European Journal of Internal Medicine 64 (2019) 21–23

Contents lists available at ScienceDirect

European Journal of Internal Medicine

journal homepage: www.elsevier.com/locate/ejim

Special Article

Grantsmanship writing tips: the experimental design

ARTICLE INFO

Keywords:
Grantsmanship
Funding
Grants
Experimental design
Clinical research

1. Introduction

Our prior editorials have discussed the basic principles of grantsmanship [1] and the writing approach for the background, hypothesis, specific aims sections [2]. Herein we present the effective writing strategies for the experimental design section of a research grant proposal.

2. The experimental design

The experimental design is the core part of the grant proposal and should give all the necessary technical information as well as a solid rationale to illustrate how the aims and objectives will be accomplished. It may be referred to as "Research Strategy" or even a "Project description". Regardless of name, this portion of the grant is where you must describe your experimental approach in a clear, convincing and precise way without over-writing unnecessary details. Word choice is a pivotal element. Show that you are knowledgeable and confident with a clear plan by using the future tense ("we will") and avoid terms like "could" or "might" [3]. The organization of the experimental design section should reflect the requirements of the sponsor and be at least 50% of the page allowance. The space allocated for each aim should be balanced and reflective of the importance, or amount, of work/detail required by that aim. We and others recommend using a modular structure that repeats for each aim and includes the following four subsections: *i.* rationale and preliminary data; *ii.* experimental approach and methods; *iii.* potential pitfalls and alternative strategies; *iv.* expected outcomes [3,4].

2.1. Rationale and preliminary data

The opening of the experimental design of each aim should include the supporting rationale and preliminary data. Some funding agencies specifically call this initial part "Justification and Feasibility" because here you have to: i. justify why you propose this aim, explaining the rationale behind the experimental design; and ii. support rationale and feasibility by presenting preliminary data.

Begin each aim with an overview of the rationale behind your proposed scientific approach. Support the rationale with preliminary original data from your own team presenting the grant application. Preliminary data should be mostly unpublished and presented with the aid of graphs, tables, figure legend as in scientific publications. Select preliminary data that are relevant to the grant proposal without trying to impress the reviewer with all that was done in recent years. This section establishes your credibility with the reviewer.

2.2. Experimental approach and methods

When writing the experimental approach and methods, be "reviewer friendly" by using visual aids to break up blocks of text. Infographics, flowcharts, graphs, and figures can clearly display the study design and reinforce/summarize the key concepts introduced in the text. When grants are over six pages long, including graphics are the perfect solution to emphasize and define the major concepts you are presenting. This is very helpful in translational research studies that encompass many experimental groups with different interventions. A figure that visually displays the trial and intervention(s) enables the reader to understand the general strategy without reading the methods section multiple times. Also remember to include the "why" and not just the "what" of the experiments. Answer the question, "Why does this need to be done?" instead of just listing *what* you want to do.

Here are five important tips on how to approach the writing of the experimental design and Table 1 details the basic checklist to use when writing grants for clinical and basic/translational studies.

Tip 1: *Define the groups.* At the beginning of the experimental design, it's important to clearly define the characteristics and rationale of both the experimental and control groups (Table 1). *Translational research studies* using animal models require details (race, strain, background, origin source) that present a clear justification for the choice and number of model animals. There should be information on the husbandry conditions (temperature, diet, etc.…) and on the procedure(s) performed. Defining and justifing the studied subjects has a critical role in *clinical research* [5]. One should consult the EQUATOR Network [6,7], which outlays recommendations for reporting research. Based

https://doi.org/10.1016/j.ejim.2019.02.003
Received 1 December 2018; Accepted 10 February 2019
Available online 26 February 2019

Table 1
Basic checklist for the experimental design section.

	Clinical research	Basic/Translational research
Study groups	• Are the inclusion/exclusion criteria well defined and justified? • Have you checked for potential selection biases? • Is the control group well described? • Have you checked the EQUATOR guidelines? • Have you consulted a biostatistician for sample size calculation? • Have you written the exact number of subjects to be studied? And do you have available an adequate number of participants?	• Are the cell lines/animal models well characterized and justified? • Have you given information on race, strain, background, origin source, husbandry conditions of your animals, if applicable? • Is the control group well described? • Have you consulted a biostatistician for sample size calculation? • Have you written the exact number of animals/replicates to be studied? • Have you used graphs/flowcharts?
Intervention	• Is the intervention well described, justified, standardized and reproducible? • Have you stated who will administer the intervention? • If applicable, have you stated if there is blind administration of the intervention? • If applicable, have you stated how subjects will be randomized? • Have you described how you'll monitor adherence and safety?	• Is the intervention well described, standardized and reproducible? • Is the intervention scientifically justified? • Are the novel reagents, dugs, and procedures well described? • Have you given reference for your laboratory instruments and reagents? • Are your methods valid and realiable? • Have you given evidence of feasibility (preliminary data, citation of your own publications)?
Data collection and analysis	• Have you described measures for assuring quality of data collection? • Have you stated how to monitor and assure validity and reliability of data? • Is/Are the outcome/s well defined? • Have you consulted a biostatistician for data analysis? • Have you discussed how you'll deal with potential confounders and missing data? • Have you stated if you'll use an intention-to-treat approach?	• Have you consulted a biostatistician for data analysis? • Is the data analysis of all the experiments well described? • Is/Are the outcome/s well defined?

upon your particular type of study, they outline the most pivotal information needed in reporting data. Thus, by using the appropriate EQUATOR recommendation, you can ensure you are designing a study that will collect all of the pivotal information needed for proper analysis. Inclusion and exclusion criteria for all the study groups should be clearly listed in order to show that potential biases have been taken into account and that the selected sample is representative of the population. We also advise openly addressing any potential biases or limitations to assure reviewers that the results and their applicability will not be invalidated. Finally, consider that both NIH and Horizon 2020 require gender balance in the study design. Exclusions of race, gender or age should be justified with scientific evidence.

Tip 2: Write the numbers. When describing the experimental groups, state exactly how many subjects will be enrolled and/or how many animals will be studied in both the experimental and control groups. The numbers should be justified by providing the details of the performed sample size calculation [8] for the primary outcome (statistical test, power, estimate of effect size from pilot work, standard deviation when required). Make sure to work together with a biostatistician when defining the sample size, especially for clinical research studies. Also, provide data showing that an adequate number of patients will be available for the study in your clinic, thus reassuring the reviewer about the feasibility of the project in terms of numbers. Data from previously published studies or pilot experiments on the proposed study population are important to support the feasibility of the project in your hands.

Tip 3: Describe the intervention. In both translational and clinical studies [5] the intervention (pharmacological treatment, surgical procedure, etc.) should be described in detail, including information on blinded administration if applicable, randomization procedures, monitoring adherence and potential contamination or co-intervention in the control group. It's important also to justify the choice of the intervention chosen (Table 1).

Tip 4: Specify the statistical analysis. It is imperative to give detailed information on how the collected data will be analyzed [5]. Consult a biostatistician early and work together during the project design and the grant writing process to define the sample size, set the procedures for data management (error and validity checks, entry of data, etc.) and define the analytic approach. All the biostatistical details should be given in the grant regarding statistical and analysis methods (Table 1).

Tip 5: Support feasibility and innovation. You must show that the described experiments are feasible in your hands by citing your own literature or preliminary data or including support letters from your collaborators. Also, when describing new methods and concepts, emphasize the innovative part of the approach you are proposing.

2.3. Potential pitfalls and alternative strategies

In this sub-section, you should anticipate, discuss and in turn eliminate the possible concerns that the reviewer may raise. If this portion is strong, the reviewers will understand that you have thought through your experimental design very carefully.

In case of a hypothesis-driven aim, the first pitfall to discuss is the occurrence of a working hypothesis proven to be invalid. What would you do? What alternative pathways would you study? Discuss alternative hypothesis providing scientific rationale. Then, continue discussing the possible technical problems or limitations that may arise and the alternative plans that are in place to protect the project. Discuss the logical pitfalls that may occur, for instance, delay in the enrollment of the subjects, or in the breeding of the animals. For each challenge, discuss what other strategies you could adopt.

2.4. Expected outcomes or anticipated results

For the main outcome of each experiment, describe what results you anticipate to find and discuss their implications on the field. Be realistic and try to create enthusiasm by enlightening the reviewer as to how the progress, that would be possible thanks to the specific result, will lead to future research and or practice changes. If you anticipate that your outcome will be in contrast to other research, be sure to acknowledge the paradigm shift and detail why and how the contrast is possible. In this section, you should be able to tie your results to the vision or goal of the sponsoring institution, so they are reminded that the outcome of this project emphasizes and supports their institutional goals.

3. Related elements

There are elements of the grant proposal that are strictly related, both logically and operatively, to the experimental design.

Timeline/Gantt chart. At the end of the experimental design section, we recommend including a time-line in the form of Gantt chart, even if it is not required by the sponsor. A timeline shows the feasibility of the experiments according to their temporal logical arrangement, as well as your ability to organize and lead a 5-year research plan for instance.

References. Science is ever changing, and in this modern era, published research is available online at an exponential rate. As you write your experimental design section, make sure you are including updated and current sources. Reviewers are likely to do a quick search to ensure you are using recognized standards, so be sure to identify and properly cite throughout the section research that supports your theory and methods.

Budget. The budget is a pivotal piece of the grant. We encourage you to prepare an outline of your budget after reviewing the solicitation and before you draft your experimental design. Keep this outline close as you draft the research plan and make adjustments as needed. It is important to ensure that what you are proposing will be able to fit within the confines of the budget allowance by the sponsor. Further, it is important that each element proposed in the experimental design is accurately included in the budget. When budgeting an aim, think about more than just the supplies needed to complete the task/experiments. Estimate the amount of time and personnel needed to ensure the project is a success. Make sure that this time is reflected in the personnel costs you are projecting. If your research involves humans or animals, you may need to budget supplies and support to complete regulatory processes. Do you need to travel and/or publish with open access? Be sure to include those costs as well, if they are allowable. The call should detail if any additional documentation may be needed. Often, if equipment is being purchased, the sponsor may require a letter from the manufacturer or a quote. Check with your institutional budget professional before submitting any document to ensure that all needed costs are included. A checklist is included in Supplementary Fig. 1. That said, if at the end, you find out that your budget is over the limit, then you will need to go back through your experimental design and cut back accordingly.

Once you have determined the budget needed, be sure to provide enough detail in the justification to assuage any doubt or concern of the reviewer. Morrison and Russell suggest that the “justification” should be both “appropriate and reasonable” [9]. The more detail you can provide, the more confident a reviewer will be that you have thoroughly considered the project and are prepared to begin the research. This will strengthen your proposal and ensure the project is possible once funded.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejim.2019.02.003.

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