NIH Grant Applications
The Anatomy of a Specific Aims Page

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Author: Michelle S., Ph.D., E.L.S.

The Specific Aims section is the most vital part of any NIH grant application. In this section, you must quickly gain the reviewers' trust and confidence while simultaneously convincing them that your work is important to fund. You must also convey that you and your team are the best people to complete the work you've proposed. For these reasons, the Specific Aims can be one of the most difficult sections to write. In this article, we provide some tips on structure, content, and organization of your Specific Aims page.

The Specific Aims section is central to your grant proposal. Therefore, it should be the first section you write. You may think of your Specific Aims page as an abbreviated version of the full grant. By having this page written and well-thought out, the remainder of grant application will be easier to write.

The Introductory Paragraph

In this paragraph, your goal should be to introduce your research subject to the reviewers and quickly capture their attention. This paragraph should describe the significant gap in knowledge that directly relates to the critical need the funding entity deals with. It is critical to know your funding entity's mission statement and ensure the critical need you are trying to fill fits well within its mission. It should include the following information:

First Sentence/Hook: In this sentence, briefly describe what your proposal will be about. Ideally, this sentence should convey a sense of importance or urgency to your research. Explain quickly WHAT your research topic is and WHY it is critical that you conduct the research (i.e. saving lives, preventing cancer, etc.)

What is Known: State what is currently known in the specific field. This part should not be very long (3-5 sentences) but it should ground the reader in the subject of your research. Provide the reader with only the necessary details to understand why you are proposing the work. Remember to be concise and focused on only the key points.

Gap in Knowledge: The gap in knowledge is the piece of information that is not known. Clearly state the gap in knowledge that needs to be addressed. Convey that your research will fill this gap using the funding that you are requesting. In the example Specific Aims page we use here (See Figure 1), the most critical piece of the gap in knowledge has been italicized. This technique can be useful to emphasize the most important words or phrases in your Specific Aims page. If you choose to use *italics* or underline to emphasize key points, remember to do so moderately. Overuse of italics or underlining can be distracting.

The Critical Need: The critical need is the knowledge (hypothesis-driven), technique, new compound, or treatment that you propose to develop. This need is important to increase medically relevant knowledge or improve health care. The critical need is the reason your proposal should be funded. Emphasize the significance of the problem you are trying to address. Additionally, it should be clear in this paragraph that your research proposes the next logical step to advance the field.

Below is an example of an introductory paragraph:

Viruses are thought to be involved in 15% to 20% of human cancers worldwide, thus providing critical tools to reveal common mechanisms involved in human malignancies. As the etiologic agent of adult T cell leukemia/lymphoma (ATLL), human T cell leukemia virus type I (HTLV-1) is just such a virus. HTLV-1 encodes a potent oncoprotein, Tax, which regulates important cellular pathways including gene expression, proliferation, apoptosis, and polarity. Over the years, Tax has proven to be a valuable model system in which to interrogate cellular processes, revealing pathways and mechanisms that play important roles in cellular transformation. Although the Tax oncoprotein has been shown to transform cells in culture and to induce tumors in a variety of transgenic mouse models, the *mechanism by which Tax transforms cells is not well understood*. A large number of Tax mutants have been generated and their biological activities have been thoroughly characterized, primarily in cell culture systems. *Currently, a major obstacle in the field* is that the transforming activity of Tax mutants cannot be compared using available transgenic models due to random transgene integration sites, variable transgene copy number, and inconsistent transgene expression levels, making it difficult to link the biological activities of Tax mutants with their transforming potential.

Color Key: Hook | Known Information | Gap in Knowledge | Critical Need

Figure 1. The Introductory Paragraph. Sections of the paragraph have been color coded to highlight each critical component.

The Second Paragraph

In this paragraph, your goal should be to introduce the solution that fills the gap in knowledge. It is critical to convince your reviewers

that you (and your colleagues) have the solution to address the current knowledge gap and the expertise to accomplish this solution. Keep your wording simple, relevant, and to the point. You will want to address the following points:

» What do you want to do?
» Why are you doing it?
» How do you want to do it?

There is some flexibility in this paragraph, depending upon how your proposal is structured and what your goals are. For example, your research may be strictly hypothesis-driven and seek to test several elements of one general hypothesis. In other cases, you may be seeking to develop a critical tool or technique in the proposal. Based on these variations, this paragraph will shape up differently. However, it should include the following components:

Long-Term Goal: This is your overarching research goal. Because you are asking for support from a particular funding entity, it is important to ensure that your long-term goals align with the mission of your funding entity. Keep your wording general in this sentence—you are stating your long-term plans, and the reviewers understand that the specifics may be subject to change.

Hypothesis and Proposal Objectives: Your proposal should contain both of these components, depending on the long-term goal. State your central hypothesis clearly, specifically, and with simple language. You want to demonstrate to the reviewers that you have a hypothesis-driven proposal that is testable. Describe how your project addresses the critical need, and clearly state the proposed solution. In general, avoid vague hypotheses because it will be unclear to the reviewers what you expect to determine with the proposed research.

Rationale: Explain how you arrived at your central hypothesis (for example, using past studies and published literature). Briefly, state what your project's completion would make possible (e.g., new therapeutics), and tie it to the funding entity's mission.

Qualifications: Briefly state why your experimental design and your team are the best to accomplish the research goals. You can mention factors such as your preliminary data, personnel qualifications, laboratory equipment, etc., but it is important to keep it concise.

Here is an example of a second paragraph:

To solve this problem we will develop an innovative mouse model system in which to study Tax tumorigenesis using targeting vectors containing wild-type or mutant Tax genes that are silenced by a preceding floxed stop cassette. These vectors will be knocked in to the *Rosa26* locus of recipient mice by recombination. After crossing these mice with Lck-CRE mice, the stop cassette will be specifically excised in developing thymocytes where the Lck promoter is active, allowing conditional expression of wild-type or mutant Tax proteins in T cells, the natural target of HTLV-1 infection. The feasibility of our proposed mouse model is supported by the fact that Lck-Tax transgenic mice have been developed and produce a leukemia that closely resembles ATLL. Thus, targeting of Tax expression in cells in which the Lck promoter is active is expected to produce a similar disease in our model. In our improved model system, insertion into the *Rosa26* locus will eliminate random integration sites and standardize gene copy number resulting in consistent levels of wild-type and mutant Tax protein expression.

Color Key: Long-term Goal | Proposal Objective | Rationale | Hypothesis | Pay-off

Figure 2. The Second Paragraph. Sections of the paragraph have been color coded to highlight each critical component. Note: This example does not expressly contain *Qualifications* and does include some *Pay-off*, which is described in this article as part of the final paragraph. These variations highlight the flexibility you have while creating a strong Specific Aims page.

The Aims

In this section, you will describe briefly each of the aims you will use to test your hypothesis. Ideally, the aims should be related, but not dependent, upon each other. If you do this, the failure of one aim (or an unexpected result from one aim) does not negatively influence any other aim or prevent the completion of the other aims.

Within 2-4 sentences each, you should describe the experimental approach and how each aim will help answer your larger hypothesis. A typical NIH R01 grant will have between 2 and 4 Aims. Plan to describe each aim in a separate paragraph. Additionally, these tips may help you to formulate your aims sections:

» Give your aim an active title that clearly states the objective in relationship to the hypothesis.
» Include a brief summary of the experimental approach and anticipated outcomes for each aim.
» If you have room, you may wish to include a sub-hypothesis (the small portion of the overall hypothesis) and a small description of the pay-off of each aim. Including these is helpful to creating the impression that each aim is valuable, testable, and independent of the others.
» To make it easier for the reviewers to clearly read and understand each aim, it is often helpful to use headings and/or bullets to delineate each specific aim.

Here is an example of the Aims section:

Aim 1 will establish an innovative mouse model for HTLV-1 Tax tumorigenesis. Targeting vectors containing silenced wild-type or mutant Tax genes will be knocked in to the Rosa26 locus of C57BL/6 mice. These mice will then be crossed with homozygous Lck-CRE mice, thereby excising the stop cassette and generating mice that express wild-type or mutant Tax proteins specifically in T cells.

Aim 2 will examine the effect of mutations that disable specific biological functions of Tax on Tax-mediated tumorigenesis. Tax can bind

to and regulate the activity of members of the SRF, CREB, NF-kB and PBM protein families, each of which has been implicated in oncogenesis. Mice established in Aim 1 will allow us to compare for the first time the tumorigenic potential of wild-type and mutant Tax proteins in an effort to identify pathways that are required for Tax tumorigenesis.

Color Key: Aim Title | Experimental Strategy | Outcome or Impact

Figure 3. The Aims Section. Sections of the paragraph have been color coded to highlight each critical component. Note the active voice in the titles of each aim and the use of boldface text to highlight the titles.

The Final Summary Paragraph

This final paragraph of the Specific Aims is often overlooked, but it is vital for the impact of your proposal. Think of your Specific Aims page as an hourglass, where the wide parts represent the general information and global significance, and the narrow parts are the fine details. If you end with the Aims Section (above) you will end on fine details and a narrow scope. An hourglass with a narrow base is unstable and will topple. Therefore, this final paragraph creates a firm, broad base to support your entire proposal.

The final paragraph should include the following important details:

Innovation: Plainly state what is innovative about your project. What would completion of this proposal bring to the field that is not present currently?

Expected Outcomes: Specifically state your expected outcomes for this project. Use plain language. What do you expect to see at the completion of each aim? Include this information only if you have not placed it in the Aims.

Impact: State how your project would help those who need it, (i.e. the development of a new treatment, vaccine, disease model or diagnostic tool) Include a broad impact statement about how your proposal will benefit the people or other subjects that you mentioned in the opening paragraph.

Here is an example of a Final Paragraph:

The proposed studies will establish a new mouse model that will overcome current limitations and provide greater insight into the mechanism of HTLV-1 Tax tumorigenesis, knowledge that is currently lacking and that promises to yield novel insights into viral and cellular biology. The new and improved mouse model for Tax tumorigenesis will provide a valuable resource for the wider scientific community to pursue a multitude of studies that have not previously been possible due to limitations of existing mouse models of Tax.

Color Key: Innovation | Expected Outcomes | Impact/Pay-off

Figure 4. The Final Paragraph. Sections of the paragraph have been color coded to highlight each critical component.

Final thoughts

Remember, your proposal may have some variability from these descriptions. The example given here is a strong example, but it is not all-inclusive. Each Specific Aims page is unique to the proposal. Therefore, there is a lot of flexibility in how these elements can be arranged and emphasized. Consider the novelty, innovation, and significant elements of your proposal as you decide how to organize this page; however, a great Specific Aims page will possess all of these elements. The order presented here has an ideal logic for a majority of proposals, so try applying it to your proposal to see how it works for you.

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