

CHAPTER 8

WRITING THE SPECIFIC AIMS SECTION

Instructions for PHS 398 Research Plan Component / *Specific Aims* Section:

"State concisely the goals of the proposed research and summarize the expected outcome(s), including the impact that the results of the proposed research will exert on the research field(s) involved. List succinctly the specific objectives of the research proposed, e.g., to test a stated hypothesis, create a novel design, solve a specific problem, challenge an existing paradigm or clinical practice, address a critical barrier to progress in the field, or develop new technology." You are limited to one page.

In the previous chapter, we introduced you to the purpose of each of the ten components of the *Specific Aims* section and showed you how to create a bullet outline using them. In this chapter, we will guide you through the process of expanding your bullets, which is the initial step in formulating the first draft of this section. As can be seen from the instructions in the text box, above, this section is limited to one page. Succinct writing will be required, therefore, if you expect to get everything needed into the allowed space. Only the most important, 'linchpin' references should be cited here. Set up the page using some of the same space-saving approaches that are described in chapter 5 for the one-page Introduction: use Georgia, Arial or Helvetica as your typeface at 11 points, auto-hyphenate, use full justification and single space after each sentence. We recommend, however, that you start with one-inch margins, because that is a more reviewer-friendly approach than using the minimum of 0.5 inch. For the same reason, open a line after each paragraph. If you find that clever editing of the first draft still leaves you over the one-page limit, then and only then, go to 0.5-inch margins. The last thing that you should give up, in our opinion, is the open line after paragraphs. You don't want your application to look like pages from a telephone directory! The formatting for this page should be what is used for the other documents that will constitute your Research Plan.

In terms of writing the Research Plan, we recommend that nothing be left to the interpretation of reviewers. If you allow them to interpret what you have written, they may not make the desired interpretation or – worse – they may make the wrong interpretation. To avoid this problem we recommend that you help reviewers make the connections that you want them to make. The approach we have developed allows you to 'tell' reviewers exactly why information has been included without running the risk of being seen as pedantic or condescending while doing so. The approach entails 'labeling' of the components that make up the section in such a way that there can be no question as to why you have included the information. Labeling of key sentences also helps to lead reviewers through what you have written. (A well-written proposal leads reviewers without them knowing that they are being led.) The approach makes comprehension effortless, because no work is needed to appreciate why material has been included. As you expand your bullets we will recommend where and how to use such 'labels.'

We also recommend that you increase reviewer friendliness by highlighting key words that identify components you know reviewers will need to find in order to review your proposal. We will tell you which words to highlight later in this chapter. *Judicious use of subtle highlighting* – we

recommend italics – is the key; overuse causes such highlighting to lose its effect and can even become an aggravation to reviewers. Of the four allowed typefaces, italicized *single* words or *several words* aren't that noticeable with either Arial (which is the typeface for this *Workbook*) or Helvetica. We recommend, therefore, that you also underline with these typefaces to make *single* words or *several words* stand out, as is illustrated in this sentence. More than several words, i.e., phrases or entire sentences, are sufficiently prominent in italics that you don't have to underline. To do so would be overuse of highlighting – to the point that it would be an aggravating distraction. If you are using Georgia, which is what this typeface is, italicized *single* or *several words* stand out adequately and underlining is not needed. The *same* is true for *Palatino Linotype*, which is what this typeface is. We do not recommend the latter typeface because of the extra room it requires as a result of wider line spacing (evident here).

EXPANSION OF YOUR BULLET OUTLINE INTO SENTENCES

Once you are satisfied with your outline, the next step is to expand it into your first draft of the *Specific Aims* section.

Introductory Paragraph

Opening Sentence. Expand the bullet that you wrote for your opening sentence. Make sure that it reads well and flows easily into the presentation of what is currently known. Make sure that the sentence is arresting and, as such, will immediately attract the reviewer's interest and attention.

Current Knowledge. Working from the bullets that reflect current knowledge, write two-to-four complete sentences that convey what is known about your subject area. The first sentence should be labeled to signal this component's purpose. For example, "It is well known that ..." or "It has long been appreciated that ..." The series of two-to-four sentences should narrow reviewers' focus from the most important older current knowledge to the edge of the field as it exists today. Cite only the most important references in doing so.

Gap in the Knowledge Base/Unmet Need. Next, expand the bullet that you wrote to delineate the gap in the knowledge base or the unmet need that will drive the application. Label this sentence by beginning with something like, 'What is not known is ...' or 'Thus there is an *urgent [or critical] need* for ...' Note that "*urgent need*" is highlighted in italics. If you are offering a statement of need, next, expand the bullets that provide objective evidence for existence of the need. If publications of other investigators are used to support existence of the need, cite that work.

What, Why, Who Paragraph

TIP: The first 3 components in this paragraph create a focusing progression, which the reviewer must perceive. To help ensure that s/he makes that connection, the long-term goal, objective and central hypothesis should be presented without interposed explanatory information. These three components should be juxtaposed, so that there is a seamless flow of logic from the broadest (the long-term goal) to the narrowest focus (the central hypothesis).

Long-Term Goal. Expand the bullet for your long-term research goal. It should clearly encompass the gap or unmet need that was delineated in the first paragraph. Do so by completing the following: 'Our [My] long-term goal is to' Note that the words 'long-term goal' have been italicized and underlined to make them easier for reviewers to find. Note, also, that there is a hyphen between "long" and "term." It is required because those two words created a compound adjective that modifies "goal."

Overall Objective. Now, expand the bullet you wrote for the overall objective into a single sentence that conveys what you want to produce with this research project. Make sure that what you write here links back to the gap in the knowledge base or unmet need that you presented in the first paragraph; the objective of any grant application must be to either fill that gap or meet that need. Label this sentence by beginning it with something like, 'The overall objective of this application, which is the next step toward attainment of our long-term goal, is to

Note use of the phrase, "which is the next step toward attainment of our long-term goal." Including something like it assures that reviewers will recognize that this application represents the next step along the continuum of research that is projected by your long-term goal. The words "long-term goal" should not be underlined and italicized when they are used the second time. When you have completed this sentence, make certain that it links back to the gap/unmet need component and that it relates clearly to your long-term goal.

Central Hypothesis and How Formulated. This component will not be included if your proposal is purely need driven. It will be included if you are writing either a hypothesis-driven application or a 'hybrid' – one that is driven both by a statement of need and by a central hypothesis. The expanded bullet should convey your 'best bet' as to how the objective can be attained. Ideally, it should have readily identifiable parts that will be used to set up the aims. Make sure that you label this component so that it can be found easily by reviewers. For example, 'Our central hypothesis is that' Be certain that what you have proposed is objectively testable.

Now, expand the bullet(s) that you wrote to describe how your hypothesis was formulated, i.e., why it has been chosen as your 'best bet.' If the work of others is used in addition to your own preliminary data to support formulation of your central hypothesis, the relevant publications should be cited.

Rationale. Next, expand the bullet that summarizes your rationale. 'Label' this component so that it is readily recognizable, e.g., 'The rationale that underlies the proposed research is that ...' Remember that the litmus test is to ask yourself, 'Does this tell the reviewer what will become possible after I have completed the research that is not possible now?' It should convey that you will be able to take the next vertical step in the field that is currently blocked by existence of the gap/need.

Specific Aims 'Paragraph'

Begin paragraph three with a sentence something like, 'We plan to objectively test our central hypothesis and, thereby, attain the objective of this application by pursuing the following specific aims:' Next, expand the bullets for your specific aims and the working hypothesis for each. After doing so, make certain that each clearly links back to a part of your central hypothesis. If you find that doesn't link back, either eliminate it or create a part in the hypothesis that will support its inclusion.

Because the aims are so important, we recommend that you set each off as a separate 'headline,' and that it and its subordinate paragraph be indented one tab. For the same reason, we

recommend that you present them in bolded italics. Nothing in the subordinate paragraphs should be bolded or otherwise highlighted, except for *'working hypothesis.'*

Payoff Paragraph

Expected Outcomes. Continue by expanding the bullets that present your expected outcomes. Label the opening sentence with something like, 'It is anticipated that these aims will yield the following *expected outcomes*. First, _____, Second, _____.' Continue to develop this component using the same approach for each expected outcome.

Generality Regarding Positive Impact. Conclude the fourth paragraph and your *Specific Aims* section by expanding the bullet that you wrote to generalize about positive impact. Make sure that what you write sets up an easy transition into the next section, *Research Strategy*, which will begin with the Significance and Innovation subsections. In those two subsections, you will provide specific detail that validates the general statement about positive impact that you write here. This sentence should also be used to segue into the next section. To accomplish these things, we recommend that you begin and end the sentence with something like, 'These outcomes are expected to have an important *positive impact* because, as will now be detailed in the next section.'

FINALIZING YOUR SPECIFIC AIMS SECTION

As the next step, revise and refine the sentences that you have written until they flow well. Add material, if needed, to link the sentences appropriately and blend them into readable prose. Edit until you have no more than a single page. Convert to a PDF file for upload into the PHS 398 Research Plan component at the site indicated, below.

OMB Number: 0925-0001

PHS 398 Research Plan																												
<p>1. Application Type:</p> <p>From SF 424 (R&R) Cover Page. The response provided on that page, regarding the type of application being submitted, is repeated for your reference, as you attach the appropriate sections of the Research Plan.</p> <p>*Type of Application:</p> <div style="border: 1px solid black; padding: 2px; display: flex; justify-content: space-between;"> <input type="checkbox"/> New <input type="checkbox"/> Resubmission <input type="checkbox"/> Renewal <input type="checkbox"/> Continuation <input type="checkbox"/> Revision </div>																												
<p>2. Research Plan Attachments:</p> <p>Please attach applicable sections of the research plan, below.</p> <table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 60%; padding: 5px;">1. Introduction to Application <small>(for RESUBMISSION or REVISION only)</small></td> <td style="width: 15%; padding: 5px;"><input type="text"/></td> <td style="width: 10%; padding: 5px;"><input type="button" value="Add Attachment"/></td> <td style="width: 15%; padding: 5px;"><input type="button" value="Delete Attachment"/></td> <td style="width: 10%; padding: 5px;"><input type="button" value="View Attachment"/></td> </tr> <tr> <td style="padding: 5px;">2. Specific Aims</td> <td style="padding: 5px;"><input type="text"/></td> <td style="padding: 5px;"><input type="button" value="Add Attachment"/></td> <td style="padding: 5px;"><input type="button" value="Delete Attachment"/></td> <td style="padding: 5px;"><input type="button" value="View Attachment"/></td> </tr> <tr> <td style="padding: 5px;">3. *Research Strategy</td> <td style="padding: 5px;"><input type="text"/></td> <td style="padding: 5px;"><input type="button" value="Add Attachment"/></td> <td style="padding: 5px;"><input type="button" value="Delete Attachment"/></td> <td style="padding: 5px;"><input type="button" value="View Attachment"/></td> </tr> <tr> <td style="padding: 5px;">4. Inclusion Enrollment Report</td> <td style="padding: 5px;"><input type="text"/></td> <td style="padding: 5px;"><input type="button" value="Add Attachment"/></td> <td style="padding: 5px;"><input type="button" value="Delete Attachment"/></td> <td style="padding: 5px;"><input type="button" value="View Attachment"/></td> </tr> <tr> <td style="padding: 5px;">5. Progress Report Publication List</td> <td style="padding: 5px;"><input type="text"/></td> <td style="padding: 5px;"><input type="button" value="Add Attachment"/></td> <td style="padding: 5px;"><input type="button" value="Delete Attachment"/></td> <td style="padding: 5px;"><input type="button" value="View Attachment"/></td> </tr> </table>				1. Introduction to Application <small>(for RESUBMISSION or REVISION only)</small>	<input type="text"/>	<input type="button" value="Add Attachment"/>	<input type="button" value="Delete Attachment"/>	<input type="button" value="View Attachment"/>	2. Specific Aims	<input type="text"/>	<input type="button" value="Add Attachment"/>	<input type="button" value="Delete Attachment"/>	<input type="button" value="View Attachment"/>	3. *Research Strategy	<input type="text"/>	<input type="button" value="Add Attachment"/>	<input type="button" value="Delete Attachment"/>	<input type="button" value="View Attachment"/>	4. Inclusion Enrollment Report	<input type="text"/>	<input type="button" value="Add Attachment"/>	<input type="button" value="Delete Attachment"/>	<input type="button" value="View Attachment"/>	5. Progress Report Publication List	<input type="text"/>	<input type="button" value="Add Attachment"/>	<input type="button" value="Delete Attachment"/>	<input type="button" value="View Attachment"/>
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EXAMPLE OF A HYPOTHESIS-DRIVEN *SPECIFIC AIMS* SECTION

Interferon gamma (IFN- γ) is central to the maintenance of homeostasis, as well as to host defense against a variety of pathogenic microorganisms and tumor cells. In addition, it can have an active role in the pathogenesis of a number of diseases. IFN- γ mediates all of these effects through a single binding protein (the α subunit of the IFN- γ -receptor complex), which is present on the surfaces of all normal nucleated cell types (Granger & Coe, 1994). While it is known that the binding protein initiates signal transduction (Yu, 2000), and it is understood mechanistically how it does so (Griffin *et al.*, 2004; Campbell, 2008), what is not clear is how this critically important protein is produced. Lack of such knowledge is an important problem, because, without it, acquiring the ability to modulate the number of receptors on cells pharmacologically is highly unlikely.

Our *long-term goal* is to understand how the receptor for IFN- γ can be manipulated for preventive and therapeutic purposes. The *objective here*, which is our next step in pursuit of that goal, is to determine how production of the receptor's α subunit is regulated transcriptionally. Our *central hypothesis* is that both constitutive and stimulated regulation are required through different sets of *cis*-acting response elements in the gene's promoter. Our hypothesis has been formulated on the basis of our own preliminary data produced using the promoter that we recently cloned (Galaway *et al.*, 2008; see Justification and Feasibility sub-subsection under *Research Strategy-Approach*). In addition, the work of Adams & Seagram (2008) is supportive of the hypothesis. The *rationale* for the proposed research is that, once it is known how transcription of the α chain's gene is regulated, production of the subunit can likely be manipulated either up or down pharmacologically, resulting in new and innovative approaches to the prevention and treatment of a variety of diseases.

We plan to test our central hypothesis and, thereby, accomplish the objective of this application by pursuing the following two *specific aims*:

1. *Identify the DNA response elements that regulate constitutive transcription of the subunit's gene.*

Based on the preliminary data referred to above, our *working hypothesis* is that one or more Sp1 sites are critical to the regulation of constitutive transcription.

2. *Determine how stimulated transcription is up-regulated by different stimuli.*

We *postulate*, again on the basis of our preliminary data, that cyclic AMP response elements (e.g., CRE and AP-2) regulate stimulated transcription of the subunit's gene, regardless of how stimulated transcription is activated.

With respect to *expected outcomes*, the work proposed in aims 1 and 2 is expected to identify the full complement of response elements and the cognate transcription factors that are responsible for constitutive and stimulated transcription of the subunit's gene. Such results are expected to have an important *positive impact*, because the identified components are highly likely to provide new targets for preventive and therapeutic interventions in addition to fundamentally advancing the fields of receptor biology and immunotherapy, as will now be detailed in the next section.

The 'hybrid' approach would be similar, except that the first paragraph would contain a statement of need and a summary of objective evidence in support of its existence. The central hypothesis would be the applicant's best bet as to how to meet the need. Research proposals driven purely by need rarely succeed at NIH, which is why we do not recommend them for that purpose. Need-driven proposals to NIH are usually for things like equipment.

DEVELOPMENTAL STEPS FOR CHAPTER EIGHT:

1. Set up the page for the *Specific Aims* section to maximize space, with two exceptions: (i) open a line after each paragraph and use 1-inch margins, left and right, if at all possible.
2. Expand the bullets for your *Specific Aims* section into complete sentences.
3. 'Label' them in such a way that reviewers will know precisely why the related information has been included.
4. Cite only key references in this section.
5. Highlight key words using either underlined italics (Arial or Helvetica typefaces) or italics alone (Georgia).
6. Avoid the use of Palatino Linotype because of the extra space it requires.
7. Present the ten components that make up the *Specific Aims* section in four separate paragraphs.
8. Make your specific aims and the related subordinate paragraphs stand out by indenting them 1 tab and presenting the aims, themselves, in bolded italics.
9. Edit and refine the section until it reads well and occupies no more than 1 page.
10. Convert the *Specific Aims* section into a PDF file.
11. Upload the *Specific Aims* section into the PHS 398 Research Plan component.