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Significance and innovation: cornerstones of a successful grant application

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ABSTRACT

The Significance and Innovation sections of a grant application are the cornerstones to a successful application. These sections emphasize the importance of the problem being studied, highlight what is novel about the proposal, and are an opportunity to get the reviewers excited about the application. To the novice grant writer, it may be difficult to know what "Significance" and "Innovation" are meant to describe. In this article we define the role of the Significance and Innovation sections and provide suggestions on what to include in each section and potential pitfalls to avoid.

Introduction

In most grant applications the "Significance" and "Innovation" sections are standard content that must be written in a clear and compelling fashion. These sections emphasize the importance of the problem being studied, highlight what is novel about the proposal, and are an opportunity to get the reviewers excited about the application. These sections are of fundamental importance and represent scorable elements of the grant that will be read carefully and critically by reviewers. Indeed, the National Institutes of Health's (NIH) internal analysis of individual criterion scores shows that Significance and Innovation closely follow the Approach in driving the overall impact score of a grant proposal[1] (Fig 1).

The Significance and Innovation of the grant are first introduced in the final paragraph of the Specific Aims page and are then expanded upon in the sections that follow thereafter.[2] To the novice grant writer, it may be difficult to know what "Significance" and "Innovation" are meant to describe. Do these terms refer to you, the investigator? Are they meant to highlight aspects of your scientific environment? Are they referring to the central question or hypothesis or could they refer to the methodologies proposed? In this article we answer these questions and provide suggestions on what to include in these sections and what pitfalls to avoid.

Significance

Historically, the Innovation and Significance subsections were bundled together. In recent years, funding bodies such as the NIH have separated these subsections, emphasizing their distinct importance. However, these sections remain adjacent to each other in the application and therefore repetition or redundancy should be avoided. The role of the Significance section is to clearly state the importance of the problem and the critical barrier to progress in the field that the proposed study addresses. When thinking about whether or not your proposal is significant, ask yourself the following questions: Am I tackling an important problem? How many people does the condition affect? How much morbidity does it cause? What are the costs? Will completing my aims have a major impact and move the field forward?

The grant proposal needs to address an important problem in which success will yield improved scientific knowledge and/or clinical practice. In short, the proposal needs to have potential for impact on the field. It represents the applicant's opportunity to tell the reviewer why they should care about the study and get them excited about the work. Disinterest on the part of the reviewer is a

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Fig 1. Distinctions between how applications are written and perceived by the applicant and the reviewers. As you prepare your application, it is important to be cognizant of the differences in how you write the proposal and how it is perceived by reviewers.

major reason for a low score. A strength that clinician-scientists generally have is a clear understanding of the translational significance of their work. Clinician-scientists usually focus on a human disease driven by the patient population they care for and study the underlying biology as a means to a therapy, cure, or prevention. Defining significance will be more challenging for a researcher who is passionate about a particular protein or pathway but is not aware of its clinical relevance or impact on human health or disease.

The perceived magnitude of the problem is an important aspect of how reviewers score the significance of the study. Disease processes such as cancer or heart disease affect millions of people worldwide and therefore any advancements in these fields are potentially highly impactful and therefore "significant." The study of a rare disease that only affects a small number of people per year may be considered less of a priority by some funding agencies. Nevertheless, rare diseases can represent a significant cause of morbidity or high cost, or the proposed study may lead to generalizable knowledge with broader applicability. It is important to describe the target population, disease prevalence, cost, associated mortality and morbidity statistics, and how the project will improve knowledge and/or outcomes, as all of this gives the reviewer an idea of the potential impact. Additionally, some funding agencies will issue calls for proposals specific to understudied diseases. At times, funding bodies will identify issues that are "hot topics," such as the coronavirus disease 2019 pandemic.

A well-written Significance subsection should include details pertaining to the strengths, weaknesses, and limitations of previously published research as well as your own preliminary data that are crucial to support your application (Table I). The suggested length is typically 1 to 2 pages in an NIH R01 application, but this varies depending on the grant type and agency. In writing this section, you

Table I
Conveying significance in 4 paragraphs

Paragraph	Goals
1	Justify the need for your proposed work. Explain the importance of the problem or critical barrier to progress in the field
2	Provide a scientific foundation for your studies. Include strengths/weaknesses of published research or your preliminary data
3	Explain how the project will improve scientific knowledge, technical ability, or clinical practice in 1 or more fields.
4	Describe how the concepts, methods, technologies, treatments, etc., that drive the field will be changed if the proposed aims are achieved.

Table II
Pearls for significance

The significance section is about the "problem"
Why is it important?
Who does it impact?
Why is a solution currently missing?
What have people tried? (be brief with this, don't do a literature review)
Why is a solution needed *now*?
What has happened that makes you think you and your team have a solution?
In which aim will you solve which problem?
Why is your team qualified to solve the problem(s)?

should assume that the reviewers are not aware of the significance of your field. It should be presented in a way that is compelling and obvious (Table II). Details provided should include new information and citations that build upon and validate statements made in the Specific Aims. Although a "premise" is no longer required in NIH proposals, there should be a strong scientific foundation for the proposed project. The NIH provides guidance on Significance for grant writers and reviewers, stating that there should be a description of how the concepts, methods, technologies, treatments, services or preventative interventions that drive this field will be changed if the proposed aims are achieved.[3] The Significance section should present the "idea" to the reader and highlight the critical gap in knowledge that the proposal will fill in order to have them become interested and excited about the proposal. If this is accomplished the reviewer will look forward to reading the finer details presented later in the proposal. By writing an easy to read and convincing proposal demonstrating that the work is important and that you are knowledgeable and poised to complete it, provides an opportunity to recruit the reviewer as an advocate for your proposal.

Innovation

The Innovation section focuses on how you plan to tackle the problem, specifically from the viewpoint of "what is new and different about your solution that makes it innovative?" (Table III). It should describe a departure from the current *status quo* and highlight that what you are proposing is a new idea that will change or impact the field. It should explain how you plan to push knowledge forward starting from what is currently known. Therefore, this section needs to include an assessment of where the field is now, where the current leading edge lies, and how your grant will advance it. The scoring criterion from the NIH asks whether the application, "challenges and seeks to shift current research or clinical practice paradigms by utilizing novel theoretical concepts, approaches or methodologies, instrumentation or interventions".[3] They inquire whether the concepts, approaches, methods, or interventions are novel to the field or extend the science in general—for example, adopting a particular type of imaging from one field to use in another. A refinement, improvement or new application of theoretical concepts, approaches or methods, instrumentation or interventions are also included.[3] The Innovation section is about what you know that others do not, what you can do that others cannot, and how you can solve a problem that others have failed to solve. In essence, the Innovation section is what makes your proposal unique (Table IV).

Innovation should be succinct, and it is important not to exaggerate or list innovations where there are none. Innovations should be about the current project rather than where it may lead in the future. An example of successful innovation would be to use a new research method or to apply an existing method in a different way. For example, the development of a novel vaccine using mRNA for coronavirus disease 2019 is innovative. Less successful strategies would be to use an old and tested methodology in a different population. In the Innovation section the goal is not to cover the entire

Table III
Conveying innovation in 3 paragraphs

Paragraph	Goals
1	Explain how the application challenges and seeks to shift current paradigms
2	Describe any novel theoretical concepts, approaches or methodologies, instrumentation, or interventions to be developed or used (and advantages over existing)
3	Explain any technical refinements, improvements, or new applications

Table IV
Pearls for innovation

The innovation section is about how you will "fix" the problem
What is new and different about your solution?
What do you know that others do not?
What can you do that others cannot or at least what can you do better than others?
How will you solve a problem that others have failed to solve?

solution, but rather to discuss *what's new and useful* about the solution(s) that are described in the Approach section. A mistake is to provide too much detail. That should be saved for the Approach. Another pitfall to avoid is being too innovative. Don't move away from the scientific mainstream. It is best not to challenge commonly held beliefs unless there are sufficient and compelling preliminary data to do so. Innovation is the goal, but it must be grounded on reliable published work and/or preliminary results.

In conclusion, the importance of the "Significance" and "Innovation" subsections cannot be overstated. Although our perceptions of how we see, write, and review our proposals may differ, these sections are critical areas of review and should be explicit and easy to understand. The use of phrases such as, "This study is significant because…" and, "This study is innovative because…" are highly recommended in order to lead the reviewer. The reviewer will be able to quickly find and reference such statements. The "Significance" section allows for a clear description of the impact and relevance of the proposed work, and the "Innovation" section speaks to its uniqueness and importance. Indeed, even if a proposal describes a flawless approach, but offers nothing innovative and/ or studies an area with minimal significance, it will not be successful.

Conflict of interest/Disclosure

The authors declare no conflicts of interest.

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