Special Article

Grantsmanship writing tips: background, hypothesis and aims

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1. Introduction

In the current article, we discuss the effective writing strategies for research grant proposal's background/introduction and specific aims/objective sections. These key components are often found in the beginning of the proposal and highlight the needs for the project and funding.

2. Anatomy of the grant proposal

While certain funding agencies or sponsors give precise guidelines on how to structure each part of the grant proposal, other sponsors provide more general instructions [1]. Table 1 summarizes some of the most common sections that may be required in a grant application. It is important to note that similar sections may go by different names. For instance, while the NIH requests a "Specific Aims" page, the EU grants often refer to this as the "Aims and Objectives" page. Generally speaking there is always a scientific part and accompanying documents (such as budget, facilities and infrastructures, etc.) that should be provided in support of the application [1].

In this special article series, we will focus on the scientific part [2]. When writing any proposal, the intent is to guide the reader (your reviewers) through a narrative that starts with the identification of a problem and a gap of knowledge/need (Background) and the formulation of a central hypothesis that would fill the gap or meet the need (Central Hypothesis). Next, the proposal story continues with details on how the hypothesis will be tested (Aims/Objectives) and what will be done specifically (Experimental design/Methods and

means). Then the grant should focus on feasibility by explaining the strategies to be adopted in case of problems (Potential pitfalls and alternative strategies) and the timeline for executing the experiments (Gantt chart). Finally, you can create enthusiasm stating what you expect to find (Expected outcomes) and where your research will lead (Future Direction). Many agencies require also to describe the rationale behind the proposed research with the positive impact that the research will bring once completed (Significance) and the novel parts of the experimental approach that will bring progress (Innovation). Writing the scientific approach by guiding the reviewer through a clear, interesting, novel research project, means creating partnerships with those in charge of evaluating your project [3].

3. Background

The background is the very first part of the proposal that the reviewer will read. Thus, it should be immediately engaging, generate interest and emphasize the current problem or need. This section may vary in title based upon the sponsor. Alternatives include: "Problem analysis including evidence base", "Introduction", "Review of the literature", "State of the art", or "Needs Statement". Regardless of title, this section's intent is to summarize the current status in such a way that reveals the *need* for the proposal. The section is much more than a literature review. Grantsmanship skills must be employed to deliver a *critical review* that clearly justifies why it is necessary to perform the proposed research and, when possible, it should identify key contributions your team has already made to the field in order to create a rational and evidence-based foundation for the proposed research. The

Table 1
Main sections of a grant proposal with their related purpose and content.

Section of the proposal	Purpose and content
1. Background/Introduction	• Defines the current status of the field • Pronounces the problem, gap of knowledge and/or the need • Uses published evidence to establish credibility and a foundation for the scientific rationale
2. Hypothesis	• Based upon peer-reviewed literature and/or preliminary data • Addresses the need or gap of knowledge • Concise and clear statement
3. Aims/Objectives	• Discreet goals that will test the hypothesis or fulfill the need • Provides the overall outline of the research strategy
4. Experimental Design and Methods/Approach	• Details what experiments will be done in each aim and what methods will be used • Includes a rationale for the design
5. Potential pitfalls and alternative strategies	• Identifies potential pitfalls and includes alternative strategies to address these possible challenges
6. Expected outcomes and future directions	• Anticipate what results would be produced by the research project • Relays the overall vision of the program and where the project would lead in next phases
7. Significance/Impact	• Describes the scientific rationale and rigor for the project • Logically related to the background section • Present the positive impact that filling the gap of knowledge/meeting the need will bring
8. Innovation	• Communicates the novel elements of the proposal and the potential progress as positive impact
9. Timeline	• Gives a temporal overview on how the experiments will be organized in a specific timeframe • Often uses a Gantt chart format
10. Budget and budget justification	• Details the costs of executing all the project • Describes the justification of every expense (personnel, supplies, equipment, etc.)
11. Principal Investigator Profile and Team	• Used to highlight the achievements of the PI and his/her team • Portrays experience to carry out all the proposed experiments
12. Facilities and Infrastructures	• Illustrates the resources that are available and relevant to the proposals • Includes descriptions of the facilities and equipment to be used • May discuss personnel or patient populations
13. Abstract	• A "stand alone" document that provides a shortened summary of the project • May be written in lay terminology if required (lay abstract) • Typically available to the public, so should not include proprietary information
14. Target groups	• Identifies the population(s) aided by this proposal • Required for 3rd Health Programme • Similar to Project Narrative Statement in NIH proposal
15. Policy relevance	• Describes the contribution of the project to Programme priorities, the added value to EU public health, the geographical coverage, and the consideration of social, cultural and political context • Required for 3rd Health Programme • Similar to Project Narrative Statement in NIH proposal
16. Dissemination	• Designates the plan on how the research results will reach the scientific community and the society
17. Title	• Emphasizes the payoff of the project • Includes key terms
18. Letters of support	• Written by key persons (chairmen, mentors, collaborators) in support of the applications
19. Compliance documents	• Research protocol descriptions and ethical approvals,if required
20. Cover letter	• Gives overview of the project for the funding agency's staff • Helps selecting reviewers • Provides contact information

content of this section should be structured as a "funnel", starting with more general facts and then proceeding with more specific details [4]. For physician scientists who work on clinical and translational research, the opening should give information on the burden of the studied disease using objective facts such as epidemiological data regarding mortality or morbidity, incidence or recurrence rate, or financial impact. This opening should include a "hook" to gain the reviewer's interest. For instance: "*ABC is a highly fatal and aggressive disease arising from the X epithelium (cit.). It is the second most common malignant tumor of the respiratory system with both incidence and mortality that are increasing worldwide (cit.). Overall, the estimated five-year survival rate is 21.8 % (cit.).*" In just three sentences, the writer has described the peril of the disease and underscored its devastation to the community. Importantly, the literature cited must be *relevant*. This means you should look for current literature as well as highly cited literature. When summarizing the evidence found, ensure that you do not just describe what was found in the study. An additional sentence that describes how this applies to the problem or solution your are proposing is imperative.

It is also important to define the perimeters of what is known and unknown or currently debated. Identifying the gaps in knowledge or current uncertainties about the problem or disease must be done by reviewing the literature and existing data with a critical but constructive approach. Be clear in stating the gap and when appropriate, highlight the statement with italics or bolding to ensure the message

resonates with the reviewer. For instance: "*Despite the two clinical trials in ABC patients that have been completed (cit.), research has failed to elucidate an effective treatment for disease X. Preclinical studies have shown that drug Y significantly reduces the proliferation rate of X cells in ABC animals; however, the mechanism is still poorly understood in humans.*"

Finally, the conclusion of the background section should give a very brief overview of the proposed project by linking it with existing data: "*Built on previous data, this proposal will determine the efficacy of drug Y in reducing the occurrence of bleeding events in ABC patients. Thus, it would lay the foundation for future randomized controlled trials. Regardless of efficacy, the pilot study will generate significant data that will enable future research on the mechanisms of action of…*". The concluding transition is also important to set the project up for success. Whenever possible, design the project so that regardless of outcome, new data will be generated that can inform the field. This reassures the reviewers that this project will indeed contribute.

The sponsor may ask for proposals that will address a need or gap in knowledge that has already been identified by the sponsor itself. In these cases, ensure that your project and literature review does not just duplicate what has already been put forth in the call. Take time to read about the sponsor's mission and vision statements to ensure that your project is in congruence with the goals and mission of the sponsor. If the sponsor has completed prior work that could be relevant, be sure to include and properly cite that work in your background. Ignoring

pivotal research that was previously supported by the sponsor could signal to the reviewers that this project was not thoroughly researched. Further, you want to ensure that your project is not a duplication of a project they are already sponsoring.

4. Central hypothesis

The majority of calls for applications, especially for basic and translational research, are for proposals that are "hypothesis-driven", i.e. the investigators should formulate the central hypothesis that will be tested with the execution of the research project. In common words, the hypothesis is a supposition made on the base of partial evidences [5]. In clinical practice, the physician generates a "diagnostic hypothesis" that arises from two main evidence sources: what the patient refers to as the complaint and what the physician personally detects at the physical examination. A similar logic applies to the formulation of a research hypothesis that originates from both what is known (data from the literature) and from what is the investigator's personal observation (preliminary data/evidence) [6]. Hypothesis need to be evidence-based and should also be clearly testable. This second element is pivotal. When developing the hypothesis, be sure that it is phrased and designed in such a way that it can be tested to be proven valid or invalid. The hypothesis is the investigator's "best bet" on what would fill the gap of knowledge or meet the need that was defined in the background section [7]. Thus, when writing the hypothesis, it is very important to be sharp and clear in defining the elements from which the hypothesis raises (literature and preliminary evidence) and to frame hypothesis within a broader goal of research. Draft phrasing could include: "*Our long-term goal is to design a preventive protocol for… For this project, the central hypothesis is …We formulated this hypothesis based on …and on our preliminary data showing that…*". Using the key terms "central hypothesis" "preliminary data" "long-term", etc. trigger the reviewer to pay closer attention. These are key sentences that are the foundation of the proposal. When appropriate highlight these sentences with italics or bolding.

There is a second category of calls for applications for projects that may be considered "hypothesis generating" [8]. They are specific to support, for instance, big data acquisition using high-throughput technologies such as genomics, metabolomics or proteomics that will be the base to formulate in a second phase, a specific central hypothesis [3,6]. In those grant proposals, the hypothesis, when required, should strongly stand on the literature data and support the premise that the generation or collection or the proposed data or tools will enable future research and discovery. For these proposals, feasibility and pay-off may be more strongly weighted in the review process. Thus, the background research should underscore that the project is clearly possible and additional research should address why the work has not been completed to date and why your team is the best one to accomplish the goal.

5. Aims and objectives

The NIH requests for a one-page document that describes specific aims of a project while the 3rd Health Programme requests a "Aims and Objectives of the Project section". For the purposes of this article, we will use the terms "aims" and "objectives" interchangeably. Other sponsors will typically require a section that delineates the goals of the research. This section is where the investigator has to state clearly and succinctly what objective have been planned in order to test the central hypothesis of the proposal and/or what milestones will be met in order to successfully complete the proposed project. Thus, the aims and objectives should be logically related to the two main pillars on which the hypothesis stands: the literature and the preliminary data. Aims should be focused and logically related to each other. However, the outcome of one aim should not prevent the execution of the other aims. This can be referred to as a fatal flaw. Each aim should be able to be initiated and accomplished regardless of how the experiments in the prior aim are

completed. For example, if your first aim is to create a model, your second aim shouldn't be completely depending on successful model creation. The second aim instead could test the newly created model *and* a standard model for biomarkers, etc. That way if the model creation (Aim 1) isn't successful, you can still attain biomarker data from an alternative/standard model. Thus, significant time should be spent on the phrasing and careful delineation of the aims of the project. Review and rephrase the aims until they are stated with clarity, feasibility and purpose.

It is also important to not overload your project with excessive aims. This is a common pitfall for junior investigators. One may design the aims of a proposal that are unrealistic for the budget or time allotted and overly ambitious plan [3]. That's why the aims should not be just a list of experiments, but they should be a thoughtful progressive list of targets, each contributing to an overall goal or objective. This section should be structured in a clear and logical list of no more than 3–4 specific aims or objective. Sometimes, only two objectives may be needed. When writing the aims, it is imperative to draw attention to them as they are the crux of the proposal. Thus, we would suggest the following:

i. The headline of the aim should use *active* and clear language with a bold or italicized font.
   Aim 1: Validate the scaled impact of…
   Avoid generic words like "describe", "correlate", "estimate", because they are used to state "what" you are wanting to do instead of "why" you want to do the project/experiment. Generic verbs may also indicate you are not sure of what is going to happen and this reduces the reviewers confidence as it looks like more of a "fishing expedition" instead of a directed project [3];
ii. Include a working hypothesis for each aim. The working hypothesis should be a narrowing of the central hypothesis in the experimental setting of the aim (es. In-vivo study or patients with ABC disorder). It will guide the reader as to what questions will be answered by this specific portion of the grant.
iii. Within one to two sentences, provide a brief overview of the experimental approach that is planned for each aim. Specifics are not needed, but the reviewer should know in general terms what experiments and analysis is planned.
iv. Finally, close each aim with one sentence on what the expected results are.

After describing each aim, a transition paragraph should be included that underscore the impact that the project will have on the field in general.

6. Conclusion

In conclusion, these are general elements that will aid the clinical researcher in drafting the initial portions of a grant application regardless of sponsor. Specific advice on the required elements of the NIH proposals and 3rd Health Programme will be discussed in separate articles. It cannot be underscored enough that each sponsor will set criteria and expectations that are individual. Reading the solicitation carefully (and repeatedly) is the only way to ensure that the proposal is properly prepared.

References

[1] Gholipour A, Lee EY, Warfield SK. The anatomy and art of writing a successful grant application: a practical step-by-step approach. Pediatr Radiol 2014;44:1512–7. https://doi.org/10.1007/s00247-014-3051-8.
[2] Sauer MR, Gabbi C. Grantsmanship: what? Who? How? Eur J Intern Med 2018 Nov;57:22–4.
[3] Santen RJ, Barrett EJ, Siragy HM, Farhi LS, Fishbein L, Carey RM. The Jewel in the crown: specific aims section of investigator-initiated Grant proposals. J Endocr Soc 2017;1:1194–202. https://doi.org/10.1210/js.2017-00318.

[4] Hofmann AH. Chapter 22: background and significance. Scientific Writing and Communication: Papers, Proposals, and Presentations. 2014. p. 427–44.

[5] Oxford University Press. Oxford English Dictionary. 1992.

[6] Biesecker LG. Hypothesis-generating research and predictive medicine. Genome Res 2013;23:1051–3. https://doi.org/10.1101/gr.157826.113.23.

[7] Russell SW, Morrison DR. Chapter 7: specific aims section. The Grant Application Writer's Workbook. 2012. p. 62–70.

[8] Özdemir V, Badr KF, Dove ES, Endrenyi L, Geraci CJ, Hotez PJ, et al. Crowd-funded micro-grants for genomics and "big data": an actionable idea connecting small (artisan) science, infrastructure science, and citizen philanthropy. Omi A J Integr Biol 2013;17:161–72. https://doi.org/10.1089/omi.2013.0034.