QUESTIONS FOR EXPERIMENTAL STUDY DESIGN

COMMUNITY OF PRACTICE FOR STATISTICS
EXPERIMENTAL WORK GROUP: Barbara Jane George, Leader (NHEERL), Diana R. Hall (SSC),
Michael D. Hays (NRMRL), Roxanne Johnson (NHEERL), Martin Blake Phillips (ORISE),
Jane Ellen Simmons (NHEERL)
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These questions and criteria are focused on study design and best practices to enhance reproducibility of science and have been developed for use in study planning activities. The intended audience includes scientists, branch chiefs, and quality assurance managers for guidance in preparing and reviewing QAPPs and research protocols.

1. **Study Overview**
   a. What is the research problem?
   b. What is (are) the study objective(s)?
   c. What are the research question(s) that will be answered to address the objectives?
2. **Experimental Design and Data Elements**
   a. What type of study is planned (e.g., pilot study, exploratory study, confirmatory study)?
   b. What is the experiment design (e.g., randomized block, counterbalancing)?
   c. Will replicates be used (e.g., biological replicates, field duplicates, split samples, analytical lab duplicates)?
   d. What primary variables (i.e., the key dependent variables and independent variables) are in this experiment?
   e. Will sources of variability be controlled (e.g., by strain of lab animal)?
   f. What covariates will be examined?
   g. What is the variable type (e.g., continuous, categorical) and measurement unit (e.g., milligrams per liter) for each primary variable and covariate?
3. **Statistical Analyses:** For each experiment included, address the questions below.
   a. Is a statistical analysis plan included?
   b. What statistical analyses will be performed?
      i. What is the unit of analysis (e.g., animal litter, person, truck)?
      ii. What statistical parameters will be estimated (e.g., mean, standard deviation, regression coefficients)?
      iii. What statistical relationships (between measurement variables) will be quantified?
      iv. What statistical hypotheses will be tested and what hypothesis tests will be performed?
      v. What are the assumptions behind the statistical analyses (e.g., normal distribution)?
         1. What are the methods for evaluating that these assumptions?
         2. Might data transformations be needed?
4. **Sample Size**
   a. Will a power analysis be performed?
      If Yes

  i. How will the power analysis be performed?

  ii. What are the assumptions for the power analysis and why are they necessary?

  iii. What is considered acceptable power for the study?

  iv. What is the pre-specified effect size and why was this chosen?

  v. How does the sample size support the power level and effect size?

  vi. For which variables will repeated measurements be collected?

  vii. How will the number of repeated measures and the correlation among them be taken into account in the power analysis?

  If No

  i. Why is a power analysis not applicable to the proposed study?

5. **Randomization and Blinding**
   a. Will animals and/or samples be randomized?
      i. If yes, how will randomization be carried out?
      ii. If no, why not?
   b. Will the experiment be partially or fully blinded?
      If Yes
      i. If partially blinded, what portions of the experiment will be blinded?
      ii. How will the blinding be carried out?

6. **Bias**
   a. What are the potential known sources of bias (e.g., sampling bias, measurement bias, analytic bias)?
      i. What approaches will be used to minimize or eliminate them?
   b. What will be done to avoid reporting bias and publication bias?

7. **Data Inclusion/Exclusion**
   a. What are the data inclusion and data exclusion criteria?
   b. What are the proposed methods for detecting and treating outliers and spurious values?

8. **Data Analysis Considerations**
   a. How will missing data be coded in the data set and treated in statistical analyses?
   b. How will covariates be evaluated as confounders or effect modifiers/interactions?
   c. How will values below a detection limit/quantitation limit be represented?
   d. Are negative measurement data possible (e.g., as a result of background correction if applicable) and how will these data be used?

9. **Multiple Comparisons**
   a. Will multiple test correction (i.e., an adjustment for multiple comparisons) be performed?
      i. If yes, what method will be used (e.g., Benjamini-Hochberg approach to controlling the false discovery rate)?
      ii. If no, what is the explanation for not performing a multiple test correction?

10. **Data Management and Sharing**
    a. How will the data be archived? (e.g., paper copies, laboratory notebooks, digital backups, etc.)
    b. For data stored in digital-only format, what steps will be taken to ensure that the data are accessible using non-proprietary or open source software?

c. What database will be used and why?

Additional Resources (Note that material in Wikipedia is not peer-reviewed.)

Experiment Design and Data Elements	
pilot study	http://en.wikipedia.org/wiki/Pilot_experiment http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3081994/
exploratory study	http://en.wikipedia.org/wiki/Exploratory_research
confirmatory study	http://en.wikipedia.org/wiki/Confirmatory_trial
experiment	http://en.wikipedia.org/wiki/Experiment
randomized block	http://en.wikipedia.org/wiki/Randomized_block_design http://www.tfrec.wsu.edu/anova/RCB.html
counterbalancing	http://www.unc.edu/courses/2008spring/psyc/270/001/counterbalancing.html
replicates	http://www.stat.ucla.edu/~sabatti/statarray/textr/node3.html http://euler.bc.edu/marthlab/scotty/help.html (See graphic in "What type of replicates should I use?" section)
unit of analysis	http://en.wikipedia.org/wiki/Unit_of_analysis http://en.wikipedia.org/wiki/Statistical_unit
dependent variables	http://en.wikipedia.org/wiki/Dependent_and_independent_variables
independent variables	http://en.wikipedia.org/wiki/Dependent_and_independent_variables
covariates	http://en.wikipedia.org/wiki/Covariate
variable type	http://en.wikipedia.org/wiki/Statistical_data_type
measurement unit	http://en.wikipedia.org/wiki/Units_of_measurement
distributions	http://en.wikipedia.org/wiki/Probability_distribution http://en.wikipedia.org/wiki/Normal_distribution http://en.wikipedia.org/wiki/Log-normal_distribution
Statistical Analyses	
statistical parameters	http://en.wikipedia.org/wiki/Statistical_parameter
statistical relationships	http://en.wikipedia.org/wiki/Correlation_and_dependence
statistical hypotheses	http://en.wikipedia.org/wiki/Statistical_hypothesis_testing
hypothesis tests	http://en.wikipedia.org/wiki/Statistical_hypothesis_testing
Sample Size	
power analysis	http://www.ats.ucla.edu/stat/seminars/Intro_power/default.htm http://www.ats.ucla.edu/stat/gpower/indepsamps.htm http://www.gpower.hhu.de/en.html http://biostat.hitchcock.org/MeasurementError/Analytics/PowerCalculationsforLogisticRegression.asp http://www.ats.ucla.edu/stat/dae/ (see bottom of page)
power	http://www.ma.utexas.edu/users/mks/statmistakes/power.html http://udel.edu/~mcdonald/statsampsize.html http://www.stat.columbia.edu/~gelman/stuff_for_blog/chap20.pdf

	http://www.nature.com/nrg/journal/v15/n5/abs/nrg3706.html
effect size	http://en.wikipedia.org/wiki/Effect_size
sample size	http://en.wikipedia.org/wiki/Sample_size http://en.wikipedia.org/wiki/Statistical_power#Software_for_Power_and_Sample_Size_Calculations http://biostat.hitchcock.org/MeasurementError/Analytics/SampleSizeCalculationsforLogisticRegression.asp

Randomization and Blinding

randomization	http://en.wikipedia.org/wiki/Randomized_controlled_trial
blinding	http://dx.doi.org/10.1126/science.342.6161.922

Bias

sampling bias	http://en.wikipedia.org/wiki/Biased_sample
measurement bias	http://en.wikipedia.org/wiki/Information_bias_(epidemiology) http://pubs.rsc.org/en/content/articlepdf/1997/an/a704789d
reporting bias	http://en.wikipedia.org/wiki/Reporting_bias
publication bias	http://www.ma.utexas.edu/users/mks/statmistakes/filedrawer.html

Data Inclusion/Exclusion

data inclusion/ exclusion	http://en.wikipedia.org/wiki/Inclusion_and_exclusion_criteria
outliers	http://en.wikipedia.org/wiki/Outlier

Data Analysis Considerations

missing data	http://en.wikipedia.org/wiki/Missing_data http://www.stat.columbia.edu/~gelman/arm/missing.pdf
confounders	http://en.wikipedia.org/wiki/Confounding http://sphweb.bumc.bu.edu/otlt/MPH-Modules/BS/BS704-EP713_Confounding-EM/BS704-EP713_Confounding-EM_print.html
effect modifiers	https://onlinecourses.science.psu.edu/stat507/node/34
detection limit	http://goldbook.iupac.org/ http://en.wikipedia.org/wiki/Detection_limit
quantitation limit	http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2556583/

Multiple Comparisons

multiple test correction	http://en.wikipedia.org/wiki/Multiple_comparisons_problem http://en.wikipedia.org/wiki/False_discovery_rate http://udel.edu/~mcdonald/statmultcomp.html
multiple comparisons	http://en.wikipedia.org/wiki/Multiple_comparisons_problem
Benjamini-Hochberg	http://www.stat.purdue.edu/~doerge/BIOINFORM.D/FALL06/Benjamini%20and%20Y%20FDR.pdf