

# EXPERIMENTAL DESIGN

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# Experimental Design

*How are you going to complete  
the proposed Specific Aims?*

# *Overall Research Design and Concept*

- Experiments to be performed
  - ▣ Scientific Rational for each experiment
  - ▣ How each contributes to completion of the Specific Aim
  - ▣ Procedures
  - ▣ Hazardous procedures, materials, and necessary precautions
- Data
  - ▣ Collection methods
  - ▣ Data Analyses and Interpretation
  - ▣ Data-Sharing Plan
- Novelty
  - ▣ New Methodology, Approaches, Tools, Technologies
  - ▣ Advantages and Shortcomings
- Expected outcomes, Potential problems & limitations
  - ▣ Limitations of your approach and Alternatives
- Significance/Summary
- Timetable or tentative sequence

# *Organization of Experimental Design Section*

- Individual Specific Aim to be completed
  - ▣ Verbatim
- Hypothesis
- [Impact]
- Rationale
  - ▣ Justify the experimental approach taken
  - ▣ More effective if short!
- Experiment(s)
- Methods
- Expected Results
  - ▣ And the “What if the Unexpected?” .... Limitations and Alternatives
- Statistical tests, including the calculation of sample size
  - ▣ Do you have enough statistical power to find effects if they exist?
  - ▣ This is a critical section which often causes an application to fail.

# Experiments

*How are you going to test your hypothesis?*

# Experiments

- Clearly describe each planned experiment
  - ▣ How does each experiment test your hypothesis
  - ▣ Should sequentially complete the designated specific aim
  - ▣ Should be clearly understood by reviewer that is not an expert in the field
- Remember your research basics:
  - ▣ Positive and negative controls
  - ▣ Sample size
  - ▣ Must test your hypothesis
- State the expected results
  - ▣ How does each result “answer” the specific aim and build on your hypothesis
- Pictures, figures and cartoons
  - ▣ Very helpful in clarifying the experimental approach
- Tables and charts
  - ▣ Use to show experimental groups, controls & outcomes avoids penalty for omissions in text

## Methods

*What technique(s) will you use to test your hypothesis?*

# Methods

- How much detail?
  - ▣ Brief overview of methods well-described in published articles – Citation is sufficient
  - ▣ Describe in detail all methods that have not been published
  - ▣ Be honest about limitations and alternatives
  - ▣ Do NOT give more information than is needed.
    - Reviewers will look for flaws and penalize you heavily for them.
    - Don't give them ammunition by including anything in the application you don't plan

# Methods

- If your proposal is highly innovative-
  - ▣ Make a very strong case for why you are challenging the existing paradigm
  - ▣ Have data to support your innovative approach
  - ▣ Outline limitations and alternatives
  - ▣ Be Persuasive, But Be Careful of Being Too Innovative

*You have to have a very good reason and be able to prove that, despite all the thousands of NIH-funded researchers that have written grants before you, you have to use a completely new technique that no one else has thought of, or ever described, in the last hundred years!*

# Methods



*Fancy or New Techniques are helpful only if they are the best experimental approach!*

# *Expected Results – or Not?*

- State what you expect to find and what this means in terms of your specific aim and hypothesis
- What if results are negative? Or different?
  - ▣ What you will do? – Alternate plan
  - ▣ State how negative findings will also advance the field
  - ▣ Avoid using the term “failure”
- Discuss limitations of each approach
  - ▣ How they may affect results and data
  - ▣ Call attention to potential pitfalls
  - ▣ Propose alternatives

# Limitations and Alternatives

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## *Discussion of Potential Problems and Solutions, Limitations and Alternatives*

*...tells the reviewer that you've  
thought long and hard about each  
individual experimental approach*

# Experimental Design

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*Finish with a concise discussion  
of the Significance of these  
experiments and specific aims  
to patients and to the mission  
of the agency!*

# Simple Timeline Table

	Year 1	Year 2	Year 3	Year 4	Year 5
Course Study	X	X			
Specific Aim 1		X	X	X	
Specific Aim 2				X	X
Specific Aim 3	X	X	X		
Manuscript Submission			X	X	X

# *Vertebrate Animals*



*Failure to address these 5 points under Vertebrate Animal section will make your application “incomplete” –*

*And will delay review or negatively impact your score*

# Vertebrate Animals

1. Provide a detailed **description of the proposed use** of the animals in the work outlined in the Research Design and Methods section. **Identify the species, strains, ages, sex, and numbers of animals** to be used in the proposed work.
2. **Justify the use of animals, the choice of species, and the numbers** to be used. If animals are in short supply, costly, or to be used in large numbers, provide an additional rationale for their selection and numbers.
3. Provide information on the **veterinary care** of the animals involved.
4. Describe the **procedures** for ensuring that discomfort, distress, pain, and injury will be limited to that which is unavoidable in the conduct of scientifically sound research. Describe the use of analgesic, anesthetic, and tranquilizing drugs and/or comfortable restraining devices, where appropriate, to **minimize discomfort, distress, pain, and injury**.
5. Describe any **method of euthanasia** to be used and the reasons for its selection. State whether this method is consistent with the recommendations of the Panel on Euthanasia of the American Veterinary Medical Association. If not, present a justification for not following the recommendations.

# Design and Methods

## *Clinical Studies*

# *Design and Methods: Clinical Studies*

- Overview
- Study Sample
- Data Collection Procedures
- Intervention(s)
- Outcome measure(s)
- Data Analysis/Sample Size Calculations

# *Design and Methods: Clinical Studies*

- Description of subjects
  - ▣ Inclusion criteria (address biases)
  - ▣ Exclusion criteria (well justified)
  - ▣ Women, minority, and children inclusion (per NIH)
- Availability of participants
  - ▣ Recruitment plan
  - ▣ Pilot work showing ability to recruit
  - ▣ Data from previous, related studies

# *Design and Methods: Clinical Studies*

- Data collection
  - ▣ List and define all study variables
    - Consider using a table
- Procedures
  - ▣ Outline screening and enrollment procedures
  - ▣ Describe interviewer training
  - ▣ Describe quality assurance procedures

# *Design and Methods: Clinical Studies*

- Outcome measure(s)
  - ▣ Describe or specify each outcome measure
  - ▣ Who assesses outcome?
  - ▣ How is blinding achieved/maintained?
  - ▣ How is equal surveillance of outcomes assured for all groups?

# *Design and Methods: Clinical Studies*

- Intervention and Controls (if any)

Describe:

- ▣ Intervention in detail, including standardized protocols
- ▣ How intervention will be implemented
- ▣ The interventionist, their proficiency, and training
- ▣ How adherence is monitored
- ▣ How you will assess for potential sources of “contamination” in the control group

# *Design and Methods: Clinical Studies*

- Data analysis
  - ▣ Describe data management procedures
  - ▣ Describe analytic approach (intent to treat?)
  - ▣ Lay out proposed analyses for each specific aim or hypothesis
  - ▣ Discuss alternative strategies considered and why you decided on your approach
  - ▣ Discuss how you will handle confounders, missing data, and attrition

# *General Comments*

- Remember to obtain letters from everyone who agrees to help out indicating that they are aware of the commitment<sup>1</sup>

# *AHA Fatal Flaws*

- Problems with experimental approach
- Too much unnecessary experimental detail
- Not enough detail on approaches, especially untested ones
- Lack of appropriate controls
- Not directly testing hypothesis
- Correlative or descriptive data
- Experiments not directed toward mechanisms
- No discussion of alternative models or hypotheses
- No discussion of potential pitfalls
- No discussion of interpretation of data

AHA Grant writing Fatal Flaws Dec 2005

[http://www.heart.org/downloadable/heart/1133366256870Grantwriting\\_Tips.pdf](http://www.heart.org/downloadable/heart/1133366256870Grantwriting_Tips.pdf)