

The application: significance, preliminary data, and approach

Hulley – chapter 19

GW Workbook – chapters 9,10,11

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Describing the significance of a
research project is about telling a
compelling story...

Is it a good grant? (NIH Guidelines)

- Significance / Relevance
 - Is the problem important? How will science be improved?
- Investigators
 - Do investigators have appropriate experience and training to conduct research?
- Innovation
 - Does project shift current clinical practice paradigms?
- Approach
 - Are methods well-reasoned, unbiased, feasible?
- Environment
 - Are resources available to conduct project?

Significance

What is the basis for your research ('so what'?)

- What is the problem
- What do we know now
- Highlight the part of the problem you are attacking
 - Quickly move the text to your hypothesis
 - Show your judgement in uncertainty
- What will be the clinical impact
- Reviewers sometimes treat the Significance section as a 'test' for the PI
 - especially for early-stage investigators
 - Demonstrate expertise, experience, and judgement

Background & Significance Section

- Write a condensed story that introduces reviewers to the research
- First 1-3 pages, or a brief overview with detailed write-up for each specific aim
- Provides a rationale for why you have developed your hypotheses and specific aims.

Significance Section

- Need to build desire for your study
- **Do not be boring**
- What is the big picture
 - Facts, theoretical framework
- Rigor of existing science
 - Literature critique, problems and gaps
- Show your preliminary results addressing gaps
- Impact
 - Contribution to body of knowledge upon completion
 - Simple statements of credible positive impacts to patients
 - Relevance to NIH or others

Significance

- Lit review can not be comprehensive. **Get to the point.**
- Go deep only into the **most relevant research**: seminal studies and recent studies defining state of knowledge
- **Highlight controversy.** Identify problems, weaknesses, and gaps in literature
- **Cite your publications** whenever you can.
- **Show impact**
- Demonstrate **your expertise**
- Describe where we are right now, thus setting-up your aims

Your Process

- Do your homework – read...write....repeat
- Continuously re-evaluate your hypothesis and aims
- Search other fields for innovation to apply
- Find others with preliminary data that compliments your PD
- Have others read it !!!
 - Content experts
 - Editors / proof-readers
 - Educated but no content expertise

How a reviewer sees Significance

- Do I care about this question?
- Do other reviewers care about this question?
- Why do I not understand it?
- Is it well written?
- Is preliminary data compelling?
- Does it translate to a research study?
- Any impact / so what?
- Other scoring criteria are focused on study implementation and feasibility

Preliminary Data

- PD is almost always required (or expected if not required)
- Significance:
 - Establishes the foundation for each hypothesis and specific aim
 - “These are interesting results, and we should study this further.”
 - Clarity of data presentation is critical.
 - Includes tables, figures, or graphs. Use footnotes extensively, and map descriptive text to figures and tables.
 - Ties with innovation of project
 - Make sure your PD strongly supports your hypothesis
- Approach
 - Demonstrate feasibility or superiority of your data collection protocols
 - Repeat previously published approaches with references
 - PD may come from any member of the research team
 - May highlight innovation in methods

Preliminary Data

- The quality of the preliminary data is scored!
 - Reviewers look at PD carefully.
 - Considered a sample of your work, and what you think the final results might look like.
 - Do not include PD if it is of poor quality, distracting, or not relevant

Innovation

- NIH is less interested in ‘me too’ research
- Depart from the status quo.
 - Use a new theory, method, approach, or intervention
 - Then explain how novel aspects increase study significance
 - Innovative hypothesis or question
 - Sometimes a strange idea is an innovative idea
- Usually one paragraph, and re-stated throughout application
 - Define the status quo in the literature
 - State how your innovation improves your project or addresses past weaknesses

Approach

- Describe the overall strategy, methods, and analysis for each aim
 - What will be done
 - How will you do it
 - Who will do it (if not obvious)
 - What might go wrong
 - What are alternative approaches
 - What are the expected outcomes
 - Why are these results important
- This may be the easiest section to write because you have already conducted pilot work and developed research protocols.

Approach (for each aim)

- Introduction (1 paragraph)
 - overview /objective / hypothesis
 - statement of the rationale, approach, impact
- Research Design
 - Describe each study activity
 - Justify model systems
 - Power and sample size
 - Statistical methods
 - Preliminary feasibility data / publication quality
 - Reference published methods / common protocols /standards
 - Rigor
 - Expected outcomes (1-2 paragraphs)
 - Problems (make sure they are minor)
 - Alternatives (1 paragraph)
 - Timeline for all aims and benchmarks (make a table or figure)
 - Future directions / what is the next step

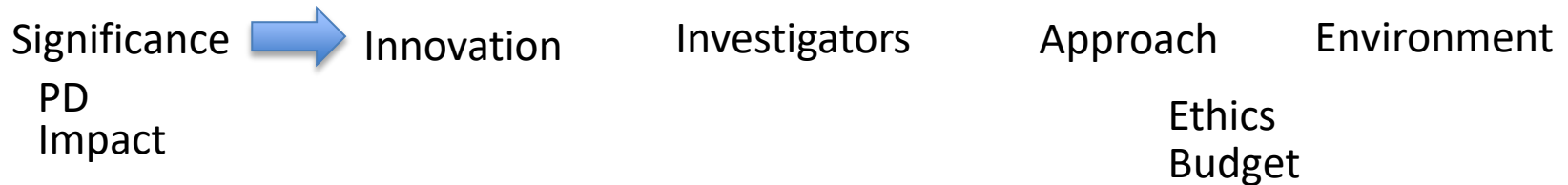
Approach

- 8-10 pages
- Try to use equal space for each specific aim
- Simplify descriptions as much as possible
- But, include enough detail in the most critical areas
- Data analysis. Do not forget the statistical analysis – get adult biostatistical support
- Advocate for the study by demonstrating expertise, feasibility, innovation, and impact

Other sections

- Investigators
 - Biosketches
 - One paragraph describing team interactions
- Environment
 - Facilities section
- Not scored, but discussed
 - Budget
 - Human Subjects / Animal protection

Will my research get funded?



Of the scored domains, Significance is sine qua non. Without significance, nothing else matters.

*Tell the story..... If Reviewers think your question is significant....
then*

Approach is usually next most criticized. Reviewers often want more clarity and detail. They do not care about page limits.

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