; **clinic start-up design**; **patient recruitment start-up design**; **trial start-up design**. rt: **close-out design**

P&P 1: Count a person as enrolled when the assignment is revealed to clinic personnel.

P&P 2: Regard the point of enrollment as the end of the baseline period of observation and the start of the followup period of observation.

P&P 3: Count a person to the group indicated by the assignment and do so regardless of course of treatment or degree of compliance to treatment.

P&P 4: Establish and maintain systems of assignment to preclude randomization absent documented consents.

P&P 5: Do not use registration and enrollment interchangeably.

P&P 6: Construct minimum and maximum time limits separating the various baseline visits.

P&P 7: Set up and maintain procedures to ensure that data collected for baseline visits are within the limits specified in relation to P&P 6.

P&P 8: Avoid recruitment quotas.

Comment

Quotas increase the time and effort needed to recruit and can raise troubling issues when recruitment are orchestrated to fill quotas. Largely, the only instances under which quotas might

be considered is when there are compelling reasons to believe that the response to treatment is quantitatively different for the subgroups represented by the quota variable – rarely the case.

P&P 9: If quotas are imposed in multicenter trials, strive to impose in regard to the overall sample size; not at the clinic level.

Comment

Achieving the overall sample size is easier and less costly in terms of effort and time if quota requirements are for the overall sample size than when they are imposed at the clinic level.

P&P 10: Set up and maintain procedures to track and summarize protocol deviations in regard to eligibility and baseline data collection.

P&P 11: Opt for start-up designs in multicenter trials allowing clinics to start when certified. Strive to avoid "big bang" start-up designs (designs in which clinics are held at the starting blocks until all clinics are in position to start).

Comment

There is generally nothing to be gained by delaying the start of a clinic so other clinics can start at the same time. The only exceptions may be with designs calling for a common period of followup and where there is concern about seasonal variation in response to treatment.

P&P 12: Avoid imposing a limit on the number of patients that may be enrolled from individual clinics in multicenter trials. If an upper limit is set, set it well above the expected number; at least 1.5 that number.

Comment

Pigs is pigs and data is data. Translation: A patient is a patient regardless of the clinic or the number of patients enrolled from a clinic.