

 <b>JOHNS HOPKINS BLOOMBERG SCHOOL of PUBLIC HEALTH</b>	<b>Human Research Protection Program Policies &amp; Procedures</b>	
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Title <b>Sample size requirements</b>	Date Effective June 10, 2005	Supercedes P&P dated

## BACKGROUND

The Federal regulations require that risks to subjects be minimized by using procedures that are consistent with sound research design and that do not unnecessarily expose subjects to risk or cause their contribution to the research to be futile. To meet this obligation the number of subjects exposed to risk must be minimized, yet sufficient to answer the question posed by the research.

## JHSPH POLICY AND PROCEDURES

CHR requires that the number of subjects to enter a study over its stated life (the sample size) be specified and approved for all studies prior to initiating recruitment. When this number has been approved it must not be exceeded without prior approval by CHR. If the approved sample size is exceeded, entry of new subjects into the study must stop and may only be resumed if, and when, CHR approves an increase in sample size.

### Sample Size Requirements

The sample size is the number of subjects from whom consent will be obtained. When consent for enrollment is the only consent obtained, or when there is a single consent for screening and enrollment, only a single sample size determination is required. If, however, a study involves two consent procedures, i.e., one for screening to determine eligibility followed by a later separate consent to enroll eligible subjects in the actual study, two sample size determinations are required, one for the number to be screened and a second for the number to be enrolled.

### Determining and Justifying Sample Size

Each new research application should provide the planned sample size(s), with appropriate justification. The information required to justify the sample size(s) depends upon the type of study being proposed.

For all clinical trials and behavioral intervention studies, and for most observational studies, surveys and pilot studies, the sample size justification should include:

- the events or outcomes (primary and secondary endpoints) under investigation and on which the sample size estimate(s) is(are) based,
- the statistical method(s) to be used to estimate or test these events or outcomes,
- the clinically relevant or substantively meaningful effect(s) of interest, and
- the sample size(s) needed over the life of the project to estimate the effect(s) with adequate precision and power.

The calculation of sample size(s) and the strategy for analysis should make allowance for such factors as expected loss due to ineligibility, loss to follow-up, crossover if relevant, clustering of outcomes, binary/continuous/categorical/ordinal or survival outcomes, confounding, etc. Consultation with a biostatistician during development of the research plan is highly recommended.

### Sample Size Requirements for Specific Types of Studies

- Record review and data analysis. When the review or analysis will involve records or data that are identifiable, the sample size must be provided and justified.
- Studies with sub-groups. In some studies, the total sample size is based on the number of subjects required for sub-groups with defined characteristics, such as age, gender, race, body weight, etc. For such studies, the sample size for each sub-group must be provided and the power of the study to assess hypotheses relevant to the subgroups should be stated. The total number of subjects to be enrolled is, however, what will be reviewed and approved by CHR.
- Studies with a pilot phase. When a study contains a pilot phase followed by a main study, the sample size for each must be provided and justified. If the sample size for the main phase will depend upon the results of the pilot phase, the sample size for the main phase cannot be reviewed and approved by CHR until the pilot phase is completed and the sample size for the main phase can be determined.
- Studies of uncertain duration. For studies of uncertain duration, such as some longitudinal cohort studies, the sample size for a period not to exceed five years should be provided. If the study will continue beyond the approved period, an amendment should be submitted to CHR requesting an increase in sample size for an additional period of five years or less.
- Qualitative studies. For studies of individual opinion, belief or experience, a formal sample size justification may not be possible. Nevertheless, the basis for the proposed sample size should be provided. This may refer, for example, to the number of subjects required to reach “saturation” or the number typically enrolled in previous studies of the same type. Studies that employ focus groups should describe both the number of groups to be studied and the number of subjects per group.

### Exceeding the Approved Sample Size

**When an approved sample size is reached, screening and enrollment of additional subjects must stop until a request to amend the sample size(s) is reviewed and approved by CHR.** Investigators must monitor the number of subjects entering a study so that a request to amend the sample size may be submitted for review by CHR prior to reaching the approved number. If the sample size is exceeded unintentionally and further recruitment of subjects is not required, the investigators should provide a brief memo to CHR explaining the over-recruitment and their intention not to resume recruitment. Continuing to screen or enroll subjects beyond the approved number(s), or exceeding the sample size when, in the judgment of CHR, this should have been avoidable, is considered non-compliance with terms of the project approval.

### Amending the Approved Sample Size

In order to increase the sample size above that originally approved by CHR, a written request to amend the sample size must be submitted to CHR with appropriate justification. If the investigators wish to increase the sample size at the time the progress report is submitted, this should be described and justified in an amendment request that is separate from the renewal application (see *Changes and Amendments in Approved Research LINK*). Screening and enrollment based on a revised sample size may not occur until CHR has formally approved the requested increase.

### **Definitions**

**Screening:** The process of selecting a pool of candidates who are qualified, or potentially qualified, by predefined criteria, as possible subjects for subsequent enrollment in one or more specific studies. A separate consent may be required for screening or the consent may be combined with that for enrollment.

**Enrollment:** The point at which a subject (or the subject's legally authorized representative) provides consent to take part in a specific study.

### **RESOURCES & REFERENCES**

*OHRP Requirement* \_\_\_\_\_  
*FDA Requirement* \_\_\_\_\_  
*AAHRPP Element* \_\_\_\_\_