OHRS Information Sheet
Statistical Guidelines for Non-Clinical Research Protocols

Research protocols that are reviewed by SRC 3 and IRB D involve non-clinical areas of research and cover a wide range of designs and subject areas. These studies contain elements that are generally more diverse than typical phase I-III randomized clinical trials. However, the basic scientific /analytic principles still apply in order to assure that results are clear, scientifically valid, and publishable. It is strongly recommended that study teams include a statistician as a co-investigator so that the statistical issues are appropriately addressed. The following guidelines have been prepared by statisticians Kathryn P. Gray, PhD and Judi Manola, MS.

Guidelines*

1. Clearly **state research questions**, in the form of objectives, aims or hypotheses.
2. **Specify the type of study** being proposed. Is it prospective or retrospective? Single arm or randomized? Is it a pilot study or a feasibility study?
3. **Describe the participant population**: define the participant group(s) that will answer your research questions:
   - What are the eligibility criteria?
   - If prospective, what is the recruitment mechanism?
   - If retrospective, how will you select participants to avoid bias (e.g., lead time bias, selection bias)? If a case-control study, how are the 'cases' defined and the 'controls' selected or matched by?
   - The population should be narrow enough to be easily described/characterized, but broad enough that findings are generalizable.
4. **Define the study endpoints**
   - What outcome measure will answer the research questions?
   - What level of evidence will represent a positive outcome?
   - Is the endpoint definition consistent with other studies in the field?
   - For feasibility studies, what are the indicators of feasibility, and how will you know if you have achieved them?
   - What is the intended "next step" in research if your study is successful? For example, if changing clinical practice is your goal, then clearly state what level of evidence the study team thinks would support implementing the investigated intervention into routine practice.
5. **Justify the sample size**
   - The primary objective requires a sample size justification.
     - Provide a sample size justification and corresponding power for an appropriate inference (from a statistical test or modeling). Be sure to

say what test/model you will use, whether the test is 1- or 2-sided, and the Type I error (alpha or false positive rate) you are assuming.

- When sample size or power justification is not possible, consider the objective to be secondary or exploratory.
- If you are choosing a sample size based on feasibility or practical limitations, provide information about the statistical precision that will be available. For example, what is the maximum width of a confidence interval on your primary endpoint, given the available number of subjects?
- Provide a rationale for the projected accrual rate.

6. **Describe your plan for data collection/measurement**
   - How, what, interval (one time or repeated measures)
   - Type of data: nominal (e.g., yes/no), ordinal (e.g., a numerical scale), counts, or a continuous numerical measure and the associated range of possible values.
   - Describe how you will prevent missing data or how you will control quality of your lab experiment.
   - Describe the methods for scoring lab tests, instruments and interviews
7. **Describe your statistical analysis plan and methods.**
   - Always have a section in the protocol, however brief or simple, that describes how you will summarize and analyze the data. Think about how the tables will look in your manuscript when the study is complete. This will help assure that you are capturing the required information in the most useful form.
   - Statistical testing (if it is to be performed) should correspond to the power and sample size calculation.
   - Describe how you will handle missing data or drop-outs. Missing data can be a source of bias, so preventing missing data is easier than accounting for it in your analysis.
   - If specific methodology from a discipline is to be used, briefly describe the methods (e.g., mixed-methods research from survey, behavioral sciences), as you would when you write your manuscript and give the relevant references.
8. Although not required in the concept, you will find it helpful to state how you will **report/disseminate the results.** Clearly state what the analysis results will mean, or how you will assure proper interpretation of the results.
9. Provide analysis methodology **references** if applicable.

* For tissue/tumor bank studies, for which the sole objective is collecting/reserving specimens for future research without any specific analytic objectives that require analysis, items 4, 5, 7, 8 may be eliminated.

For BWH investigators:

Biostatistics support is available to investigators in the Brigham and Women's and Harvard Medical research community through the BWH Center for Clinical Investigation (CCI) in partnership with Harvard Catalyst. They offer statistical consulting on issues

such as study design and data analysis for manuscripts and grant applications, as well as general education and advice. Please visit the BWH Biostatistics web site for details.