GWSW

Grant Writers' Seminars and Workshops

THE GRANT APPLICATION WRITER'S WORKBOOK

STEPHEN W. RUSSELL
AND
DAVID C. MORRISON

National Science Foundation - FastLane Version

GRANT WRITERS' SEMINARS AND WORKSHOPS, LLC

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STEPHEN W. RUSSELL, DVM, Ph.D.

DAVID C. MORRISON, Ph.D.

Queries and comments to: info@grantcentral.com

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OVERVIEW OF PART TWO

Template/Master Plan for Your Proposal

A successful proposal creates advocacy among reviewers for funding it. Our approach to writing a grant application is based on the premise that, to maximize advocacy, reviewers must be converted from persons who have to read your application to those who want to do so. Thus, this part of the *Workbook* will help you to put the conceptual, exciting side of your proposal up front, where it will be used to 'hook' the interest of the reviewers. Our intent is to make them want to read the details, which will be presented in the rest of the Project Description.

The format for the 15-page Project Description is:

1. Overview and Objectives
2. Expected Significance
3. Relation to the Principal Investigator's Longer-Term Goals
4. Background:
    - Review of Relevant Literature
    - Results From Prior NSF Support
    - Preliminary Studies
5. Relation to Other Work In Progress:
    - By the Principal Investigator
    - By Investigators Elsewhere
6. Research Plan:
    - Develop each Specific Aim
        - Introduction
        - Approaches
        - Expected Outcomes
        - Potential Problems and Alternative Approaches
    - Timetable
7. Broader Impacts

Part 2 of this *Workbook* will help you craft the template or master plan for the Project Description (chapters 6, 6-Online, and 7), as well as to maximize the programmatic relevance that it has to the NSF funding opportunity you are targeting (chapter 8).

CHAPTER SIX: Overview & Objectives Section

This part of the Project Description will be a conceptual overview of everything that is important and exciting about your application. It is designed to win the interest of the reviewer and to set up the details that follow.

CHAPTER 6

OVERVIEW AND OBJECTIVES SECTION

For the purposes of this chapter, we will assume that your proposal will be evaluated by a combination of *ad hoc* and panel review, which is the most common approach for standard applications.

> ***TIP:*** *The purpose of the* Overview and Objectives *section is to introduce conceptually what you will detail in later parts of the application. It is intended to 'hook' the reviewer's interest, thereby making him/her want to read the details of how you plan to do what is proposed.*

In our opinions, the *Overview and Objectives* section is the key to writing a first-class NSF proposal. It is our conviction that the rest of the proposal will fall naturally into place if this section works well. It must engender enthusiasm and advocacy among reviewers. The *Overview and Objectives* section must be something that can be read and understood by reviewers easily and quickly – even while someone (at the review-panel meeting) is talking to them at the same time. Even if your application is reviewed entirely *ad hoc*, this section is important because, as the title of the section implies, it is the overview for – the introduction to – the rest of your Project Description. The flow of logic in this section must be absolutely compelling, such that it leads reviewers seamlessly through what is presented – without them knowing that they are being led.

> ***TIP:*** *Setting up appropriate linkages between the individual components that constitute the* Overview and Objectives *section is the key to establishing a linear progression of logic that will lead reviewers to a position of advocacy.*

The *Overview and Objectives* section in competitive applications is characterized by a linear progression of logic. Each component that we recommend as a part of this section must be linked logically to what comes before it and what comes after it. If a reviewer has to stop and think about how one component relates to another, you will have lost his/her concentration and will have made it unnecessarily difficult for him/her to grasp what you want to convey. Most writers of grant applications fail to develop the appropriate linkages between the components of this section, a mistake that is compounded by inclusion of too much explanatory detail. To avoid the latter trap, think of this section as an 'executive summary' of the application – everything that is important and exciting about your application at a conceptual level. The details will be presented in later parts of the Project Description. Citations of the literature should be included in this section, but only for the most important, linchpin publications.

APPROACH TO WRITING THIS SECTION

There are three general approaches to writing your proposal: (1) hypothesis-driven; (2) need-driven; and (3) a hybrid of the two.

HYPOTHESIS-DRIVEN APPLICATIONS

As will be detailed later, a well-written hypothesis serves to focus the research that is proposed. Thus, in our opinions, it is usually the best approach to use, because it helps avoid criticism that what is proposed is an 'unfocused fishing expedition.' When should an application not be hypothesis-driven? When it would be contrived to do so. For example, if you were requesting funds to build a building, it would be impossible to create a non-contrived hypothesis for such an application. You would be seeking the funds because you need the building. Therefore, the application would be driven by a strong statement of need. Similarly, you would not use a hypothesis, even if you could, if it would put your proposal outside the norm for your field.

NEED-DRIVEN APPLICATIONS

In addition to the bricks-and-mortar example, above, you would most likely use a statement of need to drive an application that proposes the development of methodology or technology. It is also the best approach in some kinds of applications that are written to fund engineering, social or behavioral sciences research. Increasingly, however, research in these areas is being driven by hypothesis. If you are unsure of whether your proposal should be need- or hypothesis-driven, seek the advice of colleagues who are experienced and successful proposal writers in the field. Another source of advice – perhaps the most authoritative advice – is the Program Officer who oversees the area that you are targeting at NSF. S/he is intimately familiar with what works and what doesn't in that program's review process.

'HYBRID' PROPOSALS

In many instances an application can be driven by either a hypothesis or a statement of need. Rather than choosing between them, an alternative and often very powerful approach is to make the proposal a 'hybrid' of the two. Using this approach, the *Overview and Objectives* section opens with a strong statement of need, after which the application switches to the hypothesis-driven approach. Greater detail regarding this alternative will be provided in later parts of this chapter.

UNDERSTANDING THE PURPOSE OF EACH PARAGRAPH AND COMPONENT OF THIS SECTION

Understanding the purpose of each component is essential to creating the linkages that will assure development of the linear progression of logic that is so important to the success of this section.

> *The purpose of the first, introductory paragraph is to assure that the reviewer: (i) knows that the research problem is program-relevant to NSF; (ii) is informed with respect to what is current knowledge in the field; (iii) understands precisely what the subject (gap in the knowledge base or unmet need) of your proposal is; and (iv) understands why that deficiency represents an important problem that needs to be resolved.*

Introductory Paragraph

Opening Sentence. This should be a real 'grabber.' Its purpose is to immediately capture the attention of your reviewers and highlight the program-relevant, fundamentally important area that your application will address.

Current Knowledge. Not everyone at the review panel table will be an expert on the subject you are proposing. Accordingly, the purpose of this component is to inform all reviewers at the meeting with respect to what is currently known, thereby facilitating their ability to grasp the importance of the research you will propose. In essence, you are setting up presentation of the gap in the knowledge base / unmet need that will be the subject of your application.

Gap in the Knowledge Base / Unmet Need. You can offer either a gap in the current base of knowledge or an unmet need. The purpose of either approach – gap or need – is to define the subject of your proposal. The sentence must be simple, direct and must link back to the 'current knowledge' component as the deficiency that logically must be addressed next in order to advance the field vertically. As you will see, it is a very important sentence because all of the logic downstream will evolve from it.

Gap / Unmet Need as an Important Problem. The purpose of this component is to assure that reviewers grasp that continued existence of the gap / unmet need represents an important, fundamental problem.

'What- Why-Who' Paragraph

> *The purpose of the second, 'what-why-who' paragraph is to introduce reviewers broadly to what will be proposed and to convince them that you and your colleagues have a competitive advantage over equally qualified investigators elsewhere.*

Long-Term Goal. The purpose of this statement is to define for reviewers the continuum of research that you are pursuing. The gap / unmet need delineated in the first paragraph must be encompassed by the continuum of research that your long-term goal defines.

Objective of this Application. The purpose of this component is to define what will be accomplished by *this* application. This objective must link back to the gap in the knowledge base / unmet need that you delineated in the first paragraph, because the objective of any application must be to fill the gap / meet the need that is offered there. The objective must also link to your long-term goal: it must be seen as the next logical step along the continuum of research that is projected by your long-term goal statement.

Central Hypothesis and How Formulated. The purpose of the central hypothesis is to focus the research that is being proposed. That is why it is referred to as a 'directional' hypothesis; it gives 'direction' to the proposed research. It must logically flow from the objective, because the hypothesis is what must be tested to attain the objective. That is the linkage which must exist between them. It must convey your 'best bet' as to what explains the phenomenon you will be investigating. The 'how formulated' sentence that follows the statement of your central hypothesis should project that your own preliminary data are the basis for the central hypothesis.

Rationale. The purpose of this component is to convey why you want to do the research. Cleverly written, that can be exciting. In most cases, it will be because you are seeking new knowledge that will allow you to do something that you can't do now. The rationale must link

back to the problem that is described at the end of the first paragraph because what will become possible after the research is completed is the vertical step in your field that is being blocked by continued existence of the gap in the knowledge base / unmet need.

Well Prepared. The purpose of this component is to tell reviewers why you and your colleagues (if any) have a competitive advantage over equally qualified investigators elsewhere, i.e., what distinguishes you from them.

Specific Aims Paragraph

> *The purpose of this paragraph is to present the specifics of what you propose.*

Specific Aims. The purpose of your specific aims is either to test the parts of your central hypothesis or, if you are writing a purely need-driven application, to convey the tasks that will be undertaken in order to meet the need. With respect to linkage, your aims must grow out of, and be completely concordant with either your central hypothesis or, if yours is a need-driven proposal, the objective.

Payoff Paragraph

> *The purpose of the 'payoff' paragraph, as its name implies, is to tell reviewers what they can expect to get from their investment if they decide to fund your proposal. It is an especially important paragraph with respect to developing advocacy for funding your grant application.*

Creativity, Originality and/or Transformative. The purpose of this component is to call attention to why the proposed research is apart from what is being done elsewhere. This is one of five considerations that are listed under the major review criterion, Intellectual Merit.

Expected Outcomes. The purpose of Expected Outcomes is to tell reviewers what each of your aims is expected to produce and how those products collectively attain the overall objective of the grant application.

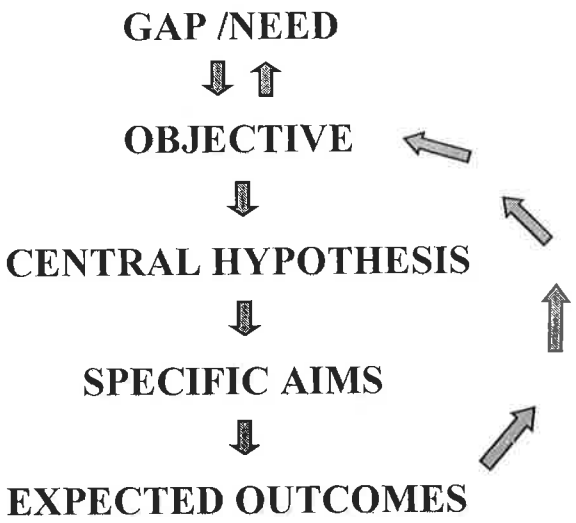
Generality Regarding Positive Impact. The purpose of this final sentence in the *Overview and Objectives* section is to point out that the expected outcomes will have positive impact on the field because they will collectively attain the overall objective of the application and, thereby, advance your field vertically. The statement should be relatively general, i.e., not contain a lot of detail that would set up redundancy with the next, *Expected Significance*, section. Thus, this last sentence should be designed to provide a transition or segue from the *Overview and Objectives* section into *Expected Significance*.

Now that you know the purpose of each of the components and how they should be linked, you are ready to develop the first draft of your *Overview and Objectives* section. We recommend that you do so by starting with a bullet outline. Accordingly, download the form at http://www.grantcentral.com/downloads-NSF.html. Follow the directions on it to develop and refine the bullet outline for this section.

EXPANSION OF YOUR BULLET OUTLINE INTO SENTENCES.

At this point, your bullet outline should be fully developed and refined. You should be satisfied that all of its elements relate to each other logically and well. The linkages should relate in such a way that they set up a linear flow of logic that is comparable to the one that is depicted in the figure, below, for either a hypothesis-driven or hybrid application. For a purely need-driven application the only change would be removal of the "central hypothesis" line from the figure.

LINEAR PROGRESSION OF LOGIC FOR A STRONG OVERVIEW & OBJECTIVES SECTION



Remember that we called attention earlier to how important phrasing of the gap in the knowledge base / statement of need is. Now you can see why in the figure, above: It literally sets up everything downstream with respect to the flow of logic.

The purpose of the remainder of this chapter is to help you expand the bullet outline you have created in your computer into the final version of your *Specific Aims* section. First, however, we want to introduce you to a very important concept.

> ***Tip:*** As you write, *'label' each component in such a way that there can be no mistake as to why you have included the information. You should not allow reviewers to interpret the meaning of anything in your grant application; you should tell them what you want them to know.*

Accomplished proposal writers walk a very fine line. The primary reviewer of your application will usually be the person on the panel who is most qualified to review the subject that you are presenting. If s/he is not an expert, s/he will be very close to being one. Many others on the panel will be far less qualified, because their expertise is in other areas for which the panel is responsible. You must get the latter, non-expert individuals up to speed with respect to the importance of what you are presenting. While doing so you cannot be perceived by your primary reviewer as either pedantic or patronizing / condescending. The strategy that we have developed, which serves both audiences while offending neither, is to 'label' each component in the section in such a way that there can be no mistake as to why it has been included. As will be

seen in the paragraphs below, that is accomplished either through the judicial use of highlighted (italicized) words or by phrasing the beginning of relevant sentences in such a way that the reviewer is 'told' what its purpose is.

First Paragraph

Opening Sentence:

Expand the bullet that you wrote as an opener into a complete sentence. Make sure that it is arresting and, as such, will immediately command the reviewer's attention. Be sure to use words that relate to what is being sought by the program description / announcement or solicitation to which you are responding.

Current Knowledge:

Working from the bullets that list the knowns in your field, create one-to-four complete sentences that succinctly describe what is currently known in your subject area. The progression of sentences should lead the reviewer from the oldest known fact that is relevant to the subject of your proposal to what is currently the edge of the field. 'Label' the first sentence in the series with something like, 'It is well known that ...'

Gap in the Knowledge Base / Unmet Need:

Create a sentence from the related bullet(s) that clearly and distinctly sets out what the subject of your grant application will be – the gap or unmet need that will be filled / met by the research you will propose. If you are using a gap in the knowledge base to drive your application, you will write a single sentence here. Open the sentence with something like, 'What is not known is ...' If you are writing a need-driven application, open with something like, 'Thus, there is an *urgent need* for ...' Note that "*urgent need*" is highlighted in italics. Use of such highlighting to call attention to things that you know reviewers will want to find is reviewer friendly and, therefore, good grantsmanship. The key is to highlight *subtly*, i.e., no bolding, underlining or changing of font. To us, the least obtrusive way to call attention to parts of your proposal is to present key words related to them in italics.

If you are offering an unmet need as the focal point of your proposal, you should have written bullets that summarize objective evidence that support existence of the need. Expand these into one or more sentences that complement and support the preceding statement of need.

Gap / Unmet Need as an Important Problem:

You should end the first paragraph by 'telling' the reviewer why the gap / unmet need represents an important problem. We recommend that you 'label' this last sentence in the paragraph with something like, 'Continued existence of this need is an important problem, because ...' or 'Lack of such knowledge is an important problem, because ...' The sentence should be completed by describing the vertical step that is being blocked – which is the problem.

The entire first paragraph should be no longer than one-third to one-half page.

Second Paragraph

Long-Term Goal:

Expansion of this bullet should create a sentence that conveys the continuum of research that you are pursuing long-term. We recommend that you highlight the words '*long-term goal*' in italics. Make sure that what you write is relevant to the program you are targeting.

Objective of This Application:

Now, expand the bullet you wrote to convey what the objective of this application is. Write a complete sentence similar to this example: 'The *objective of this particular application,* which is the next step toward attainment of our long-term goal, is to ...' The phrase, 'which is the next step toward attainment of our long-term goal' (or something similar to it) helps to link this component as a step along the continuum of research that is projected by the long-term goal sentence. Note how italics are used to highlight. Make certain that this sentence links back to the gap / unmet need that is presented in the first paragraph, because as noted earlier the objective of any application is to fill the gap / meet the need.

Central Hypothesis:

Next comes your central hypothesis and how it was formulated. Make sure that it is your 'best bet' as to how the objective can be attained. Thus, if your objective is 'to determine the mechanism of ...,' your central hypothesis must be your 'best bet' as to what that mechanism is. If your objective is to create an intervention that will ..., then your central hypothesis must be your 'best bet' as to what the intervention should be / consist of. Highlight the words, "*central hypothesis*," in italics. If possible, assure that it is written to have readily identifiable parts that will set up related aims (see *Specific Aims*, below).

Follow your central hypothesis by expanding the bullet that summarizes how your hypothesis was formulated, i.e., why it represents the 'best bet' out of all alternatives. For example, 'We have formulated this hypothesis based on preliminary findings (see *Preliminary Studies*), which suggest that ...' Create a comparable sentence that will complement and support your central hypothesis.

> ***TIP:*** *Your long-term goal, objective, and central hypothesis should be juxtaposed, thereby assuring that the flow of logic, one into the next, is seamless. Avoid the trap of interposing explanatory sentences. That detail will be provided by the rest of your application and, at the review-panel meeting, by the oral presentations of your assigned reviewers.*

Rationale:

Next, expand the bullet that summarizes your rationale. Highlight *rationale* in italics. Once the sentence is written, apply the litmus test described earlier by asking yourself, 'Does this tell the reviewer what will become possible after I have completed the research that is not possible now?' Also, make sure that your rationale links back to how the gap / unmet need was described as a problem at the end of the first paragraph – without being repetitious of that earlier sentence.

Well Prepared – Physical & Intellectual Resources:

Next, based on the bullets you wrote earlier, write a complete sentence or two that summarize why you and your colleagues have the competitive edge in this area of research. In most cases, you will underscore the constellation of your research team's strengths as distinguishing, rather than one single point. Without being redundant, call attention again to your supporting preliminary data. Emphasize the conceptual and downplay specifics. You can allude to the latter by referring to the sections in which the details will be presented (see example, below). 'Label' the first sentence to specifically convey that you are well prepared. *Regardless of what you choose to write, you must be subtle.* The last thing that you want to do is inadvertently convey that you are overly impressed with your own credentials / accomplishments. An acceptable 'well prepared' component might read something like, 'In addition to our supportive preliminary data, we are particularly well prepared to undertake the proposed research because the assembled multidisciplinary research team has the range and depth of expertise needed to address the selected problem definitively (see Biographical Sketches). Its members have been working and publishing together for over five years (refs) and have jointly developed the model that will be employed. In addition, we will be conducting the research in an environment that contains numerous other investigators who are pursuing research that is complementary to what is proposed here (see Other Resources in the *Facilities, Equipment and Other Resources* section). Because of our complementary expertise, history of collaboration and shared resources, the setting is conducive to successful completion of the proposed investigations.' Now, write your comparable sentences.

At this point – the end of the second paragraph – you should have written no more than two-thirds of a page.

Third Paragraph

Tip: *The gap, objective, central hypothesis, and specific aims should create a <u>focusing progression</u>, with the greatest specificity about what will be done projected by the Specific Aims.*

Specific Aims:

Begin paragraph three with a sentence something like, 'We plan to test our central hypothesis and, by doing so, accomplish the overall objective of this application by pursuing the following *specific aims*:' Note that the words, "*specific aims*" are italicized for emphasis. We recommend that the aims, themselves, should be presented in bolded italics as a numbered series that is indented from the left margin. Make certain that each aim you write for a hypothesis-driven or hybrid application clearly relates to a part of the central hypothesis. Each aim should be accompanied by a subordinate paragraph that provides focus to that part of the research. In a hypothesis-driven or hybrid application the only words that should be highlighted in the subordinate paragraph are '*working hypothesis*." For example, 'The *working hypothesis* for this aim, based on preliminary data that will be presented later (*Preliminary Studies*) is that ...' The aim should be broad and open-ended, with focus provided by the working hypothesis.

For a purely need-driven application, the aims should be the tasks that must be undertaken to meet the need. They should be presented in the order that they will be undertaken. Unlike hypothesis-driven or hybrid applications, the aims for a purely need-driven proposal can be descriptive. The subordinate paragraphs should briefly summarize the approaches that will be used to accomplish the tasks.

> *The third paragraph, including the aims and related subordinate paragraphs, should ideally fit on the first page of the* Overview & Objectives *section. At most, it should not extend much beyond the top of the second page.*

Fourth Paragraph

Creativity, Originality and/or Transformative:

Expand the bullets that lay claim to creativity and originality as the opening to the fourth paragraph. Don't be shy. If you have such a claim, directly state it in a 'labeled' sentence – something like: 'The proposed research is *creative and original*, because ...' Note that the words, "*creative and original*" are highlighted in italics. Your claim may be based on a different approach that you are taking, or the fact that you are challenging entrenched dogma of your field. Alternatively, it may be because you are suggesting a true paradigm shift, in which case you may want to frame the work as 'transformative.' Whatever the reason, reviewers are usually appreciative of knowing why you think that the proposed work is creative, original and/or transformative because of the relatively subjective nature of this review criterion.

Expected Outcomes:

Continue by expanding the bullets that present your expected outcomes. Link the first sentence back to the 'creativity and originality' component by beginning it with something like: 'It is anticipated that this creative, original approach will yield the following *expected outcomes*:' Highlight the words, "*expected outcomes*" in italics.

Generality Regarding Positive Impact:

Conclude the fourth paragraph and your *Overview & Objectives* section with two very important sentences. First, expand the bullet that you wrote to summarize how the expected outcomes collectively attain the overall objective of the proposal. Thus, this component must reflect – link back to – the previously written 'objective' component. Second, follow that sentence with a general comment about how attainment of the objective advances your field vertically and, therefore, will have positive impact on it. Make sure that what you write in this last sentence sets up an easy transition into the next, *Expected Significance,* section. You can do so by ending the last, positive impact, sentence with something like, '..., as will now be detailed in the next section.'

> *The entire* Overview & Objectives *section should be no longer than 1.5 pages, max.*

Finalizing Your Overview & Objectives Section.

At this point you will have your first rough draft of the *Overview & Objectives* section. Revise and refine the sentences until they flow well. Add material, if needed, to link the sentences appropriately and blend them into readable prose. If the compelling flow of logic that you need isn't there, you may have to completely rewrite the components that don't work. It may even be necessary to go back to the bullet-outline stage. Whatever it takes, invest the effort until the section meets the purpose of providing reviewers a compelling overview of what will be presented in detail in the rest of the Project Description. If you have more than 1.5 pages, prune what you have written until you meet that mark. Switching to a smaller font, narrowing the margins, or taking out the spaces between paragraphs to reach the goal of 1.5 pages should not be options.

We recommend that you cite references using author/year (one author = last name, year – e.g., Young, 1998; two authors = both last names, year – e.g., Abelson and Rafferty, 2003; more than two authors = last name of first author, *et al.*, year – e.g., Zaharias *et al.*, 2000). Your reviewers either will be experts on the subject you are offering or they will be close enough that they will recognize citations presented as author/year. This prevents them from having to flip to the *References Cited* section. No matter how intimately familiar a reviewer is with your subject area, s/he will not be able to recognize references that are cited by number (e.g., 24, 36, and 92). Asking reviewers to flip back and forth in the application to appreciate what you have cited to support your proposal is not reviewer friendly. If you are a beginning investigator and first author of most of your papers, another reason for using this approach is that it is a clever way to get across to reviewers that you did the work that is being cited – something that is impossible if numerals are used. You should avoid citing reviews to the greatest extent possible because doing so tells the reviewer nothing about your command of the field's primary literature. Please see additional discussion of how to cite the literature in chapter 11, under the Review of Relevant Literature subsection.

DEVELOPMENTAL STEPS FOR CHAPTER SIX:

1. Decide whether your proposal will be hypothesis-driven, need-driven or a 'hybrid' of the two.
2. Appreciate why it is necessary to strip this section – just this section – of unnecessary detail – to make it a conceptual 'executive summary' of all that is important and exciting about your proposal.
3. Understand the purpose of each of the four paragraphs that are recommended for the *Overview & Objectives* section.
4. Understand the purpose of each of the components that collectively constitute the *Overview & Objectives* section.
5. Understand the linkages that must exist between components of the *Overview & Objectives* section and how these must be used to set up a linear progression of logic that will lead reviewers through this section without them knowing that they are being led.
6. Understand how to avoid redundancy when creating linkages between components.
7. Appreciate why it is reviewer friendly to highlight key words and phrases in italics.
8. Understand how to 'label' sentences in such a way that reviewers will not have to interpret why you have included the information.
9. Create a bullet outline for this section using the online file at http://www.grantcentral.com/downloads-NSF.html.

10. Expand the bullet outline into sentences and the first draft of your *Overview & Objectives* section.
11. Revise and refine your draft until it reads well.
12. Cite references using the 'author, year' approach, rather than by using numerals.
13. Make certain that the entire section is no more than 1.5 pages long.

CHAPTER 10

RESEARCH PLAN: NARRATIVE DESCRIPTION OF WHAT'S TO BE DONE

Providing you have been conscientious in the development of your *Overview & Objectives* section, although the *Research Plan* is the longest section of the Project Description, it will be one of the easiest to write. We recommend that you write it now, even though this section is near the end of the Project Description, for two reasons. First, the *Research Plan* section is primarily an expansion of the *Overview & Objectives* section that you have just written. By writing it now you can capitalize on the momentum that you will have developed writing that part of the Project Description. Second, writing the *Research Plan* section at this time increases the likelihood that there will be maximal continuity with the *Overview and Objectives* section, which may not be the case if it is written in sequence, later.

GENERAL TIPS ON WRITING THE RESEARCH PLAN SECTION

This section of the Project Description provides a detailed description of what will be done during the requested period of support.

> ***Grant Proposal Guide:*** *"...outline the general plan of work, including the broad design of activities to be undertaken, and, where appropriate, provide a clear description of experimental methods and procedures and plans for preservation, documentation, and sharing of data, samples, physical collections, curriculum materials and other related research and education products."*

You should develop your *Research Plan* using as its core the specific aims that you have already formulated. The approach here will be the same one that pertains generally to your application: get the reviewers 'hooked' with a conceptual overview and then, *and only then*, follow with details. The layout of this section will look something like the following:

Specific Aim #1: Title
- 1.1 Introduction
- 1.2 Research Design:
  - 1.2.1 Study #1 (explanatory heading)
  - 1.2.2 Study #2 (explanatory heading)
  - 1.2.3 Etc.
- 1.3 Expected Outcomes
- 1.4 Potential Problems and Alternative Approaches

Specific Aim #2: Title
- 2.1 Introduction

Continue, using the format shown above for this, and any subsequent, aims.

Timetable

The title of all but the last subsection will be the eye-catching, interest-grabbing aim – copied verbatim from the *Overview & Objectives* section. It will be followed by a brief, conceptual overview of what will be done in an introductory paragraph, after which the details of what will be done will be presented under the Research Design sub-subsection. Expected Outcomes, the sub-subsection that follows Research Design, will briefly summarize anticipated results and pull them together to show the reviewer that they collectively achieve the aim's objective. A concluding paragraph, Potential Problems and Alternative Approaches, will address problems that could arise, as well as your proposed solutions to them (i.e., alternative approaches). As noted shown in the outline on the preceding page, this same format will be used to develop each of your subsequent specific aims. After the activities under each of your aims have been presented, a *Timetable* will be used to temporally relate all of the important activities during the requested period of support.

If any part of your Research Plan (or any of your Broader Impacts activities – see chapter 13) will require evaluation, it is essential that you create an effective and efficient evaluation plan. In most cases, both formative and summative approaches to evaluation should be proposed. If you have never created such a plan nor evaluated activities and research outcomes before, this is not the place to propose what you 'think' is adequate. Seek the advice of colleagues who are experienced in this area. Additionally, consult *The 2002 User-Friendly Handbook for Project Evaluation* (http://www.nsf.gov/pubs/2002/nsf02057/start.htm), which is published by NSF. It is a succinct treatment of the subject that we recommend it highly. Many universities offer evaluation resources – e.g., a fee-for-service group of experienced evaluators who are available to help plan and implement evaluation strategies. Determine whether or not your institution has such a resource. If not, are there individuals in other departments / colleges who would be willing to participate in your project as a consultant? Having a disinterested, outside person perform the evaluation is often a great asset. Such an approach overcomes the 'fox-guarding-the-chicken-coop' problem that can be associated with conducting your own evaluation. Finally, if your Research Plan will include an evaluation component, we strongly recommend that you invite someone who is a skilled evaluator to serve as a member of your Pre-Submission Review Committee (see chapter 19).

Finally, NSF encourages applicants to use metric weights and measures in their applications, as well as in the means that are used to disseminate results.

SPECIFIC TIPS ON WRITING THE RESEARCH PLAN SECTION

With these general points and the format just presented firmly in mind, begin by developing the subsection that will tell reviewers how you intend to accomplish aim #1. We recommend that you consider writing bullets first, which you then convert to text.

Using bolded Italics, write the title of your first aim — the 'headline' for this subsection.

Specific Aim #1: Title (Verbatim Repeat from Your Specific Aims Section)

1.1 Introduction sub-subsection. You should title the first paragraph, 'Introduction.' Your purpose here is to introduce what will follow in such a way that the reviewer will want to read the details. The sub-subheading should be indented and underlined. Continue writing text on the same line, as we have done here. Key words should be highlighted in italics to (e.g., *objective, working hypothesis, justification, approach, expectations, etc.*) to call reviewers' attention to them. This paragraph should be regarded as a conceptual overview of the aim. Its pur-

pose is to 'hook' the interest of the reviewers, so that they will *want* to read the details that follow.

The first sentence of the introductory paragraph should summarize the problem that aim #1 will address. It should be followed by a statement of the aim's overall *objective*, which should be to resolve the problem / question that is highlighted by the first sentence.

Next, if you are doing hypothesis-driven research, you should offer a *working hypothesis* for the aim. When you presented aim #1 in the *Overview & Objectives* section, you offered a working hypothesis in its subordinate paragraph. It should be repeated here, verbatim. You re-present the working hypothesis here, not only to remind the reviewer that the research is hypothesis-driven, but also to provide focus for what will be proposed. If you are proposing research that is driven by a statement of need, simply skip this component and write nothing here.

Next, summarize the *approach(es)* and/or *methods* that will be used to attain the objective.

The work to be proposed under this aim must be seen by reviewers as justified. Why is it necessary to do what is proposed? You should help them make that connection by offering a well-labeled *overall justification* as the next part of the introductory paragraph.

Finally, summarize what the *overall outcome* is expected to be. The outcome must be accomplishment of the aim's objective. However, you must paraphrase this last component in such a way that you are not simply restating the objective – it must come across as fresh.

To produce the first draft of the introductory paragraph for Aim #1, expand the bullets you have written into sentences. Revise and add transition sentences, as needed, to make what you have written read smoothly. When completed, the paragraph should occupy no more than ¼-to-½ page. The last sentence should be used to segue into the next sub-subsection, e.g., 'We propose to achieve this outcome through the studies / activities that are detailed in the next sub-subsection.'

1.2 Research Design sub-subsection. Here, your purpose is to detail the studies / activities that will be undertaken to accomplish specific aim #1. Note that this is where you detail what will be done. Each paragraph should be a conceptual unit, i.e., a related group of experiments designed to address a single point.

Begin by creating a bulleted list of the studies / activities that you plan for this aim. Create informative, interest-attracting titles for them — *headlines* — that can be used to introduce each of your Research Design studies / activities. Arrange the list so that one task / experiment flows logically into the next. Don't offer so many that you will have difficulty providing enough detail in the space that you have available for each of them. Assure to the greatest extent possible that there is not absolute dependence of any of the studies / activities on the expected outcome of an earlier one.

To the greatest extent possible, present each study / activity in a single paragraph. Then, make sure that you order the paragraphs in such a way that they create a compelling progression of logic that serves to lead the reviewer through what is proposed.

Detail is required for each study / activity that you propose, but it shouldn't be mindless detail, i.e., the kind that can be found in either a methods manual or the 'Methods and

Procedures' section of a journal article (see chapter 5 for an expanded discussion of this). What is needed for each study is meaningful detail, e.g., applicable parts of the following list:

Justification of the need for the particular study / activity

Approach to be used

Method(s) required

Critical reagents needed

Key equipment required (describe in the Facilities & Other Resources section)

Numbers of subjects / animals needed, and how these numbers were derived

How results will be interpreted

Statistical analyses to be used

Controls to be performed (VERY important)

Replicates that will be needed

Expected outcomes (VERY important)

Time required to complete the study / activity

Other considerations applicable to this study / activity

Use the approach described above to develop each of your aims in bulleted outline form. Then, expand the bullets for each aim into simple declarative sentences that are free of jargon and nonstandard abbreviations. Assert your confidence in being able to accomplish each study / activity by using a strong presentation format, like 'we expect to' and 'it is our conviction that.' Avoid weak words, i.e., those that unnecessarily plant a seed of doubt in the reviewer's mind regarding your ability to do what is proposed (e.g., 'hope,' 'try,' 'if,' 'might,' etc.). Emphasize the conceptual, because that is what is exciting and likely to attract the interest of the reviewer. Don't make the mistake of including too much detail; the reviewer will want to know what time it is, not how the watch was made. Methods that you have used in published studies don't have to be detailed; simply reference your use of them. Detail only those methods that either are new to you or unpublished ones that were created by you or members of your group. New investigators should generally include more detail – meaningful detail, compared to that which is required of established investigators.

With the preceding points in mind, ask yourself, 'Is there sufficient detail presented that a reviewer will have no question about feasibility of the approach(es) *in my hands*?' Also ask yourself, 'Does routine methodologic detail obscure conceptual aspects of the aim?' In other words, as recommended in chapter 5, read what you have written as though you are your application's reviewer.

If you have methods, procedures, subjects or anything else that is common to two or more aims, consider putting a 'Methods and Procedures' subsection at either the beginning or end of the Research Plan. There are pros and cons related to putting such a subsection first or last. If you put it first, the reviewer has the methodologic detail s/he needs when the subsections related to the aims are reached. The negative side to such placement is that the reviewer has to wade through a lot of methodologic detail before s/he reaches the exciting, conceptual parts. If the Methods and Procedures subsection is placed last, the reviewer doesn't have to do that, which is positive. However, this latter approach can leave the reviewer feeling anxious as s/he reads the preceding aims subsections, because s/he won't have an understanding of exactly how things will be done. Our recommendation, if you include a Methods and Procedures subsection, is that you locate it after all of your aims have been presented, i.e., just before the Timetable. If you do so, to prevent anxiety about lack of methods from developing, include a note in a very prominent text box at the beginning of the Research Plan subsection that informs the reviewer that a Methods and Procedures subsection will be presented later in the section. An approach that cannot be used is inclusion of a Methods and Procedures appendix. All information relevant to the application must be included within it – unless you have obtained a special deviation from this requirement from NSF (see the *Grant Proposal Guide*, page II-19).

1.3 Expected Outcomes sub-subsection. The purpose of this sub-subsection is to summarize the 'return on investment' that reviewers can expect. Under each study / activity you have detailed you will have included one or more expected outcomes. You should not simply list them again here. Instead, you should summarize them here and integrate them with a sentence that assures reviewers that they collectively attain the overall objective for the aim. The overview that you write here can usually be presented in a single paragraph that does not need to be extensive in its length – ¼-to-½ page, at most. To create this paragraph, we recommend that you, first, collect all of the outcomes for aim #1. After you have a good appreciation for how they relate to each other, write bullets of the kind that are suggested below.

- Summarize the first outcome and its importance
- Summarize the second outcome and its importance
- Continue summarizing outcomes and their importance
- Conclude with how the outcomes collectively attain the aim's objective

As the next step, expand these bullets into sentences, which will be the first draft of the Expected Outcomes subsection for the first aim. Repeat this process for each of your aims. Spend the time necessary to refine and optimize these subsections, because they represent another opportunity that you have to create excitement. Be enthusiastic in the way that you write this paragraph. However, at the same time, be realistic and provide appropriate caveats, if they are needed. You must not overstate your expectations to the extent that they (and you) lose credibility.

1.4 Potential Problems and Alternative Approaches sub-subsection. Your purpose here is to anticipate and then eliminate justified concerns of your reviewers. You do so by acknowledging potential problems that you could encounter, but probably won't, accompanied by alternative approaches that you would use to overcome such problems, should they occur. Reviewers will expect you to include such plans because they know as well as you do that no matter how hard one plans and prepares, research can unexpectedly take an entirely unexpected

direction. These are not meant to be big and/or unavoidable problems; those must be dealt with in the Research Design sub-subsection for the related aim. Instead, as noted above, these are meant to be problems that probably won't develop but, just in case they do, you have anticipated them and have the means in place to overcome them.

If you are proposing hypothesis-driven research, *first and foremost among problems that reviewers will expect you to address is the potential invalidity of your aim's working hypothesis*. Think about it: implicit in the fact that you are offering it as a hypothesis must be the potential for invalidity when it is tested objectively. Otherwise, what you are proposing is not a real hypothesis. You can't write this as though the sky were falling, however, or you will inadvertently make the aim appear problematic. What you want to do is honestly acknowledge that this possibility exists while, at the same time, you emphasize that such an outcome is unlikely. You would do so by writing something like: 'Although our preliminary data (see Preliminary Studies) and published studies by others (Wong et al., 2003; Logan, 2004) strongly support the working hypothesis for this aim, there is a remote possibility that it will prove invalid when tested objectively by the approaches described above. In this unlikely event, we would ...' You would go on to offer one or more credible alternative to which you would then turn. If you include this consideration under each of your aims you will convince reviewers that, no matter how your working hypotheses test, you will land on your feet and accomplish the aims' objectives. In other words, they will be impressed that you aren't naïve enough to believe that the outcomes of your hypothesis testing will be as expected – that you have alternative approaches that would 'defuse' that unlikely possibility.

As other examples of the kinds of things that should be considered in this sub-subsection, reviewers will be concerned about the availability of critical reagents: Will they be available and will they perform as expected? Will sufficient subjects be available to reach statistical significance? And will assays be as discriminating as you expect? You need to list equivalent kinds of problems and alternative approaches to them here. Begin with what you would do, should your working hypothesis for the aim prove to be invalid. List other potential problems as separate bullets. Follow each with a second bullet that succinctly states what the solution/alternative approach would be.

- Problem #1: Invalid working hypothesis
  Solution:

- Problem #2:
  Solution:

- Problem #3:
  Solution:

Now, using the bullets that you have just created, write the related paragraph. In doing so, make certain that you have chosen only the most important and plausible problems that might occur, and make sure that the alternative approaches that you have offered are feasible and credible.

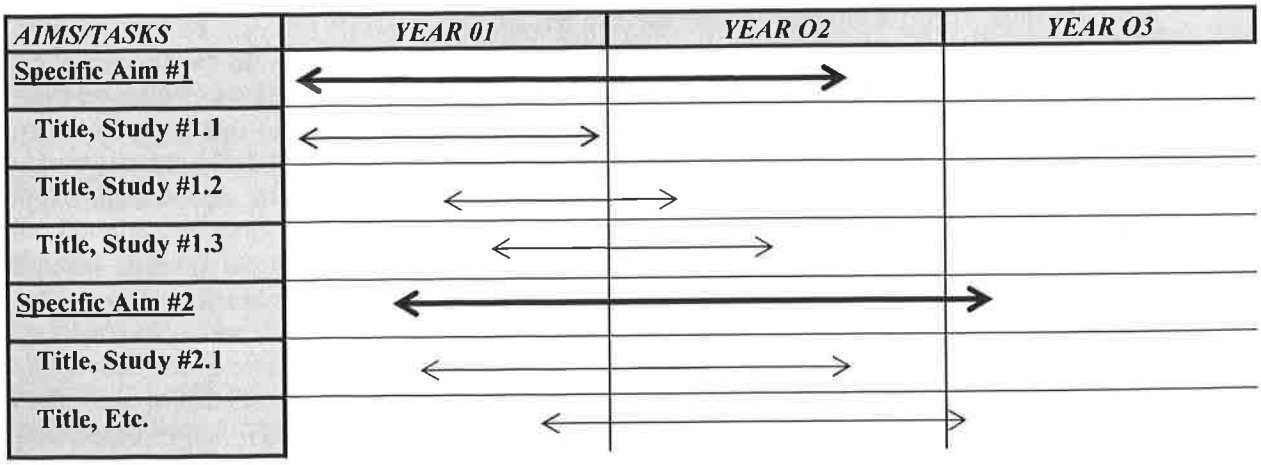
You should not belabor the problems that you identify. Rather, treat them with the brevity that they deserve. For each problem identified, address 1) the nature of the perceived problem; 2) the reason(s) why you don't think that the problem is likely to arise; and 3) what alternative approach(es) you would employ, should the problem be encountered. For example:

"In the studies described above, our working hypothesis is _____. Although the weight of our preliminary data (see *Preliminary Studies*) and complementary supporting evidence that is extant in the literature (Albright et al., 2004; Compton, 2005) strongly argue that our working hypothesis for this aim will test valid, there is a remote possibility that it will not. In that unlikely event, we would turn to _____ as the next most likely explanation for the phenomenon. This is a credible alternative because _____. Another possible problem is the way in which we have proposed to determine whether _____ will result in _____. We expect this new approach to work, because _____. As an unlikely possibility, this new technology may not prove sufficiently sensitive to detect _____ in 5% of the samples. Were this problem to arise, we would employ an alternative approach of _____, which is much more expensive and labor intensive. It has been used successfully by Wolf and her colleagues (1999) and Cantor *et al.* (2006) in similar kinds of studies to those proposed here at sensitivity levels are well above those that will be needed here. Were it necessary to employ this more expensive and time-consuming approach for a small number of samples, it is already available in our laboratory. Etc."

In writing this part of each aim, make sure that you paraphrase enough that the same choice of words and phrasing is not used in subsequent aims. A common mistake is to use exactly the same wording. Making this mistake detracts greatly from what is written because it makes it appear 'canned.' This sub-subsection should be no more than ½-page long.

Timetable.

This important section of the *Research Plan* section is not included by most grant writers. We recommend that you do so. It is important to include one like that which is depicted below, because a well-conceived timetable can give your reviewers perspective about your project that they would otherwise lack. It can't come across as an afterthought; it should be as *detailed* as is necessary to convince your reviewers that you have thoroughly thought through how long you expect that it will take to complete each component of your program. Enter years of support that are requested on the horizontal axis and your specific aims/proposed studies in the left column. The duration of each aim (bolded, double-headed arrows), and the expected duration of the major studies that will be conducted under each aim (non-bolded, double-headed arrows), should be indicated in the timetable.



The titles of studies in the left column should be sufficiently explanatory that the reviewer will understand the specific investigations / activities that will be required to accomplish the aim. If it

would make the timetable more understandable, substitute the titles of specific tasks for the arrows in the table.

This same timetable should be copied and pasted into the Budget Justification as a means of summarizing for reviewers why you are requesting the number of years of support that you are proposing (see chapter 14).

DEVELOPMENTAL STEPS FOR CHAPTER TEN:

1. Make sure that the formatting for your *Research Plan* section is consistent with that which you used to write the *Overview & Objectives* and *Expected Significance* sections.
2. For aim #1, write bullets that reflect the principal components of the 'Introduction' paragraph. In particular, make sure that there is a clear objective stated for the aim.
3. After making the list, expand each bullet into a sentence. Revise / add to the sentences that you have created in order to make a paragraph that reads clearly and smoothly.
4. Create a bulleted list of the studies / activities that will be undertaken under aim #1's Research Design sub-subsection.
5. Develop each of the studies / activities by first creating a bulleted list of specifically what will be done and the outcomes that can be expected.
6. Expand the bullets for each study / activity into sentences that create a single paragraph, if possible. Make sure that only meaningful detail is included.
7. Order the paragraphs to create a compelling flow of logic
8. Make a list of the outcomes that can be expected collectively from aim #1. Summarize them in as few sentences as possible.
9. Write an integrating sentence that tells reviewers how the outcomes collectively accomplish the objective for the aim.
10. Make a bulleted list of unlikely, but potential, problems that could be encountered while pursuing aim #1. If you are doing hypothesis-driven research, begin with the problem of potential invalidity of the working hypothesis for aim #1.
11. Develop a credible alternative approach that will solve each of the problems you have identified.
12. Expand your bullets into sentences that will collectively constitute the Potential Problems & Alternative Approaches paragraph for aim #1.
13. Repeat the process described, above, for each aim after #1.
14. Create a timetable that summarizes for reviewers when the main studies / activities under each aim will take place.
15. Copy and paste the timetable into the Budget Justification as a means of summarizing why you are requesting the years of support that you will propose.

EXAMPLE OF A RESEARCH PLAN:

RESEARCH PLAN

We will detail, below, the three specific aims that will be pursued to characterize induction of the gene that encodes the α subunit of the receptor for human interferon-γ.

Specific Aim #1: Identify DNA segments that regulate stimulated transcription of the human α chain's gene.

1.1 Introduction. Although the promoter for the human α-chain gene has been cloned (Goldwin and Homer, 2000), inferential analysis has failed to reveal the response elements that regulate transcription that is stimulated by either PGE_2 or TNF-α. The *objective* of this aim will be to identify the relevant response elements. Based on our own preliminary data (see *Preliminary Studies*), the *working hypothesis* is that stimulated transcription will be regulated by segments of the promoter that are chronically activated, such as XYZ, in concert with an additional set of stimulus-responsive elements. The *approach* will be to systematically narrow the focus to specific response elements in the promoter that will support regulatory activity when transfected *in vitro*. Principal methods will include primer-directed deletion, bead-assisted transfection, Elbert's optimized gene-induction strategy (Elbert et al., 1999), and *in vivo* footprinting, The *justification* for the approach is that there are too many computer-identified candidate sites to explore each of them by mutational analysis or electrophoretic mobility-shift assay (EMSA). At the conclusion of this specific aim, it is our *expectation* that we will know precisely which segments of promoter DNA regulate stimulated transcription of the gene that codes for the human α chain.

1.2 Research Design. We plan to accomplish the objective of this aim by conducting the following studies:

1.2.1 *Establish the Least Amount of Promoter DNA That Will Support Stimulated Transcription*. The approach will be the same as the one that we previously used in studies of the mouse inducible nitric oxide synthase promoter (Paterno *et al.*, 2003). Briefly, using the restriction map of the *Sau*3A I fragment (see Figure 6), unique restriction sites will be chosen that will allow the DNA to be shortened progressively. Each of the truncated DNA fragments will then be cloned into the GeneLight luciferase vector (pGL2-Basic). Alternatively, the entire 814 bp fragment will be introduced into the vector, after which combinations of uniquely cleaving restriction enzymes will be used to remove specific segments, followed by religation of the plasmid. Each of the resultant constructs (4 pmol of each) will then be transiently transfected by electroporation into human THP-1 cells as we have done before (Edwards *et al.*, 2001). To minimize differences, the cells from multiple electroporations will be pooled to obtain enough cells for constitutive and stimulated studies of the same construct. The cells will then be divided equally among 60 mm-diameter dishes (~1-5 x 10^6/plate) and allowed to recover for 24 hr (which serves to reduce the background levels of luminescence to a minimum). Next, plates will be exposed either to medium alone or medium containing either PGE_2 or TNF-α. For studies of stimulated transcription, dose-response studies will be performed for each stimulus. The promoterless pGL2-Basic vector will serve as the baseline control for constitutive expression in unstimulated cells. The baselines for stimulated transcription studies will be the values obtained with each construct in cells incubated in medium alone, i.e., unstimulated cells. In all experiments, the positive control will be the amount of luminescence produced by the unaltered 814 bp insert. Luminescence produced by induction of the luciferase reporter gene (Enhanced Luciferase Assay, Analytical Luminescence Laboratory, San Diego) will be measured in a lumi-

nometer (Monolight 2010, also from Analytical Luminescence Laboratory; see Facilities & Other Resources section). At the conclusion of these studies we expect to have defined the minimal amount of promoter DNA that will support full expression of the luciferase reporter gene in human THP-1 cells under the conditions of stimulated transcription.

1.2.2 *Characterization of Response Elements Most Likely Involved in Regulating Stimulated Transcription*. The approach here will be footprinting via dimethylsulfate (DMS)-mediated methylation of living cells (either stimulated or unstimulated). *In vivo* footprinting is a powerful technique for directly demonstrating which response elements have bound transcription factor proteins in living cells. We have successfully used this approach in the past in similar kinds of studies (Ancien *et al.,* 2005). This technique minimizes binding artifacts that can occur with *in vitro* approaches because binding of proteins to DNA occurs prior to the time that the cells are harvested and lysed. Briefly, THP-1 cells (2×10^7) will be plated (150 mm-diameter dish) and incubated overnight to allow them to recover from passage. Cultures will then be exposed to either medium alone (for identification of chronically active sites) or to either PGE_2 or TNF-α (identification of stimulus-responsive candidates). Stimulated transcription will be analyzed at the peak effect of each stimulant, as determined in nuclear run-on time-course studies. We have also used this approach before (Campbell *et al.,* 2006). Pilot studies will also be performed to ascertain whether or not there are proteins that bind transiently at earlier times. This will ensure that transcription factors that are involved in the initial activation of the gene, but which do not contribute to prolonged transcription of the gene, will be detected (Hoffstetter, 2006). After an appropriate period of treatment, cultures will be treated for 5 minutes at room temperature with medium containing 0.2% DMS in the continued presence of stimulators. Genomic DNA will then be isolated, treated with piperidine to cleave DNA at methylated G residues, and then subjected to the ligation-mediated PCR amplification procedure of Garrity and Wold (1999). The control for each of these experiments will be the ligation-mediated PCR amplification of *in vitro* methylated, protein-free genomic DNA. This will provide a sequencing ladder of all G residues, to which the *in vivo*-treated samples can be compared. Completion of these studies is expected to yield direct proof in living cells of the response elements that are most likely involved in stimulated transcription.

1.2.3 *Definitive Identification of Response Elements that Regulate Stimulated Transcription*. Continue with description of next study.

1.3 Expected Outcomes. Accomplishment of this aim is expected to yield knowledge of the least amount of promoter DNA that will support transcription, which will allow identification of the most likely candidates for response elements that regulate stimulated transcription. That, in turn, is expected to set the scene for definitive analyses that are expected to confirm which of the candidate response elements are, in fact, actively involved in regulating stimulated transcription of the gene that codes for the α chain of the human IFN-γ receptor, thereby accomplishing the objective of this aim.

1.4 Potential Problems and Alternative Approaches. Although the possibility is considered remote, given the strength of our supporting preliminary data (see *Preliminary Studies*), our working hypothesis for this aim could prove to be invalid when it is tested objectively. Although we do not expect such an outcome, in that unlikely event we would shift our focus to the next most likely regulatory regions, which are the ABC response elements. As noted in the *Preliminary Studies* section, there are suggestions that these could be involved, probably as complementary regulatory regions, but they may, in fact, be the principal regulators. Other potential problems could include: (1) For deletion / transfection studies, the efficiency of transfection could vary sample to sample. To minimize this problem, relative luciferase values will be

normalized against a transfection control. We will use the one that we have used in the past (Omer *et al.*, 1998), i.e., human growth hormone. To do so, the plasmid, pXGH5, which contains the cDNA for human growth hormone, will be co-transfected with each of the luciferase reporter gene constructs. Amounts of human growth factor secreted into the medium will be radioimmunoassayed and relative light units normalized by dividing them by the relevant cpm from the human growth hormone radioimmunoassay. Results will be reported as relative luciferase activity. Should it become apparent that human growth hormone has an unwanted stimulatory effect on THP-1 cells, we are prepared to create a secreted alkaline phosphatase expression vector as an alternative transfection-efficiency control. (2) Although we expect most or all of the functional response elements to be in the 220 bp segment that is located immediately upstream from the coding region, they may not be. In such a case, a possible problem is the fact that there are segments in the flanking DNA that contain too few unique restriction sites for detailed deletional analysis. An alternative approach that will resolve this problem, if it arises, will be to PCR- amplify specific regions to be assayed, after which they will be cloned into the pGL2-Basic vector. To do this we will synthesize an oligonucleotide based on the sequence adjacent to the Sau3A I site located within the coding sequence (the rightward Sau3A I site in Fig. 8). Additional oligonucleotides will be synthesized according to sequences upstream and will define the 5'-most endpoint of the region to be assayed. (3) Should little or no reporter-gene activity be obtained with the 814 bp fragment that we have cloned (an outcome that we consider highly unlikely but possible), larger fragments cloned from our primary 70-100 kb genomic clone will be analyzed. These will include the first intron, as well as sequences upstream of the 814 bp fragment.

Specific Aim #2: ***Identify the DNA response elements responsible for regulation of constitutive transcription of the α chain's gene.***

2.1 Introduction.
2.2 Research Design.
2.3 Expected Outcomes.
2.4 Potential Problems and Alternative Approaches.

Timetable:

TIMETABLE FOR THE RESEARCH PROGRAM

	YEAR 01	YEAR 02	YEAR 03
Specific Aim #1: RESPONSE ELEMENTS: STIMULATED TRANSCRIPTION	Deletion / transfection *In vivo*	tion footprinting	
Specific Aim #2: RESPONSE ELEMENTS: CONSTITUTIVE TRANSCRIPTION	Point	mutational analyses Combinatorial	Mutation EMSA supershifts