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(Friday 6:16am) 12 January 2001

Memorandum

To: Center for Clinical Trials faculty and staff

Fr: Curt Meinert

Re: Sample size good practice policies and procedures (GPPP)

Definitions

ad hoc subgroup comparison *n* - A **comparison** based on an **ad hoc subgroup**. ant: **designed subgroup comparison**

calculated sample size *n* - The **sample size** desired or required for a **study**, as derived from a **sample size calculation**. ant: **pragmatic sample size**

conditional power *n* - The **power** expected by the completion of a **study**, given the **results** up to some point in the course of a study. rt: **expected power**, **observed power**, **stochastic curtailment**

designed subgroup comparison *n* - A **subgroup comparison** in a **subgroup** enrolled to a **quota**, especially one based on a **sample size** calculated to yield a specified level of **precision**. ant: **ad hoc subgroup comparison**

detectable difference *n* - [**trials**] A hypothesized **difference** in **treatment effect** considered to be important and worthy of detection; such a difference specified for purposes of a **sample size calculation**. rt: **clinically meaningful difference**, **treatment difference**

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**.

equivalence trial *n* - A **trial** designed or conducted to test or establish **equivalence** of a **treatment** relative to another, usually as determined by **comparison** against a **standard treatment**. ant: **superiority trial**

expected sample size *n* - 1. **enrollment goal** 2. The **sample size** expected under an idealized circumstance or as dictated or derived under a **model**. rt: **achieved sample size**, **observed sample size**

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observed sample size *n* - The **number** of **observation units enrolled** at a given point in the course of a **study**; **achieved sample size** on completion of the study. rt: **achieved sample size**, **calculated sample size**, **expected sample size**

pragmatic sample size *n* - A **sample size** dictated by available funding or resources, likely availability of persons for **study**, or by like considerations. ant: **calculated sample size**

power *n* - [ME, fr OF *poeir*, fr *poeir* to be able, fr (assumed) L *potēre* to be powerful] 1. The **probability** of rejecting the **null hypothesis** when it is **false**; one minus the **type II error**. 2. **exponent** rt: **conditional power**, **expected power**, **observed power**

power function *n* - A **function** for a specified **statistical test** that gives the **power** (one minus the **type II error**; 1 - β) for a **range** of values of the **parameter** of interest in the test. The function has a value corresponding to the **type I error level** of the test when the parameter has the value specified under the **null hypothesis**; elsewhere its values correspond to the power of the test for the range of **alternative hypotheses** represented by the values assumed by the parameter.

sample size *n* - 1. The number of **sampling units** to be drawn or selected for a **sample**; the number so selected or drawn. 2. The anticipated or actual number of elements or units constituting the **database** for a **study**, eg, the number of **patients** to be **enrolled** into a **clinical trial** or actually enrolled. rt: recruitment goal, **sample size calculation**

sample size calculation *n* - A mathematical **calculation**, usually carried out when a **study** is being planned, that indicates the number of **observation** or **treatment units** to be **enrolled** or studied in order to provide a specified degree of statistical **precision** for a specified level of **type I** and **type II error** protection. rt: recruitment goal

sample size design *n* - [**trials**] The **design** for determining **sample size**, broadly, either **fixed** or **sequential**; see **fixed sample size design** and **sequential sample size design**.

sample size of convenience *n* - 1. A **sample size** based on **pragmatic** considerations. 2. A **sample size calculation** based on unrealistically optimistic assumptions, especially one based on a **treatment effect** (defn 3) indicative of a **miracle treatment** (defn 3).

sample size requirement *n* - The **sample size** required, as indicated by a **sample size calculation** or specified **recruitment goal**. rt: **quota requirement**

stochastic curtailment *n* - [**trials**] **Curtailment** based on the **likelihood** of obtaining a **result** different than the one observed if the trial were to continue to its appointed end (eg, the likelihood of an observed **positive result** being reduced to a **nil result** or the likelihood of a nil result being elevated to a positive result); typically based on calculations of **conditional power**

or **conditional type I error** assuming a specified **treatment effect** from the point of assessment to the appointed end of the trial. The decision may be to stop the trial if the assessment suggests that continuing is unlikely to produce a result different from the one observed.

superiority trial *n* - A **trial** designed or conducted to test or establish the **superiority** of a **treatment** relative to another; usually as determined by **comparison** against a **standard treatment**, or **nil control treatment** when a standard does not exist. ant: **equivalence trial**

type I error *n* - [**statistics**] The **probability** of rejecting the **null hypothesis** when it is **true**, usually denoted by the Greek symbol α. rt: **significance level**, **type II error**, **type III error**

type II error *n* - [**statistics**] The **probability** of accepting the **null hypothesis** when it is **false**, usually denoted by the Greek symbol β. rt: **power**, **type I error**, **type III error**

type III error *n* - The **error** of rejecting the **null hypothesis** for the wrong reason, eg, rejecting the null hypothesis that treatment A = treatment B and accepting the alternative that treatment B is superior to treatment A, when, in fact treatment A is superior to treatment B; the correct answer to the wrong question. (David, 1947; Mosteller, 1948) rt: **type I error**, **type II error**

P&P 1: Determine the enrollment goal during design of the trial; determine by formal sample size calculation or by pragmatic considerations.

P&P 2: Specify the enrollment goal in the study protocol; indicate method of determination (sample size calculation or pragmatic considerations); give details supporting calculations or rationale.

P&P 3: In long-term trials, indicate procedures for adjustment of enrollment goal during course of the trial; outline in the study protocol.

P&P 4: If the sample size is dictated by pragmatic considerations do not present as if the product of a formal sample size calculation.

Comment

It is always possible, given a sample size, to find some combination of the event rate, α, β, and Δ to yield that number.

P&P 5: If the sample size is dictated by pragmatic considerations provide estimates of power for a range of possible treatment differences.

P&P 6: Consider the enrollment goal as a target rather than some indelible hard and absolute number.

P&P 7: For calculated sample sizes, avoid "shopping" for an outcome measure or values α, β, and Δ in order to obtain an achievable sample size.

P&P 8: Do not impose subgroup sample size goals in the absence of reasons to believe that treatment effects differ by subgroup.

P&P 9: In long-term trials with calculated sample sizes, evaluate assumptions used in making the calculation by using data accumulated in the trial; modify the enrollment goal or time for followup accordingly.
