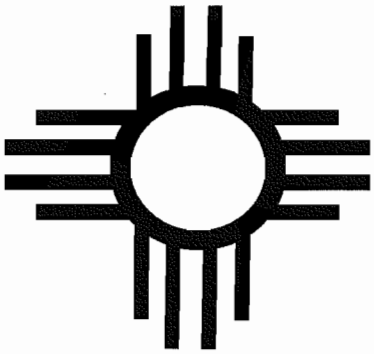

THE GRANT APPLICATION WRITER'S WORKBOOK©

Guide To A Successful Proposal

The National Institutes of Health (and any other Public Health Service agency)

PHS SF424 (R&R) Application Guide (04/2006)

Stephen W. Russell and David C. Morrison
Grant Writers' Seminars and Workshops, LLC
http://www.grantcentral.com
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November, 2006

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PREFACE

The federal government is rapidly moving toward use of the SF424 application format for all requests for most forms of research grant support, regardless of agency. All such applications will be submitted electronically through the Grants.gov Web site. Thus, there will be extensive change in the way that most applicants seek federal research grant support. Such change has already occurred with respect to applications to the National Institutes of Health. This *Workbook*, which is only available through Grant Writers' Seminars and Workshops, LLC (www.grantcentral.com), will help you to prepare a research proposal to the NIH using the *PHS SF424 (R&R) Application Guide* and forms. The *Workbook*, which is based on the July 6, 2006 [Version 2] edition of the instructions, is also applicable to other Public Health Service agencies, such as the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA) and the Agency for Healthcare Research and Quality (AHRQ). While it is true that there has been extensive change in the way that PHS proposals must be written and submitted, the good news is that the changes have been made in such a way that most of the former PHS 398 approach has been preserved.

Detailed instructions for preparing and submitting a PHS proposal are contained in Part I of the *PHS SF424 (R&R) Application Guide*. This *Workbook* is meant to complement, not replace, those instructions (refer to http://grants.nih.gov/grants/funding/424/index.htm for the latest version). By "complement" we mean that we will emphasize the tips and strategies that kept each of us continuously funded by NIH for nearly 30 years. Our intention here is to provide you with those tips and strategies, along with the principles and fundamentals of good proposal writing, none of which can be obtained by reading the instructions.

Many applicants make numerous mistakes in the preparation of their proposals, simply because they don't read and follow the instructions closely enough. Some of those mistakes are of sufficient magnitude (e.g., use of the wrong typeface or font size; exceeding the page limit for the Research Plan) that they can cause a proposal to fail its initial 'validation' review, resulting in it being rejected administratively pending correction of the mistakes. While most mistakes related to not following instructions won't lead to out-and-out rejection of your proposal, it is a fact that they can cumulatively influence a reviewer's opinion of your application negatively. Such mistakes are a clear mark of lack of attention to detail, and what is research about other than attention to detail?

In the theater, often the last encouragement that an actor hears before going on stage is, "Break a leg." We don't know what the equivalent remark is with respect to writing a grant application — "Break a pen," perhaps? Whatever it is, it would translate as, "Best of luck." But, as you'll see, luck doesn't play much of a role in this process — unless, of course, it's the kind that Thomas Jefferson was referring to when he said, "I'm a great believer in luck, and I find the harder I work the more of it I have." We agree, so let's get cracking!

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OVERVIEW: PART ONE

BEFORE YOU BEGIN TO WRITE

In our opinion, most applicants fail in their quest for research funding in large part because they don't do everything possible to position themselves to succeed. Chapters one through seven of this *Workbook* are designed to help you avoid that trap.

Chapter one, "What You Must Know About How and Why NIH Funds Research," will familiarize you with how the National Institutes of Health is organized and will introduce you to the Center for Scientific Review – the part of NIH that receives all applications and refers most of them for review.

Chapter two, "How to Develop an Irresistible Idea for Your Grant Application," will assist you in evolving the centerpiece of your proposal – an idea that will make a significant, vertical difference in your field once it is acted upon.

Chapter three, "How to Find the Appropriate Program and Granting Mechanism for Your Idea," will help you target the most appropriate part of NIH and make certain that you package and present it in the appropriate vehicle.

Chapter four, "Writing for Success, Influence of the NIH Review Process on How You Write, and How to Modify a Submitted Proposal," will familiarize you with selecting and optimizing your presentation to the most appropriate scientific review group for your proposal.

Chapter five, "Response to Prior Review," will help you to avoid the pitfalls that undercut so many resubmitted applications.

And, finally, Chapter six, "Create a Writing Schedule," will help you set up a developmental schedule for your proposal that will allow you to manage all of the competing priorities with which you are faced while, at the same time, you develop the best grant application of which you are capable.

We strongly urge you to read and follow the recommendations that are contained in Part One of this *Workbook*. From years of experience helping investigators prepare NIH grant applications, we can tell you that those who read and follow this first part of the *Workbook* enter the writing phase of the developmental process with a distinct edge over their competitors. We encourage you to be among them.

CHAPTER 1

WHAT YOU MUST KNOW ABOUT HOW AND WHY NIH FUNDS RESEARCH

To be successful, a grant application submitted to the National Institutes of Health must be concordant with its mission. Translated, that means that, by funding your proposal, one of the awarding components that comprise NIH must be convinced that the successful completion of your proposed project will help the Institute to advance its mission. It is important, therefore, that applicants understand NIH's mission and what it is striving to accomplish with its investments in medical and behavioral research.

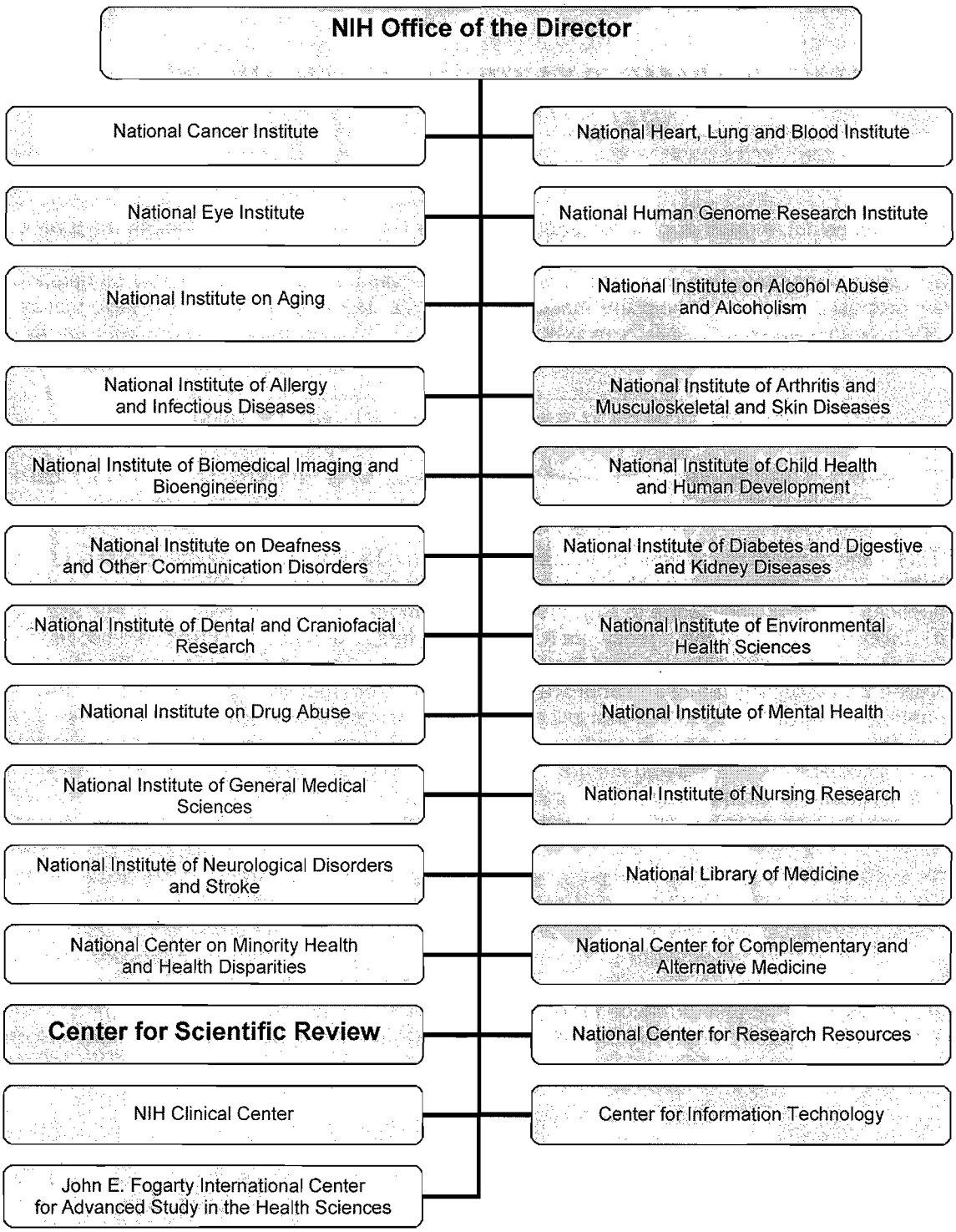
THE MISSION OF THE NATIONAL INSTITUTES OF HEALTH

"An agency of the Department of Health and Human Services, the NIH is the Federal focal point for health research."

"NIH is the steward of medical and behavioral research for the Nation. Its mission is science in pursuit of fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to extend healthy life and reduce the burdens of illness and disability. The goals of the agency are as follows: 1) foster fundamental creative discoveries, innovative research strategies, and their applications as a basis to advance significantly the Nation's capacity to protect and improve health; 2) develop, maintain, and renew scientific human and physical resources that will assure the Nation's capability to prevent disease; 3) expand the knowledge base in medical and associated sciences in order to enhance the Nation's economic well-being and ensure a continued high return on the public investment in research; and 4) exemplify and promote the highest level of scientific integrity, public accountability, and social responsibility in the conduct of science."

"In realizing these goals, the NIH provides leadership and direction to programs designed to improve the health of the Nation by conducting and supporting research: in the causes, diagnosis, prevention, and cure of human diseases; in the processes of human growth and development; in the biological effects of environmental contaminants; in the understanding of mental, addictive and physical disorders; in directing programs for the collection, dissemination, and exchange of information in medicine and health, including the development and support of medical libraries and the training of medical librarians and other health information specialists."

Note that NIH is part of the Executive Branch of our government. Thus, the director is a political appointee of the President. The organizational chart on the next page depicts how NIH is structured


NIH Office of the Director
National Cancer Institute
National Eye Institute
National Institute on Aging
National Institute of Allergy and Infectious Diseases
National Institute of Biomedical Imaging and Bioengineering
National Institute on Deafness and Other Communication Disorders
National Institute of Dental and Craniofacial Research
National Institute on Drug Abuse
National Institute of General Medical Sciences
National Institute of Neurological Disorders and Stroke
National Center on Minority Health and Health Disparities
Center for Scientific Review
NIH Clinical Center
John E. Fogarty International Center for Advanced Study in the Health Sciences
National Heart, Lung and Blood Institute
National Human Genome Research Institute
National Institute on Alcohol Abuse and Alcoholism
National Institute of Arthritis and Musculoskeletal and Skin Diseases
National Institute of Child Health and Human Development
National Institute of Diabetes and Digestive and Kidney Diseases
National Institute of Environmental Health Sciences
National Institute of Mental Health
National Institute of Nursing Research
National Library of Medicine
National Center for Complementary and Alternative Medicine
National Center for Research Resources
Center for Information Technology

THE CENTER FOR SCIENTIFIC REVIEW (CSR)

NIH supports both intramural ('within the walls' of NIH) and extramural ('outside the walls' of NIH) research programs. We, in the extramural community, are the ones who make grant applications to NIH. The Center for Scientific Review (http://www.csr.nih.gov/) is particularly important to extramural applicants, which is why it is highlighted in the preceding organizational chart. As can be seen from the chart, it is independent of the Institutes and other Centers – a so-called 'cross-cutting' organization. CSR is responsible for the receipt and referral of all grant applications submitted to NIH and oversees the peer review of most of them (~70%), regardless of the Institute or Center to which they are assigned. Approximately 90% of CSR's efforts and resources are focused directly on peer review, which is conducted under the auspices of its four scientific review divisions (Molecular and Cellular Mechanisms; Biological Basis of Disease; Physiology and Pathology; and Clinical & Population-Based Studies). The details related to the NIH review process, including more information about CSR, will be provided later, in chapter 4.

THE NIH ROAD MAP

Those in the extramural community who make grant applications to NIH should make every effort to understand how it operates. When Elias A. Zerhouni, M.D. became Director of NIH, he used the opinions and recommendations of over 300 leading figures in academe, industry, government and the public sector to create the NIH Roadmap. It is an ongoing effort to identify and organize NIH's priorities, as well as to increase the efficiency with which it supports biomedical research. By visiting the Roadmap Web site (http://nihroadmap.nih.gov), you can familiarize yourself with the current initiatives, which started in FY 2004. At this writing, they are organized under three main headings: 1) New Pathways to Discovery; 2) Research Teams of the Future; and 3) Re-Engineering the Clinical Enterprise. To not understand the Roadmap and its areas of emphasis is to not understand the current priorities of NIH.

KINDS OF GRANT APPLICATIONS FUNDED BY NIH

The SF424 (R&R) Application Guide describes "Funding Opportunities" (section 2.4, page I-10) that are available to members of the extramural community. There are three generic kinds of proposals: 1) those that are self-initiated; 2) ones that are submitted in response to a Program Announcement (PA); and 3) those that are responses to a Request for Applications (RFA). NIH also solicits contract research, which is in a separate category. Contract opportunities are announced through Requests for Proposal (RFP).

Investigator-initiated proposals are just that; there is no solicitation of your application. You have an idea that is programmatically relevant to NIH, prepare an application, and submit it on or before one of the deadlines that are listed in section 2.12, Submission, Review and Award Cycles, of the SF424 Application Guide (pages I-21-22).

Program Announcements (PA or PAR; the former are reviewed by standing review panels through the Center for Scientific Review and the latter PAs that are reviewed by an Institute) are used for several purposes. In addition to soliciting research in a specific area, they are also used to provide the extramural community with a reminder that a given area is of continuing interest to NIH, as well as to modify an activity or granting mechanism. If you are proposing research in response to a Program Announcement, you must make that known in the 'optional'

PHS 398 Cover Letter Component that complements the SF424 R&R forms. Although the instructions ask that you include only the title of the PA, we recommend that you include both the title and number. In most cases, proposals in response to PAs are submitted on the same deadlines that apply to self-initiated applications, they are reviewed by the same Scientific Review Groups (study section or special-emphasis panel), and they compete for the same pool of dollars for which self-initiated applications compete. The only time that response to a PA makes a difference is when the applicant comes close to the funding line but doesn't quite make it. In such a circumstance, because of the area's programmatic relevance, program officials have the option of reaching across the line to fund the proposal out of priority order.

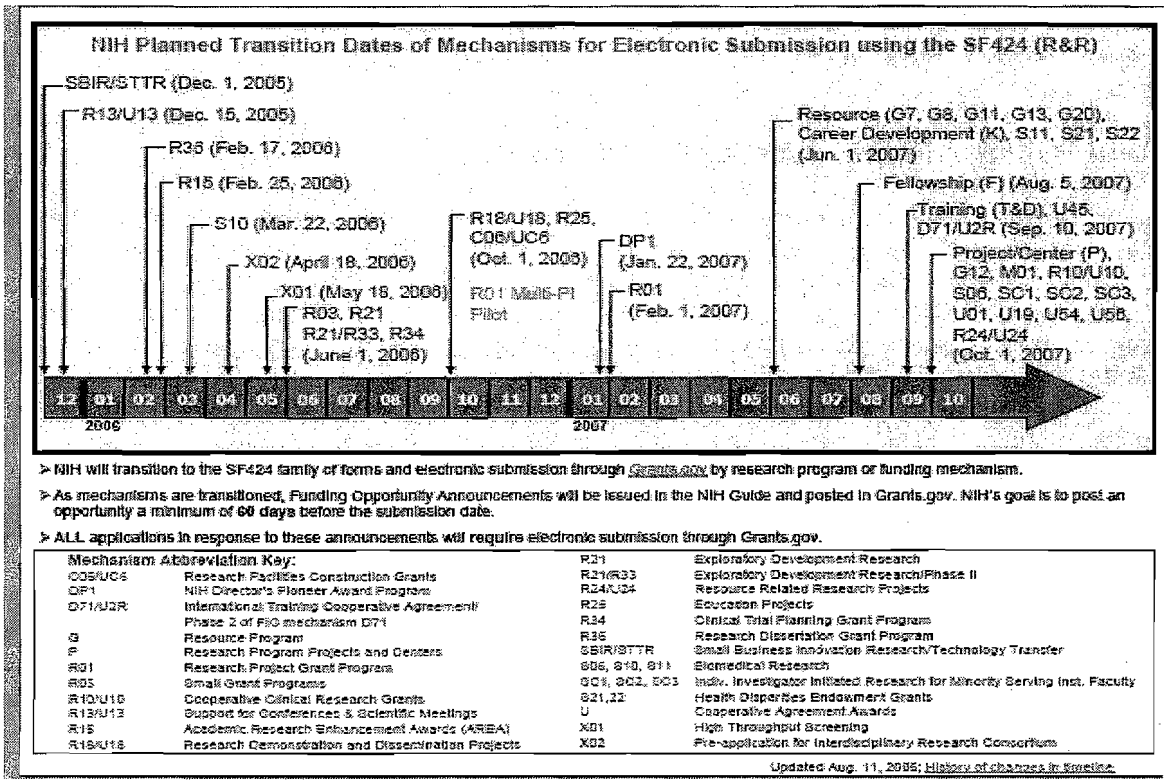
Circumstances surrounding a *Request for Applications* are quite different. Research of a very specific kind is solicited. There is a single, specified deadline or set of deadlines, which must be met. The review panel is a specially convened Scientific Review Group, not a standing study section. Set-aside funds are used to fund successful applications, the estimated number of which is stipulated in the RFA. In other words, applicants responding to a RFA are competing for a different pool of money than those who have written self-initiated applications or responses to a Program Announcement. If you have the capacity to provide the specific kind of research that is being sought, writing an application in response to an RFA should be viewed as a great opportunity to get funded. On the other hand, if you have a 'square peg' and contrive to make it look like it will fit in the RFA's 'round hole,' you are almost surely wasting your time: Such applications are usually recognized as contrived and, therefore, rarely succeed.

Program Announcements and Requests for Applications are published in three places: 1) Grants.gov "Find Grant Opportunities" (http://www.grants.gov/Find); 2) the *NIH Guide for Grants and Contracts* (http://grants.nih.gov/grants/guide/index.html); and 3) the *Federal Register* (http://www.gpoaccess.gov/fr/index.html). You can sign up for the Grants.gov e-mail alert service at http://www.grants.gov/search/email.do. You can subscribe to a listserve for the *NIH Guide for Grants and Contracts* by accessing http://grants.nih.gov/grants/guide/listserv.htm. After subscribing, each Friday you will receive a list of all Notices, Program Announcements and Requests for Applications issued during the preceding week. To receive the Table of Contents for the Federal Register, go to the Government Printing Office's listserv at: http:listserv.access.gpo.gov.

GRANTS.GOV AND ELECTRONIC RESEARCH ADMINISTRATION (eRA)

During 2006, all grant applications will be phased into electronic submission through Grants.gov. Each applicant organization must register with Grants.gov and designate an Authorized Organizational Representative (also know as the Signing Official) – the only person who can sign and submit applications for the applicant organization. Principal Investigators / Program Directors do not have to register individually, but cannot submit an application unless their academic institution has registered and designated an AOR. Each granting mechanism had / will have its own deadline for electronic submission. For the R15, February 25, 2006 was the first deadline. For the R03, R21, R21/R33 and R34 the deadline was June 1. For the R01, the deadline is currently February 1, 2007, which is a change from the original deadline of October 2, 2006. The date for transition of each granting mechanism to the SF424 family of forms and electronic submission through Grants.gov is given in the figure at the top of the next page, which was last updated August 11, 2006. To check for changes since then use the following URL: http://era.nih.gov/ElectronicReceipt/files/Electronic_receipt_timeline_Ext.pdf. Be sure to check this Web site before submitting your application, because the submission dates for the various grant mechanisms has just changed (see NOT-OD-07-001). For example, the first elec-

tronic submission date for R01s in the SF 424 format will probably change to February 5, 2007 (actually February 6, because the fifth falls on a Sunday). After submission, grant applications will be handled entirely electronically, through the eRA Commons. Each applicant organization and PD/PI is required to register with the eRA Commons (see section 2.2.2 of the SF424 Application Guide). Thus, NIH and other PHS agencies will become entirely paperless with respect to the submission and processing of grant applications during 2006



- NIH will transition to the SF424 family of forms and electronic submission through Grants.gov by research program or funding mechanism.
- As mechanisms are transitioned, Funding Opportunity Announcements will be issued in the NIH Guide and posted in Grants.gov. NIH's goal is to post an opportunity a minimum of 60 days before the submission date.
- ALL applications in response to these announcements will require electronic submission through Grants.gov.

Mechanism Abbreviation Key:			
C06/UC6	Research Facilities Construction Grants	R21	Exploratory Development Research
DP1	NIH Director's Pioneer Award Programs	R21/R33	Exploratory Development Research/Phase II
D71/U2R	International Training Cooperative Agreement/ Phase 2 of F30 mechanism D71	R24/U24	Resource Related Research Projects
		R25	Education Projects
G	Resource Program	R34	Clinical Trial Planning Grant Program
P	Research Program Projects and Centers	R36	Research Dissertation Grant Program
R01	Research Project Grant Programs	SBIR/STTR	Small Business Innovation Research/Technology Transfer
R03	Small Grant Programs	S06, S10, S11	Biomedical Research
R10/U10	Cooperative Clinical Research Grants	SC1, SC2, SC3	Indiv. Investigator Initiated Research for Minority Serving Inst. Faculty
R13/U13	Support for Conferences & Scientific Meetings	S21,22	Health Disparities Endowment Grants
R15	Academic Research Enhancement Awards (AREA)	U	Cooperative Agreement Awards
R18/U18	Research Demonstration and Dissemination Projects	X01	High Throughput Screening
		X02	Pre-application for Interdisciplinary Research Consortium

Updated Aug. 11, 2006; History of changes in timeline

and 2007. The objectives are "to lower costs and administrative effort, expedite the processing of extramural grants, and provide better quality information to the NIH and the external grantee community." Attainment of these objectives is expected to eliminate the greater-than-two-million pieces of paper that are currently associated annually with the submission of applications, peer- and secondary Council review of the submitted proposals, as well as award and post-award administrative management of those that are funded.

The National Science Foundation (NSF) has successfully employed electronic receipt and review of its grant applications since the mid-to-late 1990s using the FastLane system. Grants.gov will be NIH's equivalent to FastLane, which will continue to be used by NSF as it, too, transitions toward use of the SF424 application kit and submission through Grants.gov.

SOFTWARE REQUIRED

To access, complete and submit a grant application, Program Directors / Principal Investigators must download and install the PureEdge Viewer (see User Guide at http://grants.gov). (If you are a Macintosh user you will have to follow the special instructions that are contained in section

2.3.3 of Part I of the PHS SF424 (R&R) Application Guide. Otherwise, you will not be able to create and submit an application.) In addition, attachments to the PureEdge forms must be in Portable Document Format (pdf), which requires pdf-creation software (the free Adobe Reader software is not sufficient). A list of software that will create a pdf file from documents created with any word processing program can be found at either http://grants.gov/assets/PDFConversion.pdf or Planet PDF's "Find PDF Software" feature at http://planetpdf.com/find_software.asp. The PHS SF424 (R&R) Application Guide strongly discourages creating the required PDF documents by scanning the text, unless your scanner is equipped with proper Optical Character Recognition (OCR) capability.

UNDERSTANDING THE 'LANGUAGE' OF NIH

As with many governmental organizations, NIH is associated with a bewildering array of acronyms and abbreviations, as well as codes and definitions for its programs and granting mechanisms. Any researcher who wants to decipher and understand these should have *Activity Codes, Organization Codes, and Definitions Used in Extramural Programs* as an office resource. It can be downloaded from http://grants.nih.gov/grants/funding/ac.pdf as a pdf document.

DEVELOPMENTAL STEPS FOR CHAPTER ONE:

1. Familiarize yourself with the Center for Scientific Review and its role in receiving, referring and reviewing your application (http://www.csr.nih.gov).
2. Review the NIH Roadmap and its priority areas (http://nihroadmap.nih.gov).
3. Familiarize yourself with Grant.gov (http://grants.gov), the clearinghouse for all Federal competitive grants and the means of submitting grant applications during and after 2006.
4. Assure that your institution is registered with Grants.gov. Identify your Authorized Organizational Representative (Signing Official).
5. Become familiar with the NIH eRA Commons (https://commons.era.nih.gov/commons) and the electronic submission / review / tracking of NIH grant applications.
6. Assure that your institution is registered with the NIH eRA Commons (run List of Commons Registered Organizations query at http://era.nih.gov/commons).
7. Register with the eRA Commons through your institution (see the eRA Commons User Guide at http://era.nih.gov/commons/).
8. Download and understand how to use the PureEdge Viewer (see User Guide at http://grants.gov) and PDF-creation software (http://grants.gov/assets/PDFConversion.pdf; or http://planetpdf.com/find_software.asp), both needed to create and electronically submit a grant application through Grants.gov.
9. Download and review *Activity Codes, Organization Codes, and Definitions Used in Extramural Programs* (http://grants.nih.gov/grants/funding/ac.pdf).

CHAPTER 2

HOW TO DEVELOP AN IRRESISTIBLE IDEA FOR YOUR GRANT APPLICATION

The application you write can only be as good as the idea with which you start: If you don't have a compelling, novel idea that will drive your field vertically, you're unlikely to be funded. It's that simple! No amount of 'window dressing' — grantsmanship — can overcome a bad idea. Therefore, you (and we) must do everything possible to ensure that your starting point — your idea — is nothing short of outstanding.

The best preliminary idea of which you are capable is usually the product of a step-by-step developmental process, i.e., it will rarely occur as a spontaneous event. We recommend that you take six steps in the developmental process: 1) define the niche area that you want to systematically develop; 2) collect and critically analyze background information that pertains to the proposed area of investigation; 3) generate a preliminary idea that is pertinent to the problem you have chosen; 4) assess your preliminary idea's potential for success and modify it, if necessary; 5) seek constructive criticism from knowledgeable colleagues; and 6) refine the idea to maximize its potential for impact on your field.

1. Define The Niche Area That You Want to Systematically Develop. Your application is unlikely to be fundable if what is proposed only confirms or marginally extends the work of others. Therefore, you must identify an area of research in which you can make contributions that will drive your field vertically. This translates into identifying a niche area within the scope of your overall research interest that is not overworked, i.e., a subdivision of your broader interest that you can systematically develop as your own.

Once you have done so, identify the long-term goal you have within that niche area. It should be more than what could be accomplished under the auspices of a single grant, but not so ambitious that it would be seen as unrealistic within the context of your career. Next, conceptualize the continuum of research that would be required to attain the long-term goal you have identified.

Finally, identify the next logical step that must be taken along the continuum of research that you have conceived. In contrast to the long-term goal, the problem you select here should be one that can be resolved under the auspices of a single award. It will become the subject of your proposal.

2. Collect and Critically Analyze Background Information That Pertains To The Proposed Area Of Investigation. A comprehensive review of the literature is the next step in generating a fundable idea. This is necessary for at least three reasons. First, you need to determine what is already known – published – in the area. Second, the extent to which that body of knowledge

is reliable needs to be critically examined. And, third, you need to determine who is actively working and publishing in the field.

There are many different ways to explore the current and past literature of a field. Examples of some of the databases and services that may be helpful to you are included in the text box, below.

Literature Databases and Services

Highwire Press (http://highwire.stanford.edu/)
759,333 full-text articles are free, with about 3,000 more free each month, making HighWire the largest archive of free life science articles in the world. Includes the biological, medical, physical and social sciences. A free e-mail alert service is available.

PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi)
A service of the National Library of Medicine, PubMed includes over 15 million citations for biomedical articles back to the 1950s. These citations are from MEDLINE and additional life science journals. PubMed includes links to many sites providing full text articles and other related resources. PubMed also has a free e-mail alert service.

Thompson ISI (http://www.isinet.com/cit/)
Science Citation Index Expanded, Social Sciences Citation Index, Arts and Humanities Citation Index and more. The service offers a unique search method, cited reference searching (identification of those who have cited a relevant publication). This database is accessible through most university libraries.

Determining the extent and reliability of current knowledge requires more than reading abstracts; *detailed, critical analysis* of the pertinent past and current literature is required. One helpful approach to organizing the results of your review is to photocopy the first page of any journal article that you evaluate. The first page will almost always contain the authors' abstract. As you read the paper, annotate the photocopy with any important information that was not included in the abstract. Also include remarks about the quality of the work, as well as of the conclusions that were drawn from it. The annotated photocopy can then be filed / catalogued for future reference.

TIP: During the course of your literature review, create a list of key words that describe the field, as well as the names of investigators who have been active in the area during the last ten years.

3. How To Generate A Preliminary Idea That Is Pertinent To The Problem You Have Chosen. As you work your way through the literature, invariably, ideas will begin to occur to you. Retain such ideas, but continue to conduct your review until it has been completed. Why? Because many of your early ideas will probably prove to be sophomoric as you become more critically conversant with the literature. Also, major shifts in your insight will almost certainly occur as you view your ideas, not individually, but in the context of how they relate to each other. Finally, some of your early ideas may be ones that other investigators have had before you and have used in their own grant proposals. As you will soon see, there is nothing more 'lethal' in this business than writing a grant application that has already been written.

Once you have completed your review, go back to the notes and ideas that you have written down. As you consider them, inspiration may strike. But, if it doesn't, don't be alarmed. Don't become anxious or think that you are somehow deficient. In fact, it is unusual for your best idea to immediately occur to you. Should that be the case, simply put your notes away for a few days and then take another look at them. This time, use a different approach – e.g., try outlining or diagramming to establish better how the ideas and concepts relate to one another. The proverbial light bulb will eventually come on. When it does, you will know it, because you will be genuinely excited by the prospects that become apparent to you. At that point, you need to ask yourself one last, two-part question: *'Will this idea impact significantly on my field and, if so, can I convince others of that fact?'* If your answer to both parts is affirmative, you've crossed the Rubicon and you're on your way. On the other hand, if you find that you can't say with conviction that the idea has the potential to advance your field substantively, you have to accept that you are not yet ready to write a competitive, i.e., successful, grant application. You either need to keep trying to evolve a more novel, important idea in the same area, or shift to a new problem that has the potential to pass this 'impact' test.

4. How To Assess Your Idea's Potential For Success And Modify It, If Necessary. Once you have generated your preliminary idea, as the next step you need to assess its potential for success before you ever put pen to paper. There are three criteria that must be considered:

Your own ability to pursue the idea. Regardless of how good your idea is conceptually, it has to be one that is within your capabilities to pursue, practically speaking. For example, do you and your colleagues have the expertise necessary to accomplish the work? If not, can you mobilize the missing expertise by recruiting either co-investigators, collaborators or consultants? Do you have the resources that will be required? If not, will you be able to obtain them? Will you have the funding and personnel necessary to acquire preliminary data that will convince reviewers that the project is feasible in your hands? If your application will be clinically oriented, will you have access to sufficient patients / clinical material that a statistically valid outcome will be possible? If not, can you collaborate with investigators at other institutions? Will you, as Principal Investigator, have sufficient time to devote to the project? If you are a senior person with many different kinds of scientific, educational, and administrative responsibilities, is it credible to take on more? If you are a New Investigator, can you commit time enough to convince reviewers that you are fully committed to starting a research career? The answers to these and related questions either have to be answered convincingly in your favor or there is little point in going forward, no matter how good your idea may be conceptually.

The competition you will encounter. Good ideas are often generated independently by more than one person. You need to know, therefore, what research has already been funded in the area that you are considering. As noted above, you must avoid writing an application that is similar to one that has already been funded. Also, if such grants are out there, you want to know about them so that you can make use of them to stimulate and extend your own thinking and planning. You can electronically access grants that have been funded by the United States Public Health Service by going to the CRISP (Computer Retrieval of Information on Scientific Projects) database (http://crisp.cit.nih.gov). Most of this database pertains to extramural projects, the vast majority of which have been funded by NIH and the Substance Abuse and Mental Health Services Administration (SAMHSA). A few will be ones supported by the Centers for Disease Control (CDC), the Food and Drug Administration (FDA), the Health Resources and Services Administration (HRSA), and the Agency for Healthcare Research and Quality (AHRQ). CRISP also contains information on intramural research programs of the NIH and FDA. There

are similar databases available for the National Science Foundation (for less complete database of funded projects from 1976 on, go to http://www.nsf.gov/awardsearch/index.jsp), and the United States Department of Agriculture (Current Research Information System [CRIS] and Human Nutrition and Information Management System [HNIRMS] databases, located at http://cristel.csrees.usda.gov/). Finally, you can also access most federally funded research grants (NIH, NSF, USDA, SBIR) and those that have been funded by the United Kingdom's Medical Research Council, by going to http://fundedresearch.cos.com/. This is a Community of Science Internet site to which either you or your institution must subscribe. In addition to covering the UK's MRC this database also provides data regarding grants funded by NIH, NSF, USDA and Small Business Innovation Research (SBIR) program that is coordinated by the U.S. Small Business Administration. Eventually, all will be on Grants.gov.

To retrieve information from any of these databases, you can enter the names of individuals who either are, or have been, active in your field during the last ten years (see TIP box, above). Alternatively, you can use key words that are applicable to the idea that you are trying to fund. By using either the search strategy that is specifically recommended for the database (most are accompanied by such recommendations) or one of your own design, you can obtain numerous titles of currently / previously funded applications that are related to your idea. Clicking on a title of interest will bring up that application's abstract, the content of which may trigger useful ideas. In addition, some of the databases contain either key words or indexing terms for each application. These descriptors often will pertain to information that is not covered in the abstract (e.g., a specific method). Careful consideration of these descriptors can lead to additional useful and new thoughts/approaches that will help you to develop and refine your own idea. *A day or more spent screening these databases of already funded grants will be invaluable!!!* We predict that you will be stunned – literally – at how much better the research design of your own application becomes by using what you glean from the abstracts and key words of your competitors to improve your own proposal. Taking this approach is an important way of gaining a distinct competitive advantage, because most other writers of grant applications don't take this step.

Your idea's funding potential. Even though you have tentatively decided to submit your application to the NIH, if you haven't done so already, you need to make certain that there aren't other, equally applicable funding opportunities at other agencies. The objective here is to find other agencies that will be helped to accomplish their missions by funding your idea. To find such additional opportunities, you need to search thoroughly one or more of the funding databases that are available to you. If your institution is a member of either the Community of Science (http://fundingopps.cos.com) or InfoEd (http://www.infoed.org/ → SPINPlus → SPIN), you have access to powerful tools that will facilitate your search for additional funding. Each even has an e-mail alert service (COS = Funding Alert and InfoEd = SMARTS), which is also available through Grants.gov (http://www.grants.gov/search/email.do). You can also manually seek other federal funding opportunities through Grants.gov. By clicking on the "Find Grant Opportunities" tab and then using the "Search Grant Opportunities" functions you can selectively search for other federal funding opportunities. For help with such searches, access the "Search Tips" or click on the "Help" button that is available to you under any one of the four search strategies that are listed under "Search Grant Opportunities." While you methodically search such databases, note any agencies that have interests that coincide with your own. Even if NIH continues to be your best bet for funding, other agencies that you identify can become important backup sources of support. It is permissible – smart business – to send essentially the same application to other agencies at the same time that you submit it to NIH – with one important exception: the Biological Sciences Directorate of the NSF. If you are an established investigator you cannot submit essentially the same application to that Directorate and to other agencies unless you have obtained a written waiver (which must accompany the proposal when it is submitted).

However, if you meet NSF's definition of a "Beginning Investigator" (individuals who have not been either a Principal Investigator [PI] or Co-Principal Investigator [Co-PI] on a federally funded award, with the exception of doctoral dissertation, postdoctoral fellowship or a research planning grant – see Grant Proposal Guide, section I.A) you can. It's not that much extra work to apply to more than one source of funding, because almost all grant applications contain the same basic elements (i.e., title, summary, background, significance, research plan, budget, etc.), which simply have to be 'tweaked' to include specifics that are required by the new agency. Given this fact, with competition what it is these days, not to send an application to multiple potential sources of funding is almost unthinkable. If you decide to do so, you must indicate that fact in block 8 of the SF 424 (R&R) Cover Component. Check the "Yes" box and list the other agencies there to which the proposal has been submitted If you ultimately have the enviable problem that more than one grantor wants to fund your proposal, you either have to select one of them or make adjustments that eliminate overlap between the pending applications.

5. Seek Constructive Criticism From Knowledgeable Colleagues. Because the idea that underlies a grant application is so fundamentally important to its success, you need to do everything possible to ensure that you have the strongest idea – the strongest starting position – on which to build. An essential part of "doing everything possible" is seeking critical feedback from your colleagues; if problems exist with your idea, now is the time to find out about them — not later, from your reviewers. Once you and colleagues on the application with you have developed the idea to the fullest you can, at least two 'experts' should be consulted. Regardless of their locations, they need to be individuals who you trust. Most often, they will be investigators who are researching areas somewhat tangential to your own, but close enough that they will be able to give you the critical feedback that you seek. They could, for example, be members of your pre-submission review committee (see chapter 22). Their primary role will be to review the final draft of your draft application for scientific and technical merit before it is submitted. Your idea should be presented to them in writing. A *brief* overview (no more than one page) should be prepared that contains the following components: 1) the principal knowns on which the work would build; 2) the gap in the knowledge base that would be filled; 3) the central hypothesis that would be tested (or the need that you intend to meet, if your application will be need-driven); 4) the rationale, or underlying reason, for why the work needs to be done; 5) what could be expected from the work; and 6) why the expected outcomes are potentially important in vertically advancing the field. When you present it to them, you should specifically ask your consultants for ways in which you can improve the idea.

An alternative to getting feedback on the idea at this stage is to wait until the template or master plan for your application has been prepared (see the Overview to Part II, page 40). The positive aspect to this alternative approach is that your idea will be presented in a clearer, more complete form. The negative is that the work invested in writing the template or master plan may be wasted if its centerpiece – the idea – is found to be wanting at this later time.

6. Refine Your Idea To Maximize Its Impact. The sixth and final step is to consider critically the feedback that you receive from your colleagues and, *if you concur*, to modify the idea accordingly. If you don't fully concur, this can be a time of painful decision making. In such circumstances, you may want to seek the advice of additional colleagues before you make any changes. The bottom line is that you must have total confidence that the final product – the idea that will drive your research proposal – is completely sound and will make a difference in your field when acted upon. If you don't have that level of confidence, you won't be able to project the kind of enthusiasm and commitment that are necessary to write an outstanding proposal.

DEVELOPMENTAL STEPS FOR CHAPTER TWO:

1. Identify a relatively under-explored niche within the area of your broad research interest.
2. Develop a long-term research goal in the niche area and conceive a continuum of research that will be needed to reach that goal.
3. Conduct a comprehensive, critical review of the related literature.
4. List key words that characterize the subject you have chosen and the names of investigators who have been active in the area during the last ten years.
5. Develop a preliminary idea for your proposal.
6. Search databases of already funded grants and use what you learn to refine and improve your idea.
7. Seek constructive criticism of the idea from knowledgeable colleagues. Further refine your idea, if necessary.
8. Identify alternative / additional granting agencies to target with your application.

CHAPTER 3

HOW TO FIND THE APPROPRIATE PROGRAM AND GRANT MECHANISM FOR YOUR IDEA

HOW TO FIND THE APPROPRIATE PROGRAM FOR YOUR APPLICATION

TIP: Review panels don't fund grant applications! Review panels recommend funding.

Program officials make the funding decisions.

One of the most important misconceptions held by applicants is that review panels fund grant applications. A second common misconception is that program officials are not relevant to the development of grant applications. In fact, nothing could be farther from the truth! While standing review panels (called Scientific Review Groups or Study Sections at NIH) are critically important in evaluating the scientific and technical merit of proposals (i.e., they recommend funding), the persons who actually decide whether an application will be funded, or not, are Program Officers – the individuals who are in charge of NIH's specific programs.

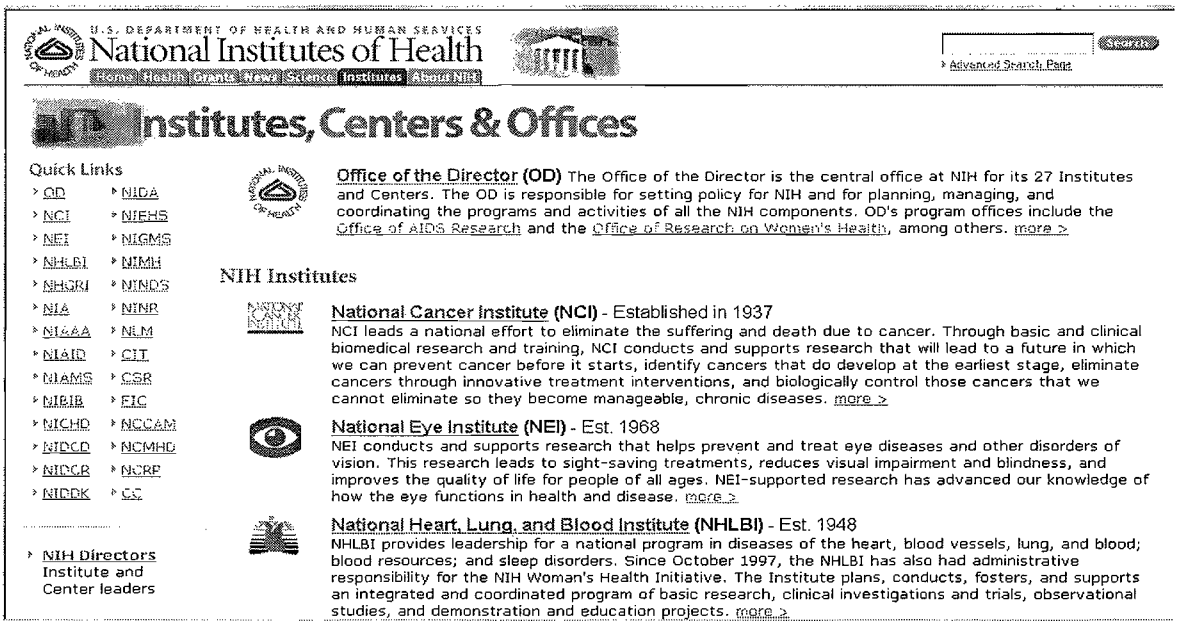
It is also not widely appreciated by applicants that each of NIH's programs has its own set of programmatic priorities. Such priorities are set according to current mission goals. To assist in setting priorities, program officials periodically inventory their portfolios of already-funded grants. The purpose is to determine how their funds are distributed. If a given research area is well- or overly represented, they may decide to de-emphasize that area when future funding decisions are made. Mission-relevant research areas that are not adequately represented, along with new programmatic goals, may be given future funding priority. Therefore, to be maximally appealing to Program, your idea should fall within an area of current programmatic relevance.

TIP: What you want to propose is not what is most important. What is important is finding an NIH program that wants to fund what you want to propose!

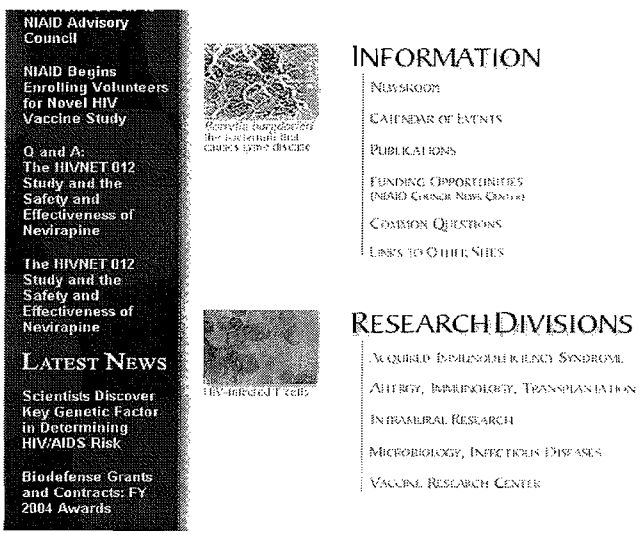
In light of the above, a critical step in developing a competitive grant application is assuring that it will be programmatically relevant when it is submitted. Ideally, you want to 'marry' what you want to do with what a program wants done, so that by funding your proposal the program will take a step toward accomplishing its mission. It is important, therefore, at this early stage in the development of your application, to identify the program at NIH that will be the target of your application.

As was noted in chapter one, NIH is organized under the Director's Office into 19 Institutes, the National Library of Medicine, and 7 Centers. Each of these entities has its own set of priorities

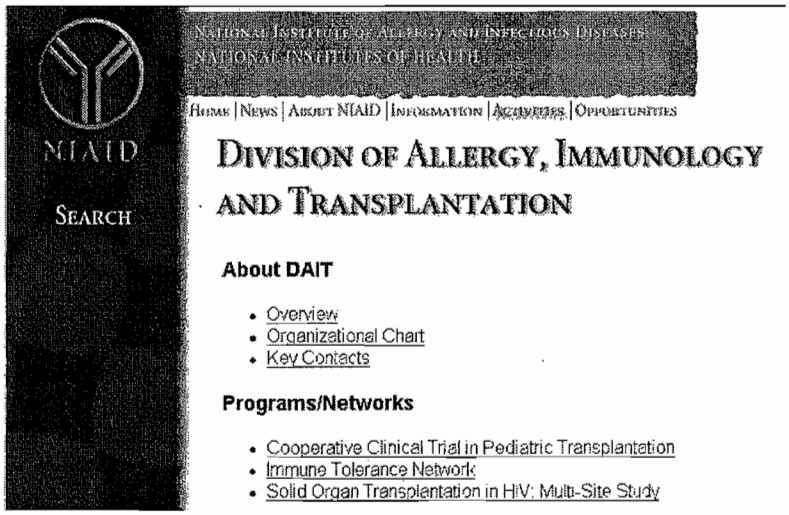
and provides research grant support as a means of accomplishing its goals. If you will be submitting a self-initiated application, i.e., one that has not been solicited (e.g., through an RFA), the first step is to determine which one (or more) of these 27 potential sources of support is most applicable to the idea that you have developed. To do so, go to the "Institutes, Centers and Offices" part of the NIH Web site (http://www.nih.gov/icd), which will give you a brief overview of the interests of each Institute and Center.



Scroll down the list and select the one that seems to mesh best with your idea. Click on its name (or click on the appropriate "Quick Link" at the upper left of the page) and you will find yourself at that Institute's / Center's home page. For illustrative purposes, let's say that your idea most closely meshes with those of the National Institute of Allergy and Infectious Diseases (NIAID; http://www.niaid.nih.gov). Part of NIAID's home page (as of this writing) is depicted below.



Note that there are four extramural Research Divisions listed, along with a button for "Intramural Research" programs. Were your interest in the area of "Allergy, Immunology, Transplantation," you would click that button, which would take you to that Division's part of the Web site.



Note that there is a "Key Contacts" button under the "About DAIT" listing. Click on "Key Contacts" and you would have a list that would include, among other things, the Branches that constitute DIAT, together with the names, telephone numbers and e-mail addresses of the related personnel. Below, the personnel who operate the "Asthma, Allergy, and Inflammation Branch" are listed. Note that, among them, are the Program Officers you are seeking to identify.

Asthma, Allergy, and Inflammation Branch

Charles J. Hackett, Ph.D. *Chief*	6610	3105	(301) 496-8973	chackett@niaid.nih.gov
Gwendolyn Ward *Secretary*	6610	Cub J-2	(301) 496-8973	gward@niaid.nih.gov
Allergic Mechanisms Section				
Marshall Plaut, M.D. *Chief*	6610	3093	(301) 496-8973	mplaut@niaid.nih.gov
Peter Bocek, M.D., Ph.D *Program Officer*	6610	3060	(301) 496-8973	pbocek@niaid.nih.gov
Sally Tinkle, Ph.D. *Program Officer*	6610	3115	(301) 496-8973	stinkle@niaid.nih.gov
Asthma and Inflammation Section				
Gang Dong, M.D., Ph.D. *Program Officer*	6610	3101	(301) 496-8973	gdong@niaid.nih.gov
Peter Gergen, M.D. *Medical Officer*	6610	3101	(301) 496-8973	pgergen@niaid.nih.gov

Each Institute and Center is different in terms of how the relevant Program Officer can be located. As a general rule, it is usually helpful to start with the Institute's / Center's "About" button or, if they have one, the "Staff Directory" button and work through subsequent layers from there. In some cases, it will be immediately clear which person is responsible for your area of interest, because a description of each Program Officer's subject area will be included with his/her contact information. If you aren't able to identify which of several Program Officers is most relevant to your idea, as would be the case for the "Allergic Mechanisms Section," above, pick one and query him/her by e-mail. S/he will undoubtedly be able to refer you to the correct individual if s/he is not your best point of contact. An alternative approach is to use the PHS Agency Contact Table (section 1.4 of the *PHS SF424 [R&R] Application Guide*), which has a phone number for each of the Institutes and Centers. That number can be used to obtain a referral to the correct Program Officer at the Institute/Center you are targeting.

If you will be responding to either a Program Announcement or Request for Applications (see chapter one), there is an easier way to identify the relevant Program Officer. The solicitation that provides the details of the funding opportunity will contain the name and contact information of the relevant individual for each Institute / Center participating in that program.

Once you have identified the Program Officer who is in charge of the program you will be targeting, you need to query him/her at this stage to assure that your idea will be of programmatic interest. Now is the time to find that out, so that you can either modify what you are planning to propose to make it more programmatically relevant or, if it is not, you can switch to an alternative source of funding that will regard your idea more highly. Your query should be submitted by e-mail, if at all possible. If you use the telephone and are lucky enough to catch the Program Officer in his/her office, s/he won't know why you are calling and will be responding off the top of his/her head. In addition, s/he may be busy at the time and not interested in holding a substantive conversation with you. Last but not least, you don't want to leave the impression inadvertently that you are a pest - a 'black hole of need.' Program Officers are not interested in associating themselves with black holes of need! By using the e-mail approach you avoid those problems. *In your e-mail message you should include three very important words: "maximize programmatic relevance."* For example, 'I would like to make an appointment to speak with you by telephone so that I can maximize the programmatic relevance of the proposal that I am planning to submit.' When you use that approach, you distance yourself greatly from being a 'black hole of need' and, instead, become someone who is being considerate of the Program Officer's job: you are offering to help him/her assure that what you submit is maximally relevant to his/her programmatic priorities. You will almost always get the substantive feedback you are seeking if you use this approach.

You don't have to worry that you are overstepping your bounds by making such a query. On page I-3 of Part One of the *PHS SF424 (R&R) Application Guide*, under section 1.4, there is the following invitation: "The PHS agencies encourage applicants to communicate with staff throughout the entire application, review and award process." On page I-4, there are specifics that pertain to development of an application. There, NIH points out that you can contact program staff to learn more about whether your proposed topic meshes with an Institute's / Center's programmatic area and/or its programmatic areas of interest (priorities).

FIND THE APPROPRIATE RESEARCH GRANTING MECHANISM FOR YOUR PROPOSAL

This *Workbook* is specifically written to support the development of a Basic Research Grant (R01) application – the most common kind of grant application that is made to NIH. As can be appreciated from Table 9 in *Activity Codes, Organization Codes, and Definitions Used in Extramural Programs* (http://grants.nih.gov/grants/funding/ac.pdf) and the descriptions that are included in Part III of the *PHS SF424 (R&R) Application Guide* (see pages III-29 through III-31), there are many other research granting mechanisms, each with its own purpose. To be successful, an idea must be packaged and presented in such a way that it meets the purpose and requirements of the chosen granting mechanism.

> TIP: Understand the purposes of the common research granting mechanisms that NIH uses to support research – especially the R01, R03, R15, R21, R21/R33, R34 and P01. Make certain that the proposal you write meets the purpose of the research granting mechanism that you have chosen to use.

The R01 Research Project Grant (http://grants1.nih.gov/grants/funding/r01.htm) is designed to fund definitive studies for up to five years and is renewable. All Institutes and most Centers support this granting mechanism. Applications for R01 funding must be supported by substantial amounts of preliminary data that establish the feasibility of its aims. Preliminary data must also support formulation of the focusing central hypothesis and the subordinate hypotheses that focus research under the aims if the proposal is hypothesis-driven. Without such data, in our experience, the likelihood of a proposal being funded at the R01 level is remote. As noted earlier, this *Workbook* focuses on the R01 research granting mechanism, because it is the one that funds the majority of research projects in the extramural program.

The R03 is a Small Research Grant (http://grants1.nih.gov/grants/funding/r03.htm). Some Institutes and Centers will consider self-initiated R03s (http://grants.nih.gov/grants/guide/pa-files/PA-06-180.html), i.e., ones that are not solicited by either a Program Announcement (PA) or Request for Applications (RFA). Other NIH Institutes and Centers and PHS-awarding components other than NIH may offer the R03, but under their own definition of the research grant mechanism. Such specifics can be obtained either by investigating funding opportunities listed on the agency's Web site or by contacting the appropriate Program Officer. Regardless of the sponsoring entity, all R03 applications must now be submitted electronically through Grants.gov using the PHS SF424 application form components. R03 grants are limited in terms of time and budget and are not renewable. Why? Because this research grant mechanism is rarely meant to support a small, definitive research project. Rather, it is most effective when written as a stepping stone to subsequent R01 funding – which is why R03s are for relatively little money, of relatively short duration, and are non-renewable. Thus, the R03 can be the means of developing preliminary data or a method or technology without which a project would not be competitive at the R01 level.

The R21 Exploratory/Developmental Grant (http://grants2.nih.gov/grants/funding/r21.htm) allows more time and money than an R03, but, like the R03, is non-renewable. Like the R03, some Institutes and Centers allow self-initiated R21s (http://grants1.nih.gov/grants/guide/pa-files/PA-06-181.html). This research grant mechanism often has the purpose of supporting high-risk (of failure) / high-impact research. In our experience, the most successful R21s are those that propose the least amount of investigation that is needed to prove a concept, establish feasibility

and/or remove risk so that subsequent definitive studies can be proposed successfully at the R01 level. That is why the granting mechanism is non-renewable. Thus, it, too, is meant to be a stepping stone to subsequent support of definitive studies (e.g., under the auspices of either an R01 or R33). The purpose of the R21 is clearly exemplified when it is combined with the R33 (a so-called Phase II grant, which is the equivalent of an R01). When the R21 is combined with the R33, the applicant writes, in essence, two grant applications. The R21 describes the least amount of research that is necessary to reduce the risk of failure and provides clear benchmarks that can be used by program staff to corroborate that the applicant has been successful in doing so. The R33 describes what will be done, once such risk has been removed. Both proposals are reviewed and approved for funding at the same time, but only the R21 is activated. As soon as R21's benchmarks have been reached, program staff can terminate the R21 and, without additional review, activate the R33, which then sponsors the definitive studies. The attraction of this approach is that no time is lost between successful completion of the R21 and the initiation of subsequent definitive studies, as there would be if an R01 proposal had to be written as a second step. Not all Institutes and Centers sponsor the R21/R33, which at this writing is available only through specific Program Announcements and Requests for Applications. It is now required that all R21 applications be submitted using the PHS SF424 (R&R) application form components through Grants.gov.

The R15 (http://grants1.nih.gov/grants/funding/area.htm) Academic Research Enhancement Award (AREA) has the purpose of stimulating research at educational institutions that provide baccalaureate or advanced training but are not currently major recipients of NIH grant support (http://grants.nih.gov/grants/guide/pa-files/PA-06-042.html). The budget and duration are capped, but unlike R03s and R21s, R15s are renewable. Thus, R15 applications can and should propose small, complete research projects that, ideally, are part of a continuum of research that is being pursued by the Principal Investigator. They can be a stepping stone to a subsequent R01, but don't have to be, because they are renewable. In addition to scientific and technical merit, R15s are also evaluated on the basis of what the award will do to strengthen the recipient institution's capacity to compete for future NIH research dollars, as well as what it will will do to expose students to biomedical research. R15s must now be submitted electronically through Grants.gov using the PHS SF424 (R&R) application form components.

R34s are Clinical Trial Planning Grants. An overview of this granting mechanism's purpose and use can be found at http://grants1.nih.gov/grants/funding/r34.htm, with details provided by the relevant Program Announcement (http://grants.nih.gov/grants/guide/pa-files/PA-06-363.html. The purpose of the granting mechanism is to provide support for the development of Phase III clinical trials. Basically, it is meant to allow investigators to pull together all of the disparate parts that must be put in place before launching a complex Phase III trial. The activities supported are primarily logistical, conceptual and/or technical in nature. The granting mechanism is not meant for the purpose of acquiring preliminary data or performing pilot studies that would be the basis for such a clinical trial. These applications also must be submitted electronically through Grants.gov using the SF424 and cannot be renewed. Thus, here again, this granting mechanism is meant to be a stepping stone to subsequent funding.

The P01 Program Project Grant has as its purpose the bringing together of independent investigators around a common theme in such a way that they become synergistically productive as a group and able to solve more complicated problems than any one of them would be able to working individually. Not all Institutes and Centers sponsor P01s. Those that do sponsor this grant mechanism offer their own version of it. It is critical, therefore, that applicants discuss their intention to develop and submit a P01 application with the relevant Program Officer before

going forward with such a proposal. P01 applications are almost always reviewed within the sponsoring Institute / Center and not through the CSR.

All of the grant mechanisms described above, excepting the R01, will be the subjects of supplements to this *Workbook*. As noted in the Introduction to this *Workbook,* many of the principles and fundamentals of grantsmanship are transposable from the R01 to the preparation of other kinds of applications. There are specifics, however, that need to be considered in the development of each. The supplements will address those specifics. In addition to the ones for research granting mechanisms, supplements will be available for the preparation of Career Development (K) and National Research Service Award (NRSA) applications. If you have an interest in any of these research / training supplements, please watch for their announcement on Grant Writers' Seminars and Workshops' Web site, www.grantcentral.com.

DEVELOPMENTAL STEPS FOR CHAPTER THREE:

1. Identify the programmatic area within NIH that will be the target of your proposal.
2. Identify the Program Officer that is responsible for the programmatic area you will target.
3. E-mail the Program Officer regarding your desire to "maximize the programmatic relevance" of your idea / application.
4. Refine your idea, if necessary, based on feedback you receive from the Program Officer.
5. Understand the purpose of each research grant mechanism you are considering for your application.
6. Identify the research grant mechanism that is most appropriate for your research project and its stage of development.

CHAPTER 4

WRITING FOR SUCCESS, INFLUENCE OF THE NIH REVIEW PROCESS ON HOW YOU SHOULD WRITE, and HOW TO MODIFY A SUBMITTED PROPOSAL

HOW TO WRITE FOR SUCCESS – COMPLIANCE REVIEW

As noted earlier, all grant applications submitted to NIH are received and distributed for review by the Center for Scientific Review. Upon receipt, each application is given a compliance review to ensure that it is responsive to the relevant instructions. Both automated (computer validation) and manual (NIH staff) reviews are conducted. If your application fails this initial screening, it may be sent back to you without being reviewed. The decision to do so is not subject to appeal.

Obtain All of the Current Instructions. As the first step in the preparation of your proposal, you owe it to yourself to obtain the most current version of the *PHS SF 424 (R&R) Application Guide*. The latest instructions can be downloaded from http://grants.nih.gov/grants/funding/424/index.htm. Updated versions of the instructions will undoubtedly be posted as NIH refines the PHS SF 424 approach to creating and submitting grant applications.

Be aware that there are instructions that are generic, i.e., that pertain to use of the SF 424 forms by any applicant. There are also agency-specific instructions. For PHS proposals, the latter instructions are denoted in the *PHS SF 424 (R&R) Application Guide* by the logo of the Department of Health & Human Services, which is reproduced to the right. These must be adhered to carefully, because they modify and/or supplement the generic SF 424 instructions to make your proposal acceptable to NIH.

If you are responding to a specific funding opportunity, that solicitation (Program Announcement or Request for Applications) will have additional instructions associated with it. These should be downloaded from Grants.gov using the approach that is described in section 2.4.3 of Part I of the *PHS SF 424 (R&R) Application Guide*. Application forms should be downloaded from the same site.

Format Specifications. There are several formatting instructions (section 2.6 of Part I of the *PHS SF 424 (R&R) Application Guide*) that absolutely must be adhered to or in all likelihood your application will be returned to you. For example:

- Page Limits and Size: The length of the Research Plan is strictly regulated. There are different limits for different research grant mechanisms (e.g., 25 for the R01 and usually

10 for the R03 and 15 for the R21). Determine how long the Research Plan can be for the research grant mechanism you plan to use, because that limit cannot be exceeded without risking rejection during the compliance review. Other parts of the application that are restricted in length include the Introduction (no more than 3 pages for resubmitted R01 and R15 applications; up to one page for R03s, R21s and revision [formerly competing supplemental] applications) and the Biographical Sketch (no more than 4 pages). Such absolute page limits should not be confused with the 'recommended' length for each section of the Research Plan. Section-length recommendations are flexible. All pages of your application must be 8.5 X 11 inches.

- Typeface: There is no flexibility regarding the typeface that can be used in an NIH grant application. It must be either Arial, Helvetica, Georgia, or Palatino Linotype. We prefer Arial, which is the typeface used in this *Workbook*.

- Font Size: The required typeface must be black and 11 points or larger. Smaller font can be used in figures, figure legends, graphs, diagrams, charts, tables and footnotes to tables. In these places the only restrictions are that a required typeface be used in black ink and that the print be legible.

- Type Density and Line Spacing: There must be fewer than 15 characters and spaces per linear inch, and line spacing must be 6 lines or fewer per vertical inch. It is required that applications be single spaced.

- Page Headers and Footers cannot be used. Page numbers will automatically be generated by the system that is used to create and submit your proposal.

- Color can be used in figures, but not for text. We recommend that, if you use color in your figures, you choose shades that have distinct grayscale differences when printed in black and white. When reference is made to each color in the legend it should be followed by the corresponding grayscale shade, e.g., dark blue (grayscale = black). This assures that color can be interpreted even when a reviewer downloads and prints a figure in black and white.

- Margins: While it is permissible to use a minimum of 0.5 inch for top, bottom, left and right margins, we recommend that you use 1-inch margins all around. Wider margins are esthetically more pleasing and, therefore, more reviewer friendly. For the same reason, we recommend that you open a line between each of your paragraphs.

HOW TO WRITE FOR SUCCESS – SCIENTIFIC AND TECHNICAL REVIEW

> TIP: The bottom line in writing a successful proposal, regardless of funding agency or discipline, is knowing how to identify the 'hot buttons' that are of importance to the targeted funding agency, and then having the grantsmanship skills needed to 'punch' those buttons.

Your objective should be to create advocacy for funding your application, not only through the quality of the science, but also by the way that you present the science. In our opinion, more

applications fail because of poor packaging and presentation of the proposed research than because of flawed science. How you write for reviewers makes a BIG difference, therefore. The tip given above is an important part of the equation. The remainder of this chapter focuses on some of the ways that you can optimize your grantsmanship.

Resources Available to You. There is a great deal of help available to you if you want to avail yourself of it. NIH has many helpful hints and examples on its Web Site designed to help you. Most of these can be found at http://grants.nih.gov/grants/new_investigators/index.htm, Resources for New Investigators. For example, the National Institute of General Medical Sciences has on part of its Web site (http://nigms.nih.gov/funding/tips.html) 25 "Tips for New NIH Grant Applicants." As another example, the National Cancer Institute offers a "Quick Guide for Grant Applications" (http:deainfo.nci.nih.gov/EXTRA/EXTDOCS/gntapp.htm), which walks an applicant through the preparation of an NIH proposal. The National Institute of Allergy of Infectious Diseases offers tutorials (http://www.niaid.nih.gov/ncn/grants/default.htm) on how to write an application, as well as a funded R01 (http://www.niaid.nih.gov/ncn/grants/app/default.htm) that Dr. Mark Smeltzer, of the University of Arkansas has allowed NIAID to annotate. Other examples of funded grants can often be obtained by directly approaching the principal investigator directly. Simply go to the CRISP database query form (http://crisp.cit.nih.gov/crisp/crisp_query.generate screen) and search for the kind of grant or contract you are interested in (e.g., a member of the Research series, such as R01, R03, R15, R21, etc.). Select the kind of funding in the "Activity" dropdown, the year(s) you want to query, and the other criteria you want used in your search. Click on the titles of the relevant grants that are displayed (e.g., R03s) and you will obtain for each the principal investigator's e-mail address (located under his/her name). Simply write the investigator a note asking whether s/he would mind sharing a copy (or a partial copy) of their funded grant. Indicate that it isn't for the purpose of competing with them. Rather, make clear that it is for the purpose of obtaining an example of that kind of application. Many investigators, especially those at your own institution, will respond positively to such a request, especially if the e-mail message or personal contact is appropriately flattering regarding the quality of the application being sought.

Hierarchical Formatting. Reviewers should be able to see at a glance what is subordinated to what in a grant application. Again, this is another part of the reviewer-friendly approach. We recommend that you choose a format and use it consistently throughout the text of your proposal. One that we particularly like is a combination of different heading/subheading/sub-subheading styles coupled with corresponding levels of indention. For example:

SECTION HEADINGS

Section headings are presented at the left margin entirely in bolded, capitalized letters. The first line of each paragraph that is subordinated to a section heading is indented one tab. Subsequent lines return to the left margin, as is shown here.

Subsection Headings

Subsection headings are in bolded italics, with the first letter of each main word capitalized. The first line of each paragraph is indented two tabs, with subsequent lines returning to the left margin.

Sub-subheadings

This level of subordination is indicated by putting the sub-subheading in underlined italics. The first line of each paragraph is indented three tabs. Subsequent lines in

each paragraph return to the left margin, thereby preventing an expanse of white space from developing as indentions progress to the right.

By adopting a system similar to the one shown, above, you make it easy for the reviewer to grasp the relationships that exist in what you are presenting.

Apply Strategies Employed by Writers of Newspaper Articles. Newspaper writers are taught to write in such a way that the reader will want to read what has been written. Reviewers, in contrast, have to read what is written in grant applications. Part of building advocacy for your proposal will entail writing in such a compelling way that its reviewers convert from 'have to' to 'want to' with respect to reading what you are presenting. Some of the tricks employed by newspaper writers can be transposed to help us accomplish this conversion.

- A newspaper headline is a conceptual distillation of the related article into the fewest words that will inform the reader of the article's content while, at the same time, it 'hooks' the interest of the reader and makes them want to read the article. Although we don't have the exact equivalent of headlines in grant applications, the specific aims, section headings and paragraph headings share characteristics with newspaper headlines: brief, informative, conceptual entities that will make the reviewer want to read what follows.

- The introductory paragraph in a newspaper article is usually complementary to the headline and is a broad overview of the content of the article. Having read the headline and the introductory paragraph, the reader knows broadly what the content of the article is and wants to read the details that follow. We will apply exactly the same approach, using introductory paragraphs in association with each major section and subsection. By doing so, reviewers will want to read the details of what is proposed.

- Paragraphing in newspapers occurs with practically every sentence. That is because each sentence represents a stand-alone thought. The order in which the stand-alone thoughts are presented sets up a progression of logic that helps to lead the reader through the newspaper article. We can't paragraph each sentence in a grant application. But we can apply the same strategy: every paragraph in your application should make one point and one point, only. Then, the ordering of your paragraphs helps to set up the progression of logic that leads the reviewer through the application. The ideal grant application, in our opinion, is one that leads reviewers through it without them knowing that they are being led.

- Style of Writing. Newspaper journalists write with a simple, direct style that emphasizes brevity and is easily read and comprehended. This approach is highlighted by one of USA Today's commercials: "It's not the most words, just the right words." This is so applicable to the writing of grant applications that we have devoted the entire next section of this chapter to developing an appropriate style of writing.

Adopt a Spare, Clear, Direct Style of Writing. Writing grant applications is not unlike writing short stories. By that, we don't mean to imply that you will be writing fiction. Rather, the similarity between the two genres is that, in both cases, every component of the 'story' must have a reason to be there. Everything that you want to convey must be contained within a limited number of pages. Therefore, every word must be the right word, and each must be chosen carefully to relate meaningfully to its neighbors. Every sentence must be crafted to convey exactly the

message that you want it to impart. Every paragraph must flow logically out of the ones that have preceded it, so that the story builds clearly and vividly in the mind of the reader/reviewer. It takes time and effort to write this way. However, there is no alternative but to make the necessary investment, because poorly written proposals are almost always preordained to fail. Why? Because reviewers rarely will take the time to decipher badly written, unclear material.

The following considerations are ones that you should keep in mind as you write. By doing so, you will avoid many of the compositional mistakes that are made by many unsuccessful grant writers.

First, write in clear, simple declarative sentences. By doing so, you will avoid tortuous, compound sentences that go on forever and are hard to understand. A reviewer should not have to read a sentence more than once to understand it. Therefore, when you have the urge to use a comma and keep going, stop and ask yourself whether it would be clearer to use a period, instead. Breaking things up into smaller 'bites' is very reviewer friendly.

Second, avoid the use of clichés and 'empty generalities.' These are words and statements that, at first, look great, but when analyzed carefully, really convey little or nothing. For example, 'The proposed state-of-the-art research is expected to advance the field significantly.' What does the cliché, "state-of-the-art," mean in terms that the reviewer can objectively evaluate? What makes the research "state-of-the-art?" What does "advance the field significantly" mean? That's a good start, but it is meaningless to a reviewer unless additional explanatory detail follows. We can't underscore enough that 'Be specific!' is one of the cardinal rules of good grantsmanship. Specificity and precision are what build credibility with reviewers. Use of meaningless clichés and generalities does the opposite.

Third, avoid the use of nouns as adjectives, which is a particularly prevalent problem among writers of grant applications. Consider: 'lower respiratory tract iron burden' or 'total parenteral nutrition catheters.' What is actually meant in these two examples is 'burden of iron in the lower respiratory tract' and 'catheters for use in administering total parenteral nutrition,' respectively. *It doesn't add that much more text to make things maximally clear.* The gain in understanding is well worth it. As will be noted in detail later, the same comments can be made about the use of non-standard abbreviations. You don't gain that much space and you run the risk of causing loss of comprehension. A related point pertains to compound adjectives – two or more words that modify another – which should be hyphenated. Thus, no hyphen is needed when referring to someone as African American. However, if you refer to an African-American patient, you need to include a hyphen.

Fourth, make sure that you avoid the use of 'weak' words, i.e., ones that unnecessarily convey doubt in your ability to do something. By weak words we mean ones like: if (if we can do X, then we will be able to do Y); try (we will try to overcome the problem that is caused by X); hope (we hope to obtain Y); believe (we believe [pray?] that we can obtain X); might (we might be able to prepare the antiserum); could/should (we could/should obtain); and may (we may be able to extend our understanding to). In every one of these examples, the word 'expect' could have been substituted (e.g., we expect to obtain, instead of we hope to obtain). Use of 'expect' is a much more positive and confident way of saying that you can do what you propose.

Fifth, the word 'whether' can create serious problems. Why? Because, although it is often used alone, it always means whether or [something else]. Usually, it is whether or *not*. Just as in the case of weak words, this latter usage of 'whether' can cause doubt in the mind of a reviewer (What happens if it comes out 'not'?). The next time that you find yourself about to use 'whether

[or not],' try 'the extent to which' as a substitute. 'Whether or not' is black and white, one way or the other. 'The extent to which' ranges from 0 to 100%. Thus, the use of this phrase can avoid the problem of 'not' (i.e., failure) being the only alternative outcome.

Sixth, make certain that you use the correct word when there is a choice between two that are closely similar in spelling and/or meaning. Some of the words that are commonly misused by applicants include: affect *vs.* effect; alternative *vs.* alternate; because *vs.* since; complement *vs.* compliment (complementary *vs.* complimentary); led *vs.* lead; principal *vs.* principle; rationale *vs.* rational; and which *vs.* that. If you need to, consult a dictionary or style manual to make sure that you use these (and others like them) correctly. This suggestion also pertains to use of singular and plural forms of the same word. The usual mistake is to use the plural form as though it were singular. Examples of words that are commonly misused in this way include: data (plural) *vs.* datum (singular); sera (plural) *vs.* serum (antisera *vs.* antiserum); criteria *vs.* criterion; media *vs.* medium; and phenomena *vs.* phenomenon. Use of the correct word can make a big difference in the clarity of your writing and, equally important, how your attention to detail is perceived by a reviewer.

THE NIH REVIEW PROCESS SHOULD INFLUENCE YOUR WRITING

While your proposal will ultimately be funded by one of NIH's Institutes, Centers or Offices, the proposal will first be evaluated for scientific and technical merit by a review panel (i.e., Scientific Review Group or 'study section,' as most review panels are called at NIH). Consequently, the application must be written to appeal to the reviewer. Your proposal will be read by individuals who are assigned this task by the study section's Scientific Review Administrator (SRA), usually in collaboration with its Chairperson. In most cases, three persons – a primary, secondary and tertiary reviewer – will be assigned to review your application. Their objective will be to identify the strengths and weaknesses of your proposal. The primary reviewer will usually be the person on the study section who is judged by the SRA to be the most qualified to review your application. If not an expert on the subject you are proposing, s/he will be close. The secondary reviewer will be the next most knowledgeable person, and so on.

Become Aware of How Study Sections Operate. Understanding the NIH review process is very important to your success. A videotape of a mock study section meeting can be downloaded from http://www.csr.nih.gov/Video/Video.asp. We strongly recommend that you view it, because if you haven't acted as an NIH reviewer before, by viewing this videotape you will gain a very good impression of what goes on during the meeting of a study section. Understanding the process and knowing what panel members have to contend with will help you to make your application more reviewer friendly.

Understand the Criteria Reviewers Must Use. A very helpful Center for Scientific Review Web site (http://cms.csr.nih.gov/ResourcesforApplicants/PolicyProcedureReview+Guidelines/) pertains to peer-review. As you will see, five review criteria are used to evaluate applications. They were updated in October 2004 (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-05-002.html) and include: "***Significance:*** Does this study address an important problem? If the aims of the application are achieved, how will scientific knowledge or clinical practice be advanced? What will be the effect of these studies on the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field? ***Approach:*** Are the conceptual or clinical framework, design, methods, and analyses adequately developed, well integrated, well reasoned, and appropriate to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternative tactics? ***Innovation:*** Is the project origi-

nal and innovative? For example: Does the project challenge existing paradigms or clinical practice; address an innovative hypothesis or critical barrier to progress in the field? Does the project develop or employ novel concepts, approaches, methodologies, tools, or technologies for this area? ***Investigators:*** Are the investigators appropriately trained and well suited to carry out this work? Is the work proposed appropriate to the experience level of the principal investigator and other researchers? Does the investigative team bring complementary and integrated expertise to the project (if applicable)? And, ***Environment:*** Does the scientific environment in which the work will be done contribute to the probability of success? Do the proposed studies benefit from unique features of the scientific environment or subject populations, or employ useful collaborative arrangements? Is there evidence of institutional support?"

Of the five evaluative criteria, in our opinion, significance is the most important. Even if there were all the money in the world, who would want to invest any of it in a project that lacks significance? That is why it is so necessary to begin with an idea that will make a vertical difference in the field, once it has been acted upon. Another criterion that deserves special comment is that of innovation. While it is a highly desirable characteristic to have in a research program, it is an 'optional' review criterion. Not all supportable research will necessarily have that characteristic. Thus, while it is ideal for a research program to be strong in all five categories, it is not an absolute necessity. In fact, if you contrive something about innovation for a project that is inherently not innovative, your credibility will be damaged.

As you write your proposal in response to this *Workbook*, we encourage you to keep these mandatory review criteria in mind. They represent important 'hot buttons' that should be given special emphasis. By judiciously highlighting such information with italics — making it easy to find it — you will increase the reviewer friendliness of your proposal.

Review of New Investigators' Grant Applications. If you are a New Investigator by NIH's definition (never have served as a Principal Investigator on a PHS-supported research project other than an R03, R15, R21 or mentored K Award [K01, K08, K22, K23, K25]) you should indicate that fact by checking the "Yes" box on the PHS398 Cover Page Supplement. Study section members are instructed, when that block is checked, to apply three of the five mandatory review criteria differently. The following is a quote from the *REVIEW OF NEW INVESTIGATOR R01s - Guidelines for Reviewers* (http://cms.csr.nih.gov/ResourcesforApplicants/PolicyProcedureReview+Guidelines/Review+of+New+Investigator+R01s.htm): "When reviewing these applications [from new investigators], reviewers should keep in mind the experience of and the resources available to the new investigator. When considering an application from a new investigator, the five updated review criteria must be evaluated in a manner appropriate to the expectations for and problems likely to be faced by a new investigator. Specifically, when considering:

> *Approach:* more emphasis should be placed on demonstrating that the techniques / approaches are feasible than on preliminary results that develop a hypothesis. Assessment of feasibility should be based more on rationale and training than on preliminary experimental data.
>
> *Investigator:* more emphasis should be placed on training and research potential than on track record and number of publications.
>
> *Environment:* there should be evidence that the necessary space, equipment, and time to perform the research are available to the principal investigator."

Given these guidelines to reviewers, you should now realize that, if you are a New Investigator, there are additional 'hot buttons' that you must punch compared to what an established investigator would have to do. For example, you should stress the feasibility of the approach *in your hands* when you write your *Research Design and Methods* section. You should make certain that you underscore in your *Biographical Sketch* that you are *independent* in your current position, and that the quality of your training is commensurate with a career in biomedical research. Other places where you can get this message across are: 1) the subsection of your *Specific Aims* section in which you describe why you are particularly well prepared to undertake the proposed research, and 2) in the *Preliminary Studies* section, wherein information is sought that will help to establish your experience and competence as an investigator. Finally, the issue of space / time for research should be emphasized in the *Resources* section.

In addition to the five mandatory evaluative criteria, "in accordance with NIH policy, all applications will also be reviewed with respect to: 1) The adequacy of plans to include both genders, minorities, and their subgroups, as appropriate for the scientific goals of the research. Plans for the recruitment and retention of subjects will also be evaluated. 2) The reasonableness of the proposed budget and duration in relation to the proposed research. And, 3) The adequacy of the proposed protection for humans, animals or the environment, to the extent they may be adversely affected by the project proposed in the application." Review of NIH applications also now requires consideration of whether children have been included in relevant human studies.

Identify the Potential Reviewers of Your Application. In addition to understanding everything that you can about the review process, itself, you also need to understand as much as possible about the actual reviewers of your proposal. Unlike most granting agencies, NIH gives you the opportunity to recommend which study section should review your application. As will be detailed later, you make that recommendation to the Center for Scientific Review (CSR) in the PHS398 Cover Letter Component that will be a part of your electronically submitted proposal. If you are not already certain which study section would be most appropriate for the review of your application, there are several approaches that can be taken to identifying it. One approach is to use the CRISP database. Enter into the CRISP Query Form (http://crisp.cit.nih.gov/crisp/crisp_query.generate_screen) the names of researchers who are currently active in the area in which you plan to work. This will produce a list of their funded grants. The last line on each printout will be titled on the left, "IRG" (Initial Review Group), with the identifying acronym of the review panel that recommended the funding of that grant on the right. If most of the applications that are similar to the subject of your proposal were reviewed and recommended for funding by a single study section, it is almost surely the one that is applicable to your needs, as well. If you don't know how to translate the study section's acronym into its name you can do so either by referring to *Activity Codes, Organization Codes and Definitions Used in Extramural Programs* (http://grants.nih.gov/grants/funding/ac.pdf) or by referring to the alphabetical list of acronyms that can be found at http://www.csr.nih.gov/Committees/rosterindex.asp. Note that there are four different kinds of study sections that are managed by the Center for Scientific Review: (1) regular standing study sections and continuing special emphasis panels; (2) fellowship study sections; (3) SBIR/STTR study sections; and (4) special emphasis study sections that meet for one time only. The first of the four will usually be the category to select. At that site (http://www.csr.nih.gov/Roster_proto/section1.asp) each entry consists of the name of the panel, its acronym, and the name of its Scientific Review Administrator. By clicking on the name of the panel, you will find its charge – i.e., a description of the spectrum of subjects it is responsible for reviewing. By clicking on the acronym, you will bring up the current roster of its members and the rosters for its last three meetings, including both permanent and temporary members. By clicking on the name of the SRA, you will open an e-mail message to him/her. Because appointments of NIH reviewers are for four years, with terms ending on June 30, at the

worst, 75% of those listed under "Membership Roster" will potentially be sitting in judgment of your application. This is the 'consumer group' to which you will be marketing your idea.

Once you have identified the study section you want to target, run a PubMed search (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi) on any of its members with whom you are unfamiliar. Also, identify each individual's current NIH funding by using his/her name to probe the CRISP database. Making these searches will give you each individual's specific expertise, allowing you to better understand your 'consumer group.' The information you obtain will help you write your application to be maximally appealing to members of the targeted panel. You also make this analysis to assure that, even though the targeted panel is the most appropriate one, there isn't a kind of expertise that is missing, without which your application could not be reviewed fairly. If you discover that there is such a lack, you cannot suggest a candidate to provide that expertise, but you can call attention to the need for that kind of input in your PHS398 Cover Letter Component. You should also follow up with a call to the Scientific Review Administrator of the scientific review group after you receive your assignment.

You also identify members of the panel to assure that one of your closest competitors is not a member. If you find that such a person is there, you are encouraged to point that out, with justification, in your PHS398 Cover Letter Component. The Cover Letter Component is never seen by the reviewers. Any other investigators who should not be involved in the review of your application should also be listed, with credible justification, just in case outside opinions are sought by the SRA. As is made clear in the *PHS SF424 (R&R) Application Guide* (section 1.4 of Part I), you should also call the SRA to express concerns about conflicts or reviewers who you are concerned may be biased in some way.

A final reason for determining who will be sitting in review of your proposal is to assure that the work of anyone on the panel who has made a particular contribution to the area you are addressing is included when you write the Background and Significance section.

TIP: After submitting your application you will receive an electronically generated "notification of assignment." It will tell you to which Institute(s) / Center(s) and scientific review group your proposal has been assigned. If you disagree, you should immediately request reassignment, in writing: Division of Receipt and Referral, Center for Scientific Review, NIH, 6701 Rockledge Drive, Suite 2030, MSC 7720, Bethesda, MD 20892-7720.

Two Audiences on the Scientific Review Group

KEY POINT: You must appreciate that you are writing your proposal for *two distinctly different audiences*: 1) your assigned reviewers and, 2) everyone else on the panel.

It is a fact of life that reviewers read the proposals to which they are assigned and rarely do much more than glance at the others until they come up for review at the panel meeting. Thus, review panels consist of two audiences: a minority audience – the primary, secondary and tertiary reviewers who were assigned to review your proposal and who have read every word of your application – and a much larger audience – everyone else on the panel – that is relatively / completely ignorant of its content. Each member of the panel has an equal vote. *It is absolutely critical, therefore, that you write in such a way that members of the majority group can become enthusiastic advocates for funding your proposal.*

At the meeting (see http://www.csr.nih.gov/Video/Video.asp), the primary reviewer – your principal spokesperson – will present your application orally to the rest of the panel. S/he will describe what you propose to do and then follow with his/her critique. The secondary and tertiary reviewers will then present anything about the application that was not described by the primary reviewer and offer their critiques. While these oral presentations are being made, the remaining members of the study section – the ones who haven't seen your grant application before – will be trying to 'catch up,' so that they can make an informed vote in the 15 or 20 minutes they have to invest in your application. To become informed they will be doing two things: listening to the oral presentations of your three assigned reviewers and, at the same time, they will be reading parts of your application in an effort to corroborate or refute what they are hearing. That is why the sections that they will read – the Project Summary/Abstract, the Specific Aims section, and the significance paragraph from the Background and Significance section – must be written in such a way that they can be comprehended by the reviewers while someone is talking to them. The strategies for doing so are covered in later chapters that are devoted to those parts of your application.

Requesting Assignment to More Than One Awarding Component. If the subject of your proposal has relevance to the missions of two or more of NIH's Institutes and Centers, you can request that your application be assigned to more than a single awarding component. You should provide justification for your request using the PHS 398 Cover Letter Component. Primary assignment should be requested to the awarding component that is most relevant to the subject of your proposal. Should that entity decide not to fund your application, if the Center for Scientific Review has honored your request (they don't have to do so), your proposal will automatically be sent to the other awarding components for consideration there. In other words, you get more than a single chance at funding. For this reason, if you have a so-called cross-cutting subject, you should definitely make a request for multiple assignment.

MODIFICATION OF A SUBMITTED APPLICATION

Withdrawing and Resubmitting a Proposal. Proposals that are submitted early can be corrected and resubmitted without penalty. If you decide to withdraw and resubmit your application after the deadline, such action will cause your proposal to be considered late. This necessitates that you provide justification for your lateness in an accompanying cover letter (PHS 398 Cover Letter Component). You cannot check the "Changed/Corrected Application" box in block 1 of the SF 424 (R&R) Cover Component on a late application.

Correcting Validation Warnings and Errors. "Warnings" and "errors" may be generated during the initial validation of your application. A "warning" pertains to something in your proposal that, while acceptable, is of concern. You have the option of making changes – or not – in response to a warning. "Errors" are completely different. They represent problems that are "unacceptable," i.e., significant inaccuracies, inconsistencies, omissions, or formatting problems that cannot be accepted by the Center for Scientific Review. If errors are identified during agency validation, they must be corrected and the application resubmitted with the "Changed/Corrected Application" box checked in block 1 of the SF 424 (R&R) Cover Component. The same approach would be used if you make changes in response to a "warning." It is also necessary to justify changes made in response to a warning or error message in an accompanying cover letter (PHS398 Cover Letter Component).

Submitting Supplemental or Corrective Information. If you discover a substantive error in your application after it has been received and validated, or you want to update it on the basis of significant new information (e.g., important new preliminary data, a new publication, or a highly relevant award) you can do so. You must wait until the application has been assigned to a Scientific Review Group, however. Once you have the name of the panel's Scientific Review Administrator, you must obtain his/her permission to send such information. If s/he agrees to accept the supplemental material, you must send it to him/her directly, i.e., not through the Grants.gov submission system. Remember, however, that such material is not an official part of the application and, while reviewers are usually willing to consider such material in the evaluation of your proposal, they are not required to do so. Therefore, if you decide to submit such material, try to limit it to no more than one page.

DEVELOPMENTAL STEPS FOR CHAPTER FOUR:

1. Obtain and read all of the instructions that are pertinent to the preparation of your application. Read them thoroughly several times.
2. Obtain electronic versions of the forms that will be used in the preparation of your application. Make certain that they are the current forms (revision of 09/2004).
3. Understand that you will have to pass a compliance review and all that it entails before your application will be reviewed for scientific and technical merit.
4. If you are a McIntosh user, make sure that you follow the special instructions that are given in section 2.3.3 of Part I of the PHS SF424 (R&R) Application Guide.
5. Appreciate the importance of grantsmanship – the packaging and presentation of your idea and the related research – in developing advocacy for funding your proposal.
6. Take full advantage of the resources that are available to you through the NIH Web site.
7. Develop a system of hierarchical formatting that will allow reviewers to discern at a glance what is subordinated to what in your application.
8. Become proficient in applying the strategies that are used by newspaper journalists to make readers want to read what they write.
9. Concentrate on developing a spare, clear style of writing that emphasizes brevity and ease of comprehension.
10. Download and view NIH's videotape of the meeting of a mock study section.
11. Understand the review criteria for evaluation of NIH grant applications.
12. Understand how the review criteria differ for new investigators.
13. Identify the most applicable study section for review of your proposal.
14. Investigate the scientific backgrounds of the members of the panel you have identified, using both their publications (PubMed database) and the abstracts of their current NIH grants (CRISP database).
15. Understand the concept that review panels consist of two audiences and what that means to the way that your application must be written.
16. Know how to correct / modify a submitted application.
17. Know how to respond to validation warnings and correct errors that are flagged during the initial, compliance review.
18. Know how to correct substantive errors / update your application after it is submitted.

CHAPTER 5

RESPONSE TO PRIOR REVIEW

TIP: The single most important reason for failure of resubmitted applications, in our opinion, is lack of full and substantive response to all of the constructive criticism offered by prior review-

The approach that is described in this chapter will help you to avoid the trap of selective response to a previous review.

Your Summary Statement (critique) will consist of a Résumé, which is a summary of the discussion of the application that occurred at the meeting. This component is not included as a part of reviews of applications that were not scored and discussed, i.e., of those that were 'triaged.' The next, "Description" component, will be the abstract (usually verbatim) that you included in your proposal. Next, you will receive each reviewer's unedited critique. Usually, there are three of these. Several additional administrative sections, including comments on the budget, will follow, with the final section being a roster of all of the reviewers who were involved in the evaluation of your proposal.

Photocopies of the Summary Statement should be made and distributed to any Co-Investigators. Each member of the research team should independently read the Summary Statement several times. With each reading, new insights will likely be acquired. During a final reading, anything that can be interpreted as criticism should be highlighted. The Principal Investigator should collect the independently highlighted copies of the Summary Statement and then make a list of all criticisms that were lodged against the previous proposal. The criticisms should be ranked from most to least important under each section of the Summary Statement, i.e., under the Résumé and the critique of each reviewer.

Once the list of all criticisms has been created, the Principal Investigator and Co-Investigators should decide how they will respond to each. If the decision is made to reject a recommendation of the previous reviewers, strong and logical justification for doing so should be formulated.

At this point, for scored applications (i.e., those that weren't triaged), the Principal Investigator should contact the relevant Program Office, a step that is encouraged in the letter that accompanies the Summary Statement, as well as in the *PHS SF424 (R&R) Application Guide* (see section 1.4 of Part I). His/her name and contact information can be found in the upper left corner of the first page of the Summary Statement. In most cases, that person was sitting in the room during the review of your application. Therefore, after you have gleaned everything that you can from what was written in the Summary Statement, s/he can tell you what is 'between the lines' of your Summary Statement. Thus, s/he can be very helpful with respect to refining the nature of your response. *You are missing a very important means of improving your response to the previous review if you do not take advantage of this opportunity.*

The response to prior review takes the form of an "Introduction" that precedes the Research Plan (up to three pages for R01s and R15s; one page for R03s, R21s and revision [formerly competing supplemental] applications). The Introduction does not count against the page limit for the Research Plan. The Introduction should be restricted to responses to criticisms of the former application. In other words, it should not be used to call attention to things that the prior reviewers identified as positive. To do so can backfire, because new reviewers may think that highlighting positive comments of former reviewers constitutes not-so-subtle influence of their thinking. In addition, it isn't necessary to refer to such positive comments, because the new reviewers will have read and taken note of the positive, as well as the negative, comments that are contained in your prior review.

To create the Introduction, for each criticism, quote in italics the first few words and the last few words separated by three-or-more periods. For example, *'Even though the applicant has ..... how she will respond.'* Beneath each quote, summarize your response to that criticism, followed by the page number where the related change in the Research Plan begins. Providing the page number is a very reviewer-friendly approach, because most new reviewers will only read your responses to the previous review. Providing the page number for each response facilitates their ability to do so.

Note that "summarize" is underlined in the preceding paragraph. One reason applicants fail to make a full and substantive response is that they think that everything must be included in the Introduction. They include so much detail that they run out of room, especially in the 1-page Introduction to an R03, R21 or revision application, before they can respond to everything that was criticized previously. They just don't have enough room to respond fully to all criticism that is contained in the prior review. Summarizing each response in the Introduction and providing a page number to the details in the Research Plan solves that problem.

Changes in the revised Research Plan must be marked so that reviewers can find them easily. NIH prohibits shading or underlining text as a means of delineating what has been changed. "Bracketing, indenting, or changing typography" are recommended by NIH. We, by contrast, recommend a more subtle, but equally effective, approach, which is marking changes with a simple, vertical line in the left margin of the Research Plan. This is the same approach that is used to mark revisions in the "Track Changes" part of the Word toolbar. *The approach used to indicate changes in the revised application should be described at the beginning of the Introduction.* If changes have been so extensive that almost everything has changed, that fact should be noted at the beginning of the Introduction, which precludes the need to mark changes in the Research Plan.

As will be seen in chapter 22, we strongly recommend that grant applications be reviewed by knowledgeable colleagues prior to submission. For revisions, it is critical that such review include scrutiny of the Introduction and the changed parts of the application. We recommend, therefore, that pre-submission reviewers be given the final draft, including the Introduction and the Summary Statement from the previous review. The pre-submission reviewers should be asked to comment, specifically, on whether the response to the previous review is full and substantive and, if not, why not.

Resubmission of 'triaged' applications is significantly more problematic, in our opinion. By definition, such applications have a lot wrong with them. Often, reviewers selectively criticize such proposals, providing only enough criticism to justify the recommendation to triage. Therefore, when an applicant fully and conscientiously responds to the review of a previously triaged pro-

posal, s/he is not working with a 'full deck.' The resubmission often is triaged again, because on the second review, the applicant learns about everything that wasn't included in the first review. As a result, it is very difficult to get initially triaged applications funded, even with all three tries that are allowed for a given idea. Even if success is ultimately realized, it usually takes all three tries and the better part of two years to reach that point. A better strategy, in our opinion, is to change an initially triaged application enough that it will become a new submission. That requires more than cosmetic changes. For example, if the initial proposal was focused on mechanisms of ischemic necrosis in a myocardial infarction model, providing the same mechanisms could be investigated by switching to stroke as the model, it would be worth considering such a change, rather than responding to the 'triaged' review. The targeted Institute would be different, the review panel would most likely be different, and the applicant would have the advantage of using the criticism from the 'triaged' review to sharpen the design of the new submission.

After preparing your Introduction you must upload it into one of the NIH/PHS-specific components of the SF424 application package, the one titled "PHS 398 Research Plan." The relevant parts are reproduced below:

OMB Number: 0925-0001
Expiration Date: 9/30/2007

PHS 398 Research Plan

1. Application Type:

From SF 424 (R&R) Cover Page and PHS398 Checklist. The responses provided on these pages, regarding the type of application being submitted, are repeated for your reference, as you attach the appropriate sections of the research plan.

*Type of Application:

☐ New ☐ Resubmission ☐ Renewal ☐ Continuation ☐ Revision

2. Research Plan Attachments:

Please attach applicable sections of the research plan, below.

1. Introduction to Application (for RESUBMISSION or REVISION only)				
2. Specific Aims		Add Attachment		
3. Background and Significance		Add Attachment		
4. Preliminary Studies / Progress Report		Add Attachment		
5. Research Design and Methods		Add Attachment		

Section 1, "Application Type," will reflect which box you checked in field 8 of the SF 424 Cover Page Component. In other words, checking "Revision" there will automatically cause "Revision" to be checked in this later component. Checking "Revision" will also activate the buttons in section 2 that are to the right of "Introduction to Application." Convert your Introduction into a PDF file and upload it using the "Add Attachment" button on line 1 of section 2.

DEVELOPMENTAL STEPS FOR CHAPTER FIVE:

1. Distribute copies of your Summary Statement to any Co-Investigators who are a part of the application.
2. Independently, each member of the research team should read the Summary Statement – read the Summary Statement – and then, after having cooled down – read the Summary Statement – again

3. Decide whether a triaged' application is one that should be responded to or whether it would be wiser to change it enough to make it a new application.
4. If the decision is to respond, each member of the research team should highlight anything in the review that can be construed as constructive criticism of what was proposed.
5. The Principal Investigator should use all highlighted copies to make a list of all constructive criticism that was lodged against the previous proposal.
6. Prioritize the list from most to least important, the most important being criticisms that were made by more than one reviewer.
7. Convene a meeting of all Key members of the research team to decide how to respond to each prior criticism. Those with 'triaged' applications should skip to # 8.
8. For scored applications (those that were not 'triaged'), contact the Program Officer using the contact information in the upper left corner of the first page of the Summary Statement.
9. Create the Introduction. First, quote each criticism by using its first and last few words. Do so in italics.
10. In a paragraph that is subordinate to each criticism, provide a summary of the response to that criticism.
11. Follow with the page number from the Research Plan where the detailed response to the criticism can be found.
12. Mark the changes made in the Research Plan with a vertical line in the left margin. If changes are so extensive that it would be impractical to mark them individually, so note at the beginning of the Introduction.
13. Before submitting your revision, have members of your pre-submission review committee (see chapter 22) evaluate the changes you have made to assure that a full and substantively response to all constructive criticism that has been provided by the prior reviewers. Be sure to provide each pre-submission reviewer with a copy of the Summary Statement so that s/he can ascertain whether you have made a full and substantive response, or not.
14. Convert your Introduction into a PDF file.
15. Upload your PDF "Introduction" file into the PHS 398 Research Plan Component.

CHAPTER 6

CREATE A WRITING SCHEDULE

Availability of time is one of the most important factors that influences the success or failure of an applicant's proposal-writing efforts. No one has an excess of time! Your competitors who are also writing NIH grant applications will be confronted by this same problem.

> TIP: Efficient time management while writing your grant application is one of the most important ways that you can gain an edge over your competitors.

Two kinds of time are needed to write a competitive grant application: (1) lead time before the deadline, and (2) quality time while you are preparing the proposal.

LEAD TIME PRIOR TO THE DEADLINE

There are two kinds of deadlines at NIH, ones that recur on a regular basis (see section II.E in Part I of the PHS 398 Instructions) and ones that are set by specific solicitations (e.g., Requests for Applications [RFAs] and Program Announcement [PAs]). Applicants have no control over the latter deadlines. Therefore, the way to maximize the amount of lead time between formal announcement of such a funding opportunity and its deadline is to have a strategy – a system – that will assure that you discover such opportunities at the earliest possible time. Thus, it is smart business, in our opinion, to subscribe to listserves and e-mail alert services that will help to assure such early discovery.

Listserves. Examples of useful listserves include the one for the NIH Guide for Grants and Contracts (http://grants1.nih.gov/grants/guide/listserv.htm). Subscribers to it are notified each Friday of every Notice, Request for Application, and Program Announcement that has been issued during the preceding week. Greater specificity can be gained by additionally consulting one of the specialized listserves listed at http://list.nih.gov/cgi-bin/show_list_archives.

E-mail alert services are very useful means of assuring early notification of a funding opportunity. We recommend the one at Grants.gov (http://www.grants.gov/SubscribeAll) and those sponsored by the Community of Science (http://www.cos.com/services/funding.shtml) and InfoEd (http://www.infoed.org; see SPINPlus, under "Pre and Post Award"). Both of the last two require that you institution be a subscriber in order to use them; most universities and other research institutions are members of one or the other.

QUALITY TIME WHILE PREPARING THE PROPOSAL

When you have the luxury of planning ahead to meet a recurring deadline, we estimate that four-to-six months are needed to do the best job of which you are capable in developing your

grant application while, at the same time, you contend with all of your other competing professional and personal priorities. In our opinion, most applicants cannot write a competitive NIH proposal within the 40-hour "paperwork burden" that is estimated in the PHS 398 instructions.

Why are four-to-six months needed to optimize the developmental process? Because, for example, time is required to thoroughly review the literature and the already-funded grants that are contained in the CRISP database. These are critically important steps in evaluating your competition and in positioning your project for success. Time is needed to maximize the programmatic relevance of your idea with respect to the priorities of the agency that you plan to target. Significant time must be invested in writing the proposal – not just the Research Plan, but every aspect of it. And finally, time is required to obtain pre-submission review of your application by knowledgeable colleagues – one of the most important steps that you can take in the developmental process

We recommend that you start by freeing up as much time as you can. Conduct an inventory of both your professional and private obligations. Anything that can be dropped, deferred and/or delegated (the three 'D's) should be eliminated from your schedule. Discuss with your unit leader and supportive colleagues how they can help you. For example, with appropriate planning and coordination, you may be able to find temporary stand-ins for committee assignments, swap clinical rotations with colleagues, and/or find short-term substitutes for teaching responsibilities. The operational words in the previous sentence are 'planning' and 'coordination.' Such arrangements can't be made at the last minute.

For any responsibilities you can't drop, defer or delegate we suggest that you deal with them in blocks of time. For example, while you are writing a grant application, telephone (including cellular) calls should be accumulated by an assistant or on an answering machine / voice-mail service. Return the calls during a scheduled block of time. E-mail messages should be handled similarly: respond to them during a single time during the day. If you are teaching, set up office hours and require that students stick to them. By using these strategies, you can minimize disruptive influences that would otherwise degrade the quality time that you need for development of your grant application.

The most efficient approach to writing your grant application involves blocking of time for that purpose, too. Set aside one-to-two hours or more per day. Protect that time by making it a formal entry in your calendar, and then have the discipline to keep that appointment with yourself. If you are a 'morning person,' set the time aside in the morning. If you are more efficient at some other time of the day, set the time aside then. To optimize the efficiency with which you utilize this block of time, we recommend that you set up a writing schedule – a timetable – that allows you to accomplish a little bit on your application each day. Consistent writing of a little bit every day results in development of the application without it being that daunting, intimidating process that we all think about in association with writing a grant application. You can do the best of which you are capable while, at the same time, you balance all of the other competing priorities that you couldn't drop, defer or delegate. The writing process is facilitated, in our opinion, by writing the parts of your application out of the order that they appear in the Table of Contents. You will put them into that order when you submit the application, but you will write the various components out of that order. By doing so, you will use the momentum that you have developed while writing one section to help write the next one, and you will minimize the potential problem of having internal inconsistencies develop between related sections that would be written widely separated in time if the 'Table of Contents' order were followed. The many applicants who have used this approach and given us feedback have uniformly found it positive. The

following timetable is the one that we recommend be used to guide the writing phase of the developmental process.

Task Set	Complete by:
Complete *Specific Aims* section, significance paragraph of *Background and Significance* section, and *Introduction* (response to previous reviewers [if applicable])	
Prepare Cover Page Component and PHS 398 Cover Page Supplement Component	
Send *Specific Aims* section and significance paragraph to Pre-Submission Review Committee (and to Program Officer, if s/he has agreed to review for programmatic relevance)	
Research Design & Methods section: develop subsection for specific aim 1; *Project / Performance Site Locations* Component	
Research Design & Methods section: develop subsection for specific aim 2; prepare *Biographical Sketch* for all Key Personnel and Other Significant Contributors	
Research Design & Methods section: develop subsection for specific aim 3; International Collaborations (if applicable); Environmental Impact; and Resource Sharing Plan(s)	
Research Design & Methods section: develop additional aims, if applicable	
Develop Human Subjects (if applicable); Vertebrate Animals (if applicable)	
Background subsection of *Background & Significance*; *References Cited* section	
Preliminary Studies *section (or Progress Report, if competing renewal)*; Appendix material, if any	
Facilities & Other Resources Component; *Equipment* Component;	
Develop *Budget Component* (Modular or Detailed) and Budget Justification	
Project Summary/Abstract; Project Narrative; *Title;* Table of Contents; *prepare Cover Letter Component*; obtain letters of support (if applicable)	
Assemble final draft. Proof, correct and make final adjustments	
Pre-submission review of the application: Submit to Pre-Submission Review Committee	
Revise draft; send to Research Office by (check this date with the Research Office):	
Submit application to meet deadline – not later than:	

Add or subtract specific aims, as needed. If you will propose to use either Human Subjects and/or Vertebrate Animals, insert those sections into the schedule. Be realistic when you set up your schedule. Take into account all of your professional and personal obligations. It is of no

value whatsoever – and is actually detrimental to the process – to set up a timetable to which you can't adhere. Generally, the span of time should be 16-18 weeks. If you have a deadline that doesn't allow that amount of time, you will have to compress the writing and pre-submission-review schedule, accordingly. Whatever you do, don't eliminate pre-submission review.

Finally, we recommend that you not try to write your proposal perfectly the first time – that you not agonize over every word. The initial goal should just be to get your thoughts down in writing, because if you're like most people, you're much better at rewriting than you are at getting it right the first time. We want you to avoid blocking on a sentence or a paragraph, to the extent that you become frustrated with your lack of progress. Just remember, if you can't find exactly the right words the first time, don't let it throw you. Simply write down whatever comes to mind at the time and go on. You'll find the inspired wording later – during the rewrite.

DEVELOPMENTAL STEPS FOR CHAPTER SIX:

1. Subscribe to relevant listserves and e-mail alert services, if you are seeking funding opportunities.
2. Identify all professional and personal obligations that you can drop, defer, or delegate in order to free up time in your schedule.
3. Identify the part of the day when you can spend one-to-two hours of quality time working on your grant application every day.
4. Set up a realistic writing and pre-submission review schedule, taking into account all other professional and personal commitments that you can't drop, defer or delegate.

OVERVIEW: PART TWO

THE TEMPLATE OR MASTER PLAN FOR YOUR PROPOSAL

Once you have completed all of the activities that are summarized in Part One, you will be positioned well to begin development of the grant application, itself. The process should begin with development of the all-important *Specific Aims* section (section A of the Research Plan) and the significance subsection of the *Background and Significance* section (section B). These parts will introduce reviewers to everything that is important and exciting about your proposal.

Chapter seven, "*Specific Aims* Section: Conceptual Overview & Creating a Bullet Outline," addresses the conceptual approach that underlies formulation of the *Specific Aims* section, provides the specific purpose for each of the thirteen components that collectively comprise this section, and will help you to develop the bullet outline that will be the foundation from which this section is developed.

Chapter eight, "Writing the *Specific Aims* Section, will take you, step-by-step, through the development of a first draft of your *Specific Aims* section. This will begin with expansion of the bullet outline, which will then be refined to provide an integrated overview of everything that is important about your proposal.

Chapter nine, "Significance Subsection of the *Background and Significance* Section," will focus on development of the paragraph that is arguably the most important one in the entire grant application. You will be guided through a three-part approach to writing this part of your proposal.

These are the parts of your application that will provide the 'blueprint' – the template or master plan – for development of the rest of your Research Plan. If these sections are written well, the rest of the Research Plan becomes relatively easy to write. Thus, we encourage you to make the investment in them that will maximize the positive impact that they can have on both the preparation and review of your application.

CHAPTER 7

SPECIFIC AIMS SECTION: CONCEPTUAL OVERVIEW & CREATING A BULLET OUTLINE

TIP: Strategically, the *Specific Aims* section should be written to create a 'partnership' with the reviewers who will represent you at the review-panel meeting. You provide a conceptual framework on which they can orally hang the details of what will be done.

The *Specific Aims* section is critical to writing a first-class NIH grant application. It is the most important section that is related to the development of your proposal, in our opinion, because as noted earlier, it becomes the template or master plan for the rest of your Research Plan; if this section works well, everything else will fall naturally into place. The *Specific Aims* section has an equally important additional role: leading the majority of reviewers decide to vote a fundable priority score for your proposal. This group of reviewers – those who were not assigned your application – will not have read your proposal before it comes up for evaluation at the review-panel meeting. Regardless, these reviewers have an equal vote in establishing your proposal's priority score. You need to appreciate that they will be doing two things at the same time: listening to your spokespersons – the primary, secondary and tertiary reviewers – as they state your case while, at the same time, they will be reading parts of your proposal – the *Specific Aims* section and the *Project Summary / Abstract* (i.e., Description) – as a means of either corroborating or refuting what they are hearing. If you have tried to read and comprehend something that is replete with detail at the same time that someone is talking to you, you know that it is impossible; either understanding of what you are reading or what you are hearing suffers. This fact informs our approach to writing the *Specific Aims* section. It must be written to help the majority of reviewers 'catch up' so that they can cast an informed vote at the end of your 15-to-20 minute window of opportunity at the review-panel meeting.

TIP: The secret to optimizing the impact of this section is writing each component to meet its purpose, which requires in-depth understanding of what each is meant to accomplish.

In addition to each component having a specific purpose, each has to be linked to others it relates to in such a way that a linear progression of logic is created. The flow of logic must be compelling – so compelling that it leads reviewers to a position of advocacy without them knowing that they are being led. An additional aid in leading reviewers is 'labeling' of each component in such a way that there can be no question in the reviewer's mind as to why the information has been included (see chapter 8). The latter strategy increases the reviewer friendliness of your proposal by reducing the amount of work that reviewers have to do as they read what you have written.

CREATE A BULLET OUTLINE

TIP: Outlining is your key to developing linkage and to avoiding unnecessary detail!

One of the most important tips that we can give you regarding development of this section is to begin by creating a bullet outline. In our opinion, outlining is the key to writing a powerful *Specific Aims* section. When extra verbiage is removed and you are dealing only with brief bullets you can see better how the various components relate to each other and can recognize and eliminate extraneous detail. Without the interfering clutter of unnecessary words, the outline approach also allows you to see whether or not the logic and the concepts flow, as they must in a competitive application. We will help you to create your bullet outline by asking you to make a series of responses in a set order. Your responses will become the bullets in your outline, which you should create in a separate computer file. Once you are satisfied with the bullets you have written and how they link to each other, we will ask you to expand them into sentences that will collectively become the first draft of your *Specific Aims* section. You can then modify, amplify, re-write and otherwise refine your first draft to produce the version that will become the template for writing the rest of your application.

The explanations that follow will give you a strong working knowledge of the purpose of each component, as well as how it must be linked to the others when you create your bullets. We recommend that they be presented in four paragraphs:

Introductory Paragraph

Opening Sentence. Begin with an interest-grabbing sentence that immediately establishes the relevance of your proposal to human health. You want to convey that, by supporting your proposal, the reviewers will be helping NIH to accomplish its goals, which are to improve the control of disease, enhance human health, and advance understanding of biological systems. For example, were you writing an application about a biochemical defect you suspect is the cause of manic-depressive illness, your bullet for this component should not focus on the fundamental biochemistry. Instead, you should create one that makes clear how important manic depression is in this country, both from the standpoint of numbers of people affected and the cost of caring for such persons. Be careful that this opening sentence does not state information that would be intrinsically obvious to the review group that you are targeting. Now, write a bullet that conveys the medical importance of your area of interest.

Current Knowledge. Your assigned reviewers will likely be the members of the panel who are most qualified to review the topic you are presenting. If not experts, they will be close to having that level of expertise. The remainder of the panel will be less knowledgeable. This component has the purpose of getting everyone at the review-panel table up to speed with respect to what is currently known about the topic of your proposal. It is not meant to be a comprehensive overview. Rather, it should consist of a few cleverly written sentences that are designed to bring reviewers from the most important, older knowledge to the edge of the field as it exists today. This component has the additional purpose of setting the scene for presentation of the gap in the knowledge base or unmet need that your application will address. Write bullets that flow logically, one into the next, in such a way that they will lead the reviewer to the 'jumping-off point' for your application, i.e., what needs to be done next.

Gap in the Knowledge Base / Unmet Need. This component is one of the most important in creating the Specific Aims section, because all of the logic downstream flows from it. It should

be simple and direct. It should very specifically identify either the gap in the knowledge base or the unmet need that will drive your application. This component must be a clear and logical extension of the 'current knowledge' component by reflecting the next logical step that is required to advance the field.

Gap in the Knowledge Base to be Addressed: Now that your reviewers have an appreciation for what is known, you need to introduce them to essential information that is missing and, therefore, holding back your field. The gap in the knowledge base that you highlight should be the one that you will address with this research proposal. Write a bullet that clearly defines the gap that you want to fill.

Statement of Need and Objective Evidence of Its Existence: If you are writing an application that will be driven either purely by need or one that will be a 'hybrid' – a proposal that offers both a statement of need and, later, a central hypothesis – you should substitute this component for the gap in the knowledge base described in the paragraph, above. Write a single bullet that denotes the need. For example, it might reflect the need for renovation of space (the kind of statement that would drive a construction grant) or purchase of an expensive piece of equipment (equipment grant). Follow with one or more bullets that provide objective evidence for existence of the need (e.g., your own assessment of need and/or the publications of others that corroborate existence of the need).

The Gap / Unmet Need as a Problem. The purpose of this component is to convey that the gap / unmet need represents an important problem. It is a problem because its existence blocks vertical advancement of the field. Write a bullet that conveys what the vertical step is that is being blocked.

At the conclusion of the first paragraph, the reviewers should understand that the research area is medically relevant, they should be up to speed with respect to current knowledge in the field, and they should understand that there is a gap in the knowledge base that constitutes an important problem.

'What, Why, Who' Paragraph

Long-Term Goal. The purpose of this component is to project the continuum of research that you will pursue over the course of multiple periods of grant support. Create a bullet that is broad enough to encompass the gap or unmet need that you have delineated in the first paragraph. Also, it must be realistic, i.e., something that is clearly achievable over a period of time. For example, if you were a cancer researcher, it would *not* be credible to write that your long-term goal is to cure cancer.

Objective of this Application. This component defines the purpose of your grant application, i.e., what it seeks to accomplish, *which must be either to fill the gap or meet the need that you delineated in the first paragraph.* It must be clear that your objective is the next logical step along the continuum of research that is projected by your long-term goal – that linkage must exist between the two. Write a single bullet that describes your objective. Be certain that your objective has a defined end point, i.e,, that it is not indeterminate in focus. For example, "to study" something would not be an appropriate goal; how would you know when you had "studied" it

enough? In addition, such an objective puts too much emphasis on process and not enough on the product of the research.

Central Hypothesis and How Formulated.

The central hypothesis must link to the objective, because the latter will be accomplished by testing the former. The purpose of the hypothesis is to provide focus for your grant application. Thus, your hypothesis must be 'directional,' i.e., it must give direction to the research. It must be your 'best bet' as to how to accomplish your objective. Write a single bullet that conveys what your central hypothesis is. A good hypothesis must be objectively testable and cannot project a predetermined conclusion. It should also have 'parts' that serve to set up the specific aims, which will be the means of testing it.

How formulated. Write additional bullets that tell your reviewers how the central hypothesis was formulated – how you focused on this starting point from among others as your 'best bet.' Your own preliminary data are the strongest basis for formulating the hypothesis. That bullet should be the first of these. Published work of others, if any, should be highlighted in additional bullets and presented as complementary to your own preliminary results.

Rationale. The purpose of this component is to convey to reviewers why you want to undertake the proposed research. In most cases, research is performed because it will yield new knowledge that will advance the field. Thus, *your rationale should tell reviewers what will become possible after the research is completed that is not possible now.* It must pass that litmus test! This component must link back to the problem that you framed at the end of the first paragraph. There, you posed the gap / unmet need as a problem because its continued existence blocks the next step in the field from being taken. Once the proposed research has been completed you will be able to take the blocked step – that is why you want to do the research. You get few opportunities in a grant application to excite reviewers. This is one of them. Cleverly written, the rationale – why you want to do the research – can truly be exciting because it conveys that the expected outcomes will clearly advance the field vertically. Now, without setting up redundancy with the 'gap as a problem' component, i.e., without using the exact same words, write a bullet that delivers that message.

Well-Prepared. As you know, two of the five mandatory criteria used to evaluate NIH grant applications are "Investigators" and the research "Environment." You should end the second paragraph by conveying why you, your colleagues, and your research environment distinguish your application from one that could be written by investigators elsewhere who are equally qualified on the basis of expertise alone. Thus, the purpose of this component is to tell reviewers why the research team you have assembled is better prepared to perform the proposed research. First and foremost among the things that distinguish your research team are your preliminary data, which both allow you to formulate a focusing central hypothesis and support the feasibility of your aims. Your competitors, though they may be equally qualified on the basis of expertise, cannot bring such direction to the research. Begin this series of bullets, therefore, with one that summarizes why your preliminary data are supportive of the project. Continue with additional, complementary bullets, e.g., such things as the combined expertise of your research team (e.g., basic and clinical researchers working together to provide the entire spectrum of expertise necessary to obtain a definitive outcome) or extensive experience with a demanding model. Conclude with a bullet or two about your research environment and why it is particularly supportive of the kinds of research that will be performed. This may be because of essential core facilities, provision of skilled technical support by the institution, or because you are surrounded by colleagues who have complementary research interests (i.e., other investigators with whom to dis-

cuss and evaluate your data). Be specific with all of your bullets here! Avoid the temptation of indulging in clichés (e.g., state-of-the-art equipment) and empty generalities (e.g., Dr. X is an outstanding molecular biologist). Write as many bullets as you can, *but make certain that they reflect things that are truly distinguishing.*

> At the conclusion of the second paragraph, the reviewers should understand: 1) in general, what you plan to do; 2) that what you are proposing will fill the gap in the knowledge base that you have delineated; 3) that your group is well prepared to undertake the proposed work, compared to others; and 4) that the work will be done in an environment that is conducive to its success.

Specific Aims 'Paragraph'

As the name implies, this component conveys specifics about the research. The approach to creating the aims differs for hypothesis- and need-driven proposals.

Hypothesis-Driven Applications. Although there are disciplinary exceptions, *most reviewers of NIH grant proposals demand hypothesis-driven research.* The aims are probably the most difficult components of the section to write. They must clearly grow out of your central hypothesis because their purpose in a hypothesis-driven proposal is to test all aspects of the hypothesis. Thus, with respect to linkage, there must be complete concordance between the aims and the parts of your central hypothesis. They need to be brief, informative, attention-getting 'headlines' that will attract a reviewer's attention and whet his/her interest. Each aim should convey why that part of the research is being proposed, not what will be done. Under no circumstance in a hypothesis-driven application should your aims be descriptive, i.e., project what is best referred to as 'look-to-see' research (I will do something, look to see what happens, and then describe whatever that outcome is – the antithesis of hypothesis-driven research.). For this reason you should avoid using words in your aims that connote a descriptive approach, such as (but not limited to) compare, correlate, describe, catalog, or investigate. Neither should they be statements regarding 'what' will be done, i.e., the process that will be involved should not be emphasized. What you want them to project is 'why' — conceptually, why do I want to do this part of the research? They should deliberately be broad and open-ended, but then focused by a working hypothesis. 'Identify the mechanism that is responsible for macrophage activation.' is an example of an aim that is written at a broad, open-ended level. If the purpose of the aim is to "identify the mechanism," then the working hypothesis must be the 'best bet' as to what the mechanism is. It might read something like, 'The *working hypothesis* for this aim, based on preliminary data that will be presented later (see *Preliminary Studies*), is that the mechanism entails binding of IFN-γ to its receptor, which activates STAT-1α and then, in concert with other transcription factors, up-regulates the expression of genes that result in activation.' By narrowing the focus to a specific entity with the working hypothesis, the applicant avoids criticism that the aim is unfocused and open-ended. The trap of writing an aim like, 'Determine whether STAT-1α initiates macrophage activation.' has also been avoided. With such an aim, if it is STAT-1α, the applicant has accomplished something important; however, if it's not, the applicant (and the reviewer) is left with nothing other than a negative outcome, which is rarely enough to satisfy NIH reviewers. This approach will minimize the likelihood that your aims will be seen either as descriptive or as an 'unfocused fishing expedition.'

The example below will illustrate further how to avoid the trap of writing descriptive aims. It should clarify why well written aims in hypothesis-driven proposals are most often an answer to the question, "Why am I proposing this part of the research."

CONVERSION OF DESCRIPTIVE SPECIFIC AIMS ('WHAT' WILL BE DONE) TO ONES THAT ARE CONCEPTUAL ('WHY' THE WORK IS PROPOSED)

'WHAT' (will be done?):

1. ***Determine genotypic allele frequencies of the AAA and BBB genes in a closed, unselected, avermectin / milbemycin-naïve helminth population.***

2. ***Determine genotypic allele frequencies of the AAA and BBB genes in a population of helminths that have been highly selected by frequent long-term treatment with avermectin / milbemycin.***

3. ***In parallel with research objective #2, select for alleles that convey resistance by frequent treatment of a naïve population of helminths with avermectin/milbemycin.***

4. ***Determine the genetic basis for resistance to avermectin / milbemycin in helminths.***

Note that each of the above is a detailed description of 'what' will be done. The first three set up different populations of helminths. When we ask 'why' the investigator wants to create these populations the answer is that the outcomes of subsequent comparisons are expected to allow him/her to identify alleles that are candidates for conferring resistance. The more appropriate aim, which combines the first three from above, is the conceptual, 'why' aim that is presented below as #1. The same approach can be used to correct aim #4, above: why does the investigator want to do that? Because s/he wants to identify which of the candidate alleles is causally responsible for the development of resistance. Writing aim #2 that way much more clearly conveys 'why' the research is proposed.

'WHY' (is it being done?):

1. ***Identify candidate resistance alleles.***

2. ***Establish which candidate alleles are causally responsible for avermectin / mibemycin resistance.***

While these are good examples of conceptual, 'why' aims, as noted above, they would be fundamentally flawed if left to stand alone. Why? Because they are open-ended and completely lacking in focus. Thus, each aim should be focused by its own working hypothesis, which the applicant would present in a paragraph that is subordinate to the related aim. This is one reason why preliminary studies are so important at the R01 level: the data generated allow formulation of a focusing hypothesis for each aim. It isn't necessary that the research proposed be complete already, as some would contend. However, enough has to have been done to allow the applicant to formulate a strong working hypothesis that provides direction – focus – for the proposed studies. Thus, for the first 'why' aim, above, the applicant would have had to have done enough preliminary work to narrow the focus from all genes to a select few. A brief sen-

tence (or two) that describes how the hypothesis will be tested should also be included. For example:

1. Identify candidate resistance alleles.

The *working hypothesis* for this aim, based on data that will be presented under *Preliminary Studies*, is that specific alleles of the AAA and BBB genes explain the development of resistance. The approach used to test this hypothesis will be comparison of genotypic allele frequencies in AM-naïve and AM-resistant helminths.

Note that the broad aim 'headline' states unequivocally that candidate resistance alleles will be identified, and that the subordinate paragraph focuses the search on a specific pair of genes, based on the investigator's own preliminary data. Later, when studies under the aim are detailed in the *Research Design and Methods* section, the investigator would present alternatives to which s/he would turn in the unlikely event that the working hypothesis would prove to be invalid. In the example above, investigation of alternative genes would be proposed, along with a brief explanation as to why they are the next most likely possibilities. The combination of the broad aim, focused by a working hypothesis, which is then complemented later by 'escape-hatch' alternatives, is a powerful way of assuring reviewers that, regardless of how the original working hypothesis test, the objective of the aim will be accomplished.

As noted in the paragraph that preceded the example, the aims you present must fully test your central hypothesis, nothing more and nothing less. Ideally, each aim should be seen as testing a specific 'part' of your central hypothesis. If an aim isn't clearly related to testing some aspect of the central hypothesis, it is likely to be rejected by the reviewers as superfluous.

Two-to-five aims are needed (we recommend two or three as ideal). The page limitation for the Research Plan precludes developing any more aims than five substantively. Each aim should be of approximately equal weight, i.e., equal in importance to the other aims and projects an approximately equal amount of work. The first aim must flow logically into the second, and so on; *however, no one of them can be absolutely dependent on an expected outcome of an earlier aim.* Why? Because, should the critical aim either not be achieved or yield an unexpected outcome the subsequent, dependent aim(s) could not be pursued as proposed. For example, consider an application on gene regulation that has as its first specific aim, 'Clone the promoter [regulator] for gene X.' Examination of the subsequent aims reveals that all of them are dependent on availability of the promoter. Such an application would be fundamentally and fatally flawed because, if the promoter isn't cloned, the rest of the work can't be done. The applicant should have realized that fact and cloned the promoter as part of his/her preliminary studies. Alternatively, an R03 could have been written to accomplish that part of the study as a stepping stone to a later R01 that would definitively develop the aims that are dependent on having cloned the promoter.

Using these tips, write bullets that summarize your aims. Follow each with another bullet that summarizes the working hypothesis for that aim. Make sure that the number of aims is concordant with the number of parts that are found in your central hypothesis.

Need-Driven Applications. The aims in a need-driven application set forth tasks that must be undertaken, in the order that they must be undertaken, to accomplish the objective. Thus, in contrast to a hypothesis-driven application, it is acceptable in a need-driven proposal to offer tasks that describe what will be done. The paragraph that is subordinate to a need-driven aim should summarize the approach that will be used to accomplish that paticular task.

'Payoff' Paragraph

> TIP: The purpose of this last paragraph is to inform reviewers what they can expect for a return if they vote to recommend funding of your application. This paragraph is particularly important in helping to develop advocacy among the majority of reviewers who have not read your complete application. It is a paragraph in which a great deal of effort should be invested, therefore.

Innovation. The purpose of the first component in the fourth paragraph is to tell reviewers why the proposed research is innovative. "Innovation" is one of the five mandatory NIH review criteria. It is the most subjective of the five. Because of this, reviewers appreciate knowing why the applicant thinks that the proposed research is innovative. Usually, it is because the proposed approach differs from that which has been taken by others. You may have created a new technology, for example, that will allow you to address problems that have thwarted others. You may be challenging dogma of your field or proposing something that will make – not in a cliché sense – a real paradigm shift. It is important to appreciate, however, that your project does not have to be innovative to be fundable; not all scientifically meritorious research is inherently innovative. Thus, this component is optional. If you are proposing valuable, must-be-done-to-take-the-next-step kind of research – but it is not inherently innovative, you will damage your credibility if you contrive something related to this mandatory review criterion. In such a case you should not try to punch this 'button,' realizing that you don't have to because it is an optional criterion.

Write bullets here, providing that you can do so credibly, that convey one or more reasons why your research/approach is innovative.

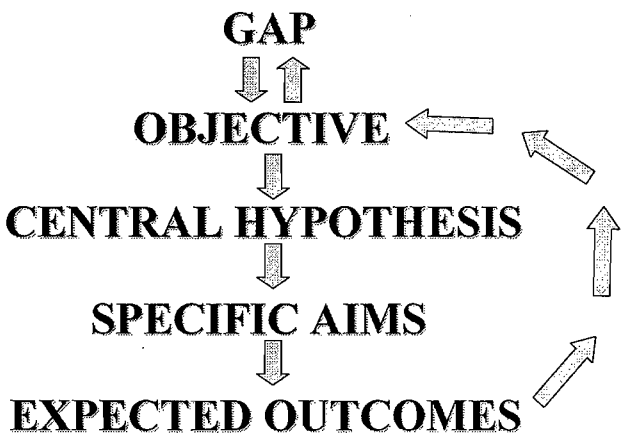
Expected Outcomes. These are the expected products of the research. In other words, these represent the 'payoff' that reviewers can except to realize if they vote to recommend funding of your application. We want you to include them here, together, rather than individually under the related aims, because reviewers can more easily see that they collectively validate your central hypothesis (that is what you expect) and, by doing so, attain the overall objective of the proposal. There should be at least one important expected outcome for each of your aims. There must be clear linkage back to the specific aims that produced them.

Now, write bullets that tell your reviewers what they can expect from your research as outcomes. As noted earlier, you need at least one for each aim.

Generality Regarding Positive Impact. This final part of the *Specific Aims* section must summarize the general impact of the expected outcomes. We recommend that you deliberately write a bullet that is a generality that segues into details that will be presented in the next, significance paragraph. In most cases, your positive impact bullet should make clear that, collectively, the outcomes will advance your field vertically, as well as contribute to the mission of the NIH Institute or Center that you are targeting.

After completing your bullet outline, print it and consider carefully how all of the elements relate to each other. Do they relate and link to each other logically and well? Remember that we called attention earlier to how important the phrasing of the gap in the knowledge base is, because that statement sets up everything downstream with respect to the flow of logic. As is shown in the figure, below, if you are proposing hypothesis-driven research, how you present the gap automatically sets up the objective, because the objective must be to fill the gap. When you write your objective, you set up your central hypothesis, because that is what must be objectively tested in order to attain the objective. When you write your central hypothesis, it ordains what the aims will be, because they are the means that will be used to test each part of your central hypothesis. The aims, in turn, dictate what the expected outcomes will be, and those, in turn must collectively result in attainment of the objective, thereby filling the gap. If you

LINEAR PROGRESSION OF LOGIC FOR A STRONG SPECIFIC AIMS SECTION©



are proposing a project that is driven purely by a statement of need, the only differences in the figure, above, would be that "GAP" would become "NEED" and the CENTRAL HYPOTHESIS would be eliminated. Otherwise, the progression of logic would be the same. Also, make sure that your long-term goal encompasses the gap in the knowledge base that you plan to fill. Check to be sure that the description of the gap as a problem, at the end of the first paragraph, links well with the rationale. The former should describe the gap as preventing an important step in the field from being taken, and the rationale should make clear that, once the research has been done, it will become possible to take that step. Spend as much time as you need to refine and perfect your bullets, making sure that they are as well crafted as they can be. If these work, the writing of this section, which is the subject of the next chapter, then becomes relatively easy.

DEVELOPMENTAL STEPS FOR CHAPTER SEVEN:

1. Appreciate that there are two audiences for whom you are writing: the minority audience (primary, secondary and tertiary reviewers) and the majority audience (those reviewers

who have not read your application prior to the time that it comes up for review at the review-panel meeting).

2. Realize that this section of the application is written for the second, majority audience.
3. Understand the strategy that underlies this section, which is to provide a conceptual framework that will allow your representatives at the meeting (primary, secondary and tertiary reviewers) to hang details on it, thereby helping reviewers who are relatively ignorant of your application reach a point where they can cast an informed vote.
4. Understand the purpose of each component that makes up the Specific Aims section and how it must be written to meet its purpose.
5. Appreciate how the components must be linked to each other to create a linear progression of logic.
6. Create a bullet outline that includes each of the thirteen components that comprise the *Specific Aims* section.
7. After leaving it alone for a day or so, return to it to determine whether it can be improved. Continue to do so until you cannot make it any better.
8. Seek constructive criticism of the bullet outline from the members of your research team.
9. Continue to work on the outline until each component meets its purpose, each is linked to the others in the way(s) that it should be, and the progression of logic is linear. When you reach this point, you are ready to proceed to chapter 8.

CHAPTER 8

WRITING THE SPECIFIC AIMS SECTION

> Instructions for PHS 398 Research Plan Component / Specific Aims Section: "List the broad, long-term objectives and the goal of the specific 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. One page is recommended."

In the previous chapter, we introduced you to the purpose of each of the thirteen 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 quoted instructions in the box, above, the recommended length for this section is one page. Appreciate that it is only a recommendation, not an absolute restriction like the page limitation for the Research Plan. We recommend that your deliberately write more than one page – about 1.25 pages. There are two reasons why. First, we want you to include more in this section than NIH wants you to. It is very difficult to get all that we want you to include on a single page without it coming across as choppy. Second, the significance paragraph, which begins the next *Background and Significance* section, begins on the second page of the Research Plan. If your application is reviewed late in the meeting, reviewers may be too burned out to turn the page if they see that the *Specific Aims* section ends at the bottom of the first page. Thus, they would miss finding the significance paragraph, which in our opinion is the most important paragraph in your grant application. By deliberately running the Specific Aims section onto the second page you force them to turn the first page, thereby guaranteeing that they will see the significance paragraph. If they have the time they will read it, because every reviewer recognizes the importance of this part of the application.

As a philosophical approach to writing grant applications 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 comprehend what is being presented in this section. The approach we have developed informs reviewers, especially those – the majority – who will not have seen your application before it comes up for consideration at the review-panel meeting, of exactly why information has been included. It minimizes the risk of being pedantic or condescending while doing so. The approach entails 'labeling' certain of the components in such a way that there can be no question as to why you have included the related information. Labeling of key sentences also helps to lead reviewers seamlessly through what you have written. The approach makes comprehension easy for reviewers, because there is absolutely no effort involved in understanding why material has been included. As you expand your bullets we will make suggestions as to where and how to create these informative 'labels.'

There is a second approach that we recommend that you use: italicize key words to make them easy for reviewers to find. As you proceed through this *Workbook,* you will find that we recommend italicizing key words, phrases and even sentences. *Judicious use* of highlighting to call attention to things that you know members of the review panel will need is reviewer friendly and, therefore, good grantsmanship. We suggest the use of italics as the least obtrusive way to do so. If you are using either Arial or Helvetica as your typeface single words or several words don't stand out that clearly when only italics are used. We recommend, therefore, that you also underline single words or several words to make them stand out. Phrases or entire sentences in these two typefaces stand out, so you should not underline them. To do so is overuse of highlighting – to the point that it can be an aggravating distraction. If you are using Georgia, *which is what this typeface is,* italics alone stand out adequately and underlining is not needed, even for single words. The same is true for Palatino Linotype, *which is what this typeface is.* As you expand certain of your bullets we will call you attention to words that we recommend you italicize in the Specific Aims section.

Finally, we recommend that you include few, if any, citations in this section. This part of the application is being written for the majority of reviewers who will not have seen your application before it comes up for review at the meeting. They will not have time at the meeting to look up references, even if you would provide them, and most of them will not be close enough to your subject that they will recognize specific references, even if you give them author / year. Thus, with the exceptions that we will call attention to, we recommend that you <u>not</u> cite the literature in this 'overview' section.

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 you write 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 convincingly convey what is known about your subject area. The first sentence should be labeled to signal what 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 that which is contemporary, i.e., to the edge of the field as it exists today.

Gap in the Knowledge Base / Unmet Need. Next, expand the bullet that you wrote to delineate the gap in the knowledge base or unmet need that will be the subject of this 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, now expand the bullets that provide objective evidence for existence of the need. If the publications of other investigators are used as one means of supporting existence of need, cite their work.

Gap / Unmet Need as an Important Problem. Now, write a sentence that expands your bullets regarding why the gap in the knowledge base / unmet need is an important problem. This will be the concluding sentence of the introductory paragraph. It should be 'labeled' in such a way that reviewers are certain to understand that the gap / unmet need is a problem. For example, you might begin it with something like, 'Lack of such knowledge represents an important problem because, until the knowledge becomes available, ...' or 'Continued existence of this need represents an important problem because, until it is met, ...' The sentence would be completed by describing the vertical step in the field that is being blocked by continued existence of the gap / unmet need.

What, Why, Who Paragraph

> TIP: An important tip that will help to better link your long-term goal, objective and central hypothesis is to avoid the temptation to interpose explanatory information – extraneous details – between them. These three components should ideally be immediately juxtaposed, so that there is a seamless flow of logic from the 'forest' (the long-term goal) to the 'tree' that will be the subject of this application (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. Write a comparable sentence 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.

Overall Objective. Now, expand the bullet you wrote into a single sentence that conveys what the objective of this application is – what you expect to accomplish. 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 either be to 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 the phrase "which is the next step toward attainment of our long-term goal." Including something like this in the statement of your objective helps reviewers connect to the fact that there is linkage between this component and the continuum of research that is reflected by your long-term goal. The words "long-term goal" should not be underlined and italicized in this second use of them. When you have completed this sentence, make certain that it links back to the gap / unmet need component and that its relationship to your long-term goal is clear.

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. Expand the bullet that you wrote previously to convey your 'best bet' as to how the objective can best be attained. 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 truly 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 you use the work of others as support for 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?' Assure that this sentence links back to how the gap / unmet need was described as a problem at the end of the first paragraph. Be aware of the fact that the potential exists for setting up horrible redundancy if you don't paraphrase cleverly. Look at the words that you used at the end of the first paragraph to convey that the gap / unmet need is a problem because it blocks the next vertical step and make certain that the same ones aren't used here to indicate that, once the research has been completed, you will be able to take the blocked step. You must make the rationale seem fresh and exciting.

Well Prepared. Next, expand the bullets into sentences that summarize why you and your colleagues have the competitive edge in this area of research. In most cases, you will want to call attention to the full range of your research team's strong points, because no one feature is likely to be that distinguishing; it is usually the constellation of strengths that prepares you well to undertake the proposed studies. As noted in the preceding chapter, your preliminary data are the most important things that distinguish you from equally qualified investigators elsewhere. If you invoked your preliminary data earlier as one basis for formulating your central hypothesis, you can call attention to them again here without being redundant. Simply begin the 'well prepared' component with something like, 'In addition to our supportive preliminary data, we are well prepared to undertake the proposed research because ...' Continue with the other things that summarize why you and your colleagues are the ones who should do what is propose. The operational word in the preceding sentence is "summarize." In other words, there should not be a lot of detail included here. For example, instead of giving specifics about each participant's expertise, the point that you want to make is that you have the scope and breadth of expertise necessary to conduct the research successfully. Thus, the related sentence might read something like, 'In addition, we have assembled a research team with the scope and breadth of expertise (molecular genetics, bioinformatics and pathology) needed to complete all phases of the research successfully (see *Biographical Sketches*).' Similarly, if you have physical or intellectual resources that distinguish you and your colleagues from your competitors, summarize those with something like, 'Also, all members of the team are full members of the Center for Molecular Pathogenesis, which gives us access to important investigative resources, as well as other funded investigators who are pursuing research that is complementary to that what is proposed here (see *Resources* section).'

Specific Aims 'Paragraph'

Begin paragraph three with a sentence something like, 'We plan to test our central hypothesis and accomplish the overall objective of this application by pursuing the following *specific aims*:' Continue by expanding the bullets for your specific aims and the working hypothesis for each. Because the aims – the 'headlines' – are so important, we recommend that you set each off as a separate paragraph indented one tab and that you present them in bolded italics. Nothing in the subordinate paragraphs should be bolded or otherwise highlighted, except for '*working hypothesis,*' which should be italicized.

Payoff Paragraph

Innovation. If you have written a bullet that describes why your research/approach is innovative, expand it into a sentence that will open paragraph four. Don't be shy. If you have a claim to innovation, be direct about it: 'The proposed research is *innovative*, because ....'

Expected Outcomes. Continue by expanding the bullets that present your expected outcomes and why they are important. If you have used an 'innovation' sentence to open this paragraph, you might begin this component with something like, 'This innovative approach is projected to yield the following *expected outcomes*. First, _____, which is important, because _____.' Alternatively, if you did not open the paragraph with a statement about innovation, begin with a sentence something like: 'At the completion of these studies, we anticipate the following *expected outcomes*.' Continue to develop this component in the same way that you would if innovation had been used to open the paragraph (see earlier in this paragraph).

Generality Regarding Positive Impact. Conclude the fourth paragraph and your *Specific Aims* section by expanding the bullets that you wrote to generalize about the positive impact that your expected outcomes will have. Make sure that what you write sets up an easy transition into the next section, *Background and Significance*, which will begin with the 'significance' subsection. In that paragraph, you will detail and substantiate with specifics the general statement about positive impact that you write here. Thus, this concluding sentence for the *Specific Aims* section might read something like, 'The outcomes are expected to have important *positive impact* because the vertical step in the field they will enable resolves a persistent and pervasive health problem, as will now be detailed in the next paragraph.'

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. 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 it works. When you are done, you should have approximately 1.25 pages. If you have more than that, prune what you have written until you meet that mark. Switching to a font smaller than 11 point (more than 15 characters and spaces per linear inch), narrowing the margins, or taking out the open lines between paragraphs to reach the goal of 1.25 pages should not be considered because making such changes compromises reviewer friendliness.

EXAMPLES OF *SPECIFIC AIMS* SECTIONS

Prior to discussing how the *Specific Aims* section is uploaded for electronic submission we want to offer you two well-written examples, one hypothesis driven and the other driven by a statement of need.

EXAMPLE OF A HYPOTHESIS-DRIVEN *SPECIFIC AIMS* SECTION

SPECIFIC AIMS

Interferon gamma (IFN-γ) has been referred to as a 'master cytokine,' because of its many effects, both direct and indirect, on cellular components of the inflammatory and immune responses. It 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.* In recent years, considerable progress has been made in showing that the α subunit must work with a species-specific accessory factor (referred to as the β subunit) to transduce signals that are initiated by the binding of ligand. While it is evident that the binding protein of the receptor complex initiates signal transduction, it is still entirely unclear how this critical 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 production of the receptor for IFN-γ can be modulated on cell surfaces for preventive and therapeutic purposes. The *objective of this application*, which is the next step in pursuit of that goal, is to determine how production of the receptor's α subunit is regulated transcriptionally. The *central hypothesis* of the application is that there are both constitutive and stimulated regulation of transcription, and that such control is mediated through different sets of *cis*-acting response elements in the promoter of the gene that encodes the α chain. Our hypothesis has been formulated on the basis of strong preliminary data produced in our laboratory, having recently cloned and characterized the promoter for the gene that encodes the human α subunit (Galaway et al., in press; see *Preliminary Studies*). The *rationale* for the proposed research is that, once it is known how transcription of the α chain's gene is regulated, its production can be either up- or down-regulated pharmacologically in new and innovative approaches to the prevention and treatment of a variety of diseases. In addition to our supportive preliminary data, we are particularly well prepared to undertake the proposed research, because a multidisciplinary research team that has been assembled that has the scope and breadth of expertise and experience needed to obtain definitive outcomes (see *Biographical Sketches*). In addition, the work will be conducted in a research environment that is conducive to its successful completion. For example, it contains numerous funded investigators and shared resources that are dedicated to complementary structure/function studies of cellular receptors (see *Resources* section).

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

1. ***Identify the DNA response elements and transcription factors that regulate constitutive transcription of the α subunit's gene.***
   Based on work that will be presented under *Preliminary Studies*, the *working hypothesis* here is that one or more Sp1 sites are critical to the regulation of constitutive transcription.

2. ***Determine how stimulated transcription is up-regulated by two widely differing stimuli.***
   We *postulate*, again on the basis of preliminary data, that cyclic AMP response elements (e.g., CRE and AP-2) are essential to regulating stimulated transcription of the gene, and that the same elements will be involved, regardless of how stimulated transcription is activated.

The proposed work is *innovative*, because it capitalizes on a new means of identifying active response elements, which was developed by our group. In addition, it takes advantage of the cloned promoter for the subunit's gene, which to our knowledge is available in no other laboratory. With respect to *expected outcomes,* the combination of work proposed in aims 1 and 2 is collectively 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 will have an important *positive impact*, because the identified components are expected to provide new targets for preventive and therapeutic interventions that will aid the growing numbers of persons in this country who have either acquired or age-related immunodeficiency. In addition, it is expected that the results will fundamentally advance the fields of receptor biology and immunotherapy, as will now be detailed in the next section.

EXAMPLE OF A NEED-BASED *SPECIFIC AIMS* SECTION

A. SPECIFIC AIMS:

While cigarette smoking has decreased significantly in the U.S. general public during the past decade, evidence suggests that smoking has actually increased among women of child-bearing age, a fact that places these women and their unborn/newly born children at significant risk of both short- and long-term adverse health effects. The problem is particularly acute for low-income women and those who are members of ethnic minorities. With respect to adverse health effects on the new-born child, these include premature birth and the problems attendant to it; chronic pulmonary disease leading to increased risk of development of asthma; and increased susceptibility to infections. Of particular importance are recent studies indicating that almost 50% of mothers who quit smoking during pregnancy resume smoking by the time the infants are only three-months old. Of mothers who resume smoking, evidence suggests that cigarette usage actually increases relative to pre-pregnancy smoking levels. The primary reason often cited for resumption of cigarette smoking among new mothers is stress associated with caring for the new child, although this issue has not been extensively studied. Given the multiple adverse consequences of secondary cigarette smoke on newborn infants, there is a *critical need* to better understand the factors that impact the decision of new mothers to resume smoking. Objective evidence for existence of this need derives from our own assessment (see *Preliminary Studies* section) and independent recognition of it by Conway and her colleagues (2003). Its continued existence represents an important problem because, until the need is met, development of effective strategies to help these mothers avoid resumption of this health-destroying habit will likely remain problematic. In the absence of new and effective interventions, tens of thousands of newborns will continue to be placed at unnecessary health risk.

Our *long-term goal* is to improve the health of at-risk newborn children, especially those who are born to low-income and minority families with histories of smoking. The *objective of this application* is to identify the risk factors that will predict postpartum smoking relapse and, based on this information, design an intervention that will reduce recidivism among low-income, recently postpartum mothers who quit smoking during their pregnancies. Study subjects will be recruited from a community-based clinical setting for low-income women (see *Facilities & Other Resources section*). The intervention that we will develop will involve an integrated approach using principles derived from the Relapse Prevention Model, first described by Marlatt (1985), and the Child Health Model published by Barnard and Eyers (1979). Our *rationale* for this project is that its successful completion is expected to provide a strong, conceptual, evidence-based intervention that will effectively reduce recurrence of smoking postpartum. Both formative and summa-

tive evaluation will be used to corroborate / refute this expectation. In addition to our supportive preliminary data, we are well prepared to pursue this project because the Principal Investigator (J. Smith) has highly relevant experience, having investigated factors that contribute to substance abuse by pregnant, low-income mothers for her Ph.D. dissertation (see *Biographical Sketch*). In addition, the research team will have ready access to strong statistical support through our nursing Clinical-Research Center (see *Facilities & Other Resources* section for details).

We expect to achieve our objective by pursuit of the following two *specific aims*:

Specific aim #1: *Identify factors that will predict relapse of smoking among postpartum mothers.* Our preliminary data (see *Preliminary Studies* section) strongly implicate perceived self image of the mother as a predictive factor and suggest equally strongly that others also exist. These include, but may not be limited to, perceived infant irritability, perceived parenting stress and peer pressure as factors that are also predictive of smoking relapse after childbirth.

Specific aim #2: *Develop an intervention that will reduce recurrence of smoking postpartum.* We will establish an evidence-based strategy for development of an intervention that will target factors that contribute to smoking, thereby assisting new mothers to resist the urge to resume smoking.

This project is *innovative* because the approach to creating the intervention uniquely targets factors that will predict smoking recurrence and, thus, mothers who are at greatest risk. It is anticipated that this innovative approach will yield the following *expected outcomes*: First, we will have identified specific factors that will predict relapse of smoking among mothers of newborns. Second, we expect to be able to use these predictors to develop an effective intervention that will target members of a large, at-risk group. We further expect that the intervention will be applicable to implementation in a comprehensive, community-based clinical setting. The proposed plan for rigorous evaluation is expected to allow us to confirm the efficacy of the new intervention. As a result, in addition to contributing vertically to the field of smoking intervention, the results of this study are expected to have an important *positive impact*, not only on the health of at-risk newborn children, but also on that of their mothers, as will now be detailed in the next section.

After you have completed your *Specific Aims* section it must be uploaded into the SF 424 application kit. You do so using the PHS 398 Research Plan Component, which is reproduced below.

OMB Number: 0925-0001
Expiration Date: 9/30/2007

PHS 398 Research Plan

2. Research Plan Attachments:

Please attach applicable sections of the research plan, below.

1. Introduction to Application			
(for RESUBMISSION or REVISION only)			
2. Specific Aims	Add Attachment		
3. Background and Significance	Add Attachment		
4. Preliminary Studies / Progress Report	Add Attachment		
5. Research Design and Methods	Add Attachment		

Once you have the final version of your *Specific Aims* section convert it into a PDF file. Don't worry if there is a lot of 'white space' on the second page of your *Specific Aims* section. It won't eat up space because it will be eliminated after your application has been received and assembled by NIH. (You will have two business days after assembly to view and check the application to ensure that such deletions have been made.) Using the "Add Attachment" button on the right of line 2, section 2, upload the file. Once you have done so the other two buttons on the line will be activated, allowing you to view and/or delete the file. If later revisions must be made, delete the uploaded file and load the revision in its place using the "Add Attachment" button, as you did originally.

DEVELOPMENTAL STEPS FOR CHAPTER EIGHT:

1. Expand the bullets for your *Specific Aims* section into complete sentences.
2. 'Label' them in such a way that reviewers will know precisely what they are included to convey.
3. Highlight key words using either underlined italics (Arial or Helvetica typefaces) or italics alone (Georgia and Palatino Linotype typefaces).
4. Present the components in four separate paragraphs.
5. Use one-inch margins all around.
6. Open a line between paragraphs and between each aim and the subordinate paragraph of the preceding aim.
7. Make your specific aims stand out by presenting them in bolded italics.
8. Deliberately make the *Specific Aims* section extend onto page 2 of the Research Plan. Edit and refine the section until it reads well and occupies no more than 1.25-1.5 pages.
9. Convert the *Specific Aims* section into a PDF file.
10. Upload the *Specific Aims* section into the PHS 398 Research Plan.

CHAPTER 9

SIGNIFICANCE SUBSECTION OF THE BACKGROUND AND SIGNIFICANCE SECTION

GENERAL CONSIDERATIONS

Instructions for Significance Subsection of the PHS 398 Research Plan Component / Background and Significance Section: "State concisely the importance and health relevance of the research described in this application by relating the specific aims to the broad, long-term objectives. If the aims of the application are achieved, state how scientific knowledge or clinical practice will be advanced. Describe the effect of these studies on the concepts, methods, technologies, treatments, services or preventative interventions that drive this field."

An important part of our proposal-writing strategy is to gradually ratchet up detail as the reviewer reads further into the application. The idea is to get the reader 'hooked' on the conceptual, exciting parts of your proposal to the extent that s/he will want to read the details that are presented later. The second, *Background and Significance* section is where you begin to increase the level of detail that is included. It is meant to provide detail and citations that will extend and validate key parts of your *Specific Aims* section.

TIP: The purpose of the significance subsection is to help justify the need for the research that will be proposed. The 'spin' that you put on what is written here should be consistent with that purpose. Many applicants make the mistake of inadequately emphasizing significance, which seriously undercuts the fundability of their application.

The significance paragraph is a brief one (no more than 1/3-to-1/2 page) that is located at the beginning of the *Background and Significance* section (Section B). It is arguably the most important paragraph in your entire application, because the review criterion "SIGNIFICANCE" is so important. It should have a bolded, italicized title, ***Significance*** or ***Significance of the proposed research***, so that the reviewer will immediately recognize that this is the part of your proposal that addresses significance. What makes research significant? It is because benefits of some kind will accrue to application of the new knowledge. It is a difficult paragraph to write because of the potential for creating obvious redundancy with the preceding *Specific Aims* section. You can do so by ensuring that the content of the significance paragraph is written with appropriate paraphrasing and expansion of detail.

Because of its relative importance, this paragraph will be read by most, if not all, of the reviewers at the panel meeting – even those who haven't read your proposal prior to that time. It is

strategically important, therefore, to ensure that it is on the second page of the Research Plan, immediately after the final paragraph of the *Specific Aims* section, where all reviewers – even those who are seeing your application for the first time at the review-panel meeting – will be guaranteed to find it.

Unlike the preceding *Specific Aims* section, it is essential that you begin to cite relevant references from the primary literature here. You should avoid citing reviews, for the most part, because they tell the reviewer nothing about your command of the field's primary literature. We recommend that you cite references using author/year (e.g., Young, 1998; or Abelson and Rafferty, 2003; or Zaharias *et al.*, 2000). Your primary, secondary and tertiary reviewers will be close enough to being experts on the subject you are offering that they will be able to recognize most of the citations if they are presented as author/year. This prevents them from having to flip to the *Literature 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 which citations you have chosen to justify the need to do what you are proposing is not reviewer friendly. If you are a New Investigator and first author of most of your papers, another reason for using this approach is that it is a clever way to impress on reviewers that you have done the work that is being cited – something that is impossible to do if numerals are used.

CREATION OF THE FIRST DRAFT OF YOUR SIGNIFICANCE SUBSECTION

We recommend that you write this paragraph to have three readily identifiable parts:

> <u>Part 1</u> should detail and expand upon the fact that a gap in the knowledge base or unmet need exists and that its continued existence is an important problem. It should conclude with a sentence that explicitly describes the contribution that you expect to make with the proposed research. The contribution sentence should link back to what you wrote for your objective in the *Specific Aims* section, because your contribution will be the result of attaining your objective.
>
> <u>Part 2</u> is the statement of significance. It should appear approximately in the middle of the paragraph and should be a simple, direct statement regarding why the expected contribution is important – why it is significant. *This sentence is arguably the most important one that you will write in the application.* We recommend, therefore, that it be highlighted by putting it entirely in italics. Even if you are using Arial or Helvetica as your typeface, do not also underline because italics alone for an entire sentence will stand well enough and will not be obtrusive, as would be the case if you also underlined.
>
> <u>Part 3</u> should validate your assertion of significance. Because significance derives from benefits that could be expected to accrue to application of the new knowledge, this third part should consist of a list of such benefits. In most cases, the benefits will relate to advancement of the field in which the research is based. Any 'fringe benefits' that might accrue to the research should also be claimed. By fringe benefits, we mean outcomes that would be beneficial when extrapolated to other venues and/or fields, such as animal health.

If you follow this three-part format, you will write a strong, compelling significance subsection. Use the suggestions provided below to trigger your own ideas. Once you have a general feel

for what you want to write, get it down on paper. *The major goal here is to produce a first draft, i.e., something that can be revised and embellished later.* The most efficient approach will likely come from the developmental sequence that you used with your *Specific Aims* section: bullet outline, followed by expanding the bullets into sentences, after which the paragraph is created by integrating and linking the sentences appropriately.

Part 1:

Opening sentences. You want to use these sentences to expand and underscore the human health relevance of the problem that you have chosen to address. You have summarized this information earlier, in the opening paragraph of the *Specific Aims* section. Now, without being redundant, you should extend and embellish what was written earlier with specific details that are supported by citations of the literature.

Succinct statement of the problem. The preceding sentences should frame a clear and succinct statement of the gap in the knowledge base or unmet need that is the focus of the proposal. Paraphrase sufficiently and expand the detail to the extent that it does not seem repetitious of the less detailed statement of the gap / unmet need that you offered in the first paragraph of the preceding, *Specific Aims* section.

Statement of what your contribution is expected to be. This statement must be both strong and credible, i.e., not just a thoughtless cliché or empty generality that fails to highlight specifically what your contribution is expected to be. This is *not* meant to be a reiteration of the expected outcomes from the last paragraph of your *Specific Aims* section. Rather, as noted earlier, it should relate to accomplishment of the overall objective of the application. For example, 'As an outcome of the proposed investigations, we expect to have determined the mechanism of / distinguished between / overcome the problem of _____.' In other words, this should reflect the new knowledge that you expect to obtain.

Part 2

Statement of significance. Near the middle of the paragraph you should specify why your contribution will be important. This is another one of those times when you can't be shy: figuratively, this sentence should knock your reviewers right out of their chairs. You don't want the reviewer to have to interpret for him/herself why your projected contribution will be significant. Rather, you should tell him/her why it is significant, leaving no room for interpretation. This statement should be 'labeled' for what it is (e.g., '*The proposed research is significant, because .....*' and, as noted above, should be fully highlighted in italics, thereby ensuring that it can be found easily. In almost all cases, the sentence will be completed by underscoring that a vertical step in the field will become possible as a result of the contribution.

Part 3

Validation of the Statement of Significance With a Credible List of Benefits. The statement of significance you have just written must now be validated by presenting the benefits that will result from the vertical advance in the field that you expect to make? For example, how will it enable subsequent thinking and research? What benefits to human health are likely to ensue? How might it reduce the cost of health care. You don't have to be the direct contributor of the benefits. If it is credible to project that others will build on what you produce, e.g., through an enabling of their research, you are justified to claim such impact.

EXAMPLE OF A SIGNIFICANCE SUBSECTION

Significance. The subunit of the receptor complex for IFN- is the means by which this important cytokine binds to cells and initiates transmembrane signaling (Yang, 1977; Telifer and Gomez, 1988; Homer et al., 1995). Through it, IFN-γ exerts a wide range of immunoregulatory activities (Klein & Klein, 1995). Serious infectious disease problems are experienced by those who become deficient in the cells that produce this cytokine, either because they are lost as part of a disease process (e.g., AIDS; Galbreath, 2002; Toliver, 2003), during chemotherapy (Aikens and Osada, 2000), or as a natural consequence of the aging process (James and Kary, 1997; Zeleny et al., 2004). In addition to its homeostatic and defensive roles, in such diseases as Hashimoto's thyroiditis and asthma, IFN-γ appears to have a pathogenetic role, either because there is an overabundance of the cytokine (Alcott and Cochrane, 1998; Jones et al., 2000) or because cells become hyper-reactive to normal, physiologic concentrations (Sandoval, 1999). Responsiveness to IFN-γ can be modulated, either up or down, by altering the number of its receptors that are present on a cell's surface (Carlson et al., 2003). Such findings suggest that cellular functions that are attributable to the effects of IFN-γ could be modulated by altering the number of subunits that are available to bind it. Our contribution here is expected to be detailed understanding of how production of the receptor is regulated transcriptionally. *This contribution is significant because it is expected to provide the knowledge needed to develop pharmacologic strategies that will allow the number of α subunits on the surface of targeted cells to be regulated, either up or down.* Once such strategies become available, there is the promise that in diseases that are associated with hyper-responsiveness to IFN-γ, cellular responsiveness could be down-regulated by reducing the number of chains that are available to bind the cytokine. Conversely, when greater responsiveness is needed – for example, to ward off pathogenic microorganisms or, in the case of immunocompromised patients, opportunistic invaders – responsiveness of host-defensive cells to IFN-γ, could be increased. Thus, important advances in the therapy of diseases and complications that are associated with cellular immune dysfunction could be expected. It is also expected that what is learned will be equally applicable to the prevention/treatment of diseases of agriculturally relevant animals. In addition, the research will be of significance, because what is learned is expected to contribute to broader understanding of how components of other receptor complexes can be modulated as an approach to therapy. Furthermore, better fundamental understanding of how receptor proteins are transcribed can be anticipated.

DEVELOPMENTAL STEPS FOR CHAPTER NINE:

1. Appreciate that, of the five mandatory review criteria used to evaluate NIH grants, "Significance" is the most important. This subsection is where that criterion is primarily addressed.
2. Understand that this section should be written to help justify the need for what you are proposing.
3. Begin citing the literature here using author/year, rather than numerals.
4. Understand and use the three-part approach that is recommended for the development of this critically important subsection.
5. File this 'Significance' subsection as the first part of the Background and Significance section, to which you will add 'Review of Relevant Literature' subsection later.
6. Seek constructive criticism of your *Specific Aims* section and significance paragraph from members of your pre-submission review committee (see chapter 22 for details regarding its composition and use).

OVERVIEW: PART THREE

DEVELOPMENT OF THE REST OF YOUR APPLICATION

Once you have finalized your *Specific Aims* section and significance paragraph using input from members of your pre-submission review committee (see chapter 22 for details) and the Program Officer for the NIH program you are targeting you will be ready to develop the remainder of your proposal. This will be discussed in detail in the following chapters.

Chapter ten, *Research Design & Methods* Section: Narrative Description of What's to be Done, addresses development of the narrative part of your proposal – the *Research Design and Methods* section. You should allocate approximately three weeks to complete this section.

Chapter eleven, Background Subsection of the *Background & Significance* Section and the *Bibliography & References Cited* Section, summarizes the strategies that should be adopted in preparing the background subsection of the *Background and Significance* section, as well as what to include in the *Bibliography & References Cited* section. Approximately two weeks should be allocated for completion of these parts of the application.

Chapter twelve, *Preliminary Studies* Section / *Progress Report*, addresses what to include in one or the other of these parts of the application, depending upon whether you are submitting a new application or a renewal (formerly competing continuation). One week should be sufficient to complete this part of your proposal.

Chapter thirteen, *Senior/Key Person Profile(s)* Component and Biographical Sketches, will allow you to describe your research team in such a way that the feasibility of what is proposed in the Research Plan is maximally supported. Allow one week for completion of these parts.

Chapters fourteen and fifteen. Chapter 14, *PHS 398 Modular Budget* Component and Justification, describes how to prepare a modular budget and budget justification for R01, R03, R15, R21 and R34 proposals that have an annual direct-cost budget of $250,000 or less. If you will be offering a modular budget, ignore chapter 15, *SF 424 (R&R) Budget* Component (Breakout Budget), Justification and Cumulative Budget, and devote less than one week to preparation of your modular budget and justification. If you will be offering a breakout budget, skip chapter 14 and substitute the tips and strategies that are included in chapter 15. As its name implies, this chapter guides the preparation of a detailed budget and budget justification. Allow approximately one week to be fully responsive to chapter 15.

Chapter sixteen covers development of the important *Facilities & Other Resources* and *Equipment* sections – the physical and intellectual assets that constitute the research environment in which you and your colleagues will be working – as well as the *Project/Performance Site Locations* component. These sections are also important in establishing the feasibility of what is proposed. They should take less than a week to complete.

Chapter seventeen addresses *Human Subjects*, *Vertebrate Animals*, *International Collaborations*, *Environmental Impact*, *Resource Sharing Plan(s)*, and *Consortium/Contractual Arrangements* should one or more of these be applicable to your proposal. This part of the application should take approximately one-to-two weeks to complete, depending on the number of sections that have to be written.

Chapter eighteen offers tips on completing the two cover-page components that are part of an NIH application, the *SF 424 Cover Component* and the *PHS 398 Cover Page Supplement.* In addition, this chapter contains suggestions regarding how to use appendix material to your maximal advantage.

CHAPTER 10

RESEARCH DESIGN AND METHODS SECTION: NARRATIVE DESCRIPTION OF WHAT'S TO BE DONE

Instructions for Research Design and Methods Section of the PHS 398 Research Plan Component: "Describe the research design conceptual or clinical framework, procedures, and analyses to be used to accomplish the specific aims of the project. Unless addressed separately in Item 14 (Resource Sharing Plan[s]), include how the data will be collected, analyzed, and interpreted as well as the data-sharing plan as appropriate. Describe any new methodology and its advantage over existing methodologies. Describe any novel concepts, approaches, tools, or technologies for the proposed studies. Discuss the potential difficulties and limitations of the proposed procedures and alternative approaches to achieve the aims. As part of this section, provide a tentative sequence or timetable for the project. Point out any procedures, situations, or materials that may be hazardous to personnel and the precautions to be exercised."

GENERAL TIPS ON WRITING THE *RESEARCH DESIGN AND METHODS* SECTION

The *Research Design and Methods* section provides a detailed description of what will be done during the requested period of funding. We assure you that, providing you have been conscientious in the development of your Specific Aims section, although this is the longest section of the application, it will be one of the easiest for you to write. We recommend that you write this section now, even though it is the last one in the Research Plan, for two reasons. First, because *Research Design and Methods* is primarily an expansion of the *Specific Aims* section that you have just written, by writing it now you can capitalize on the momentum that you have developed. Second, writing the *Research Design and Methods* section at this time increases the likelihood that there will be maximal continuity with the *Specific Aims* section, despite the fact that they appear in the application at opposite ends of the Research Plan.

Before you begin to write, consider the following general points. Development of a strong *Research Design and Methods* section requires only that you answer the following five questions for each of your aims: 1) What will be done? 2) What are the means that will be used to accomplish the aim? 3) What might go wrong? 4) What alternative strategies will be used if something does go wrong? And finally, 5) What results are expected and why are they important? If you are a New Investigator, be especially clear that the work is feasible in *your* hands.

It is imperative that you develop your *Research Design and Methods* section using as its core the specific aims that you have already formulated. If your specific aims have been balanced appropriately, each should have approximately equal weight with respect to the number of pages that is devoted to it. To determine approximately how many pages you will have available for each aim, simply divide the total number of pages you expect to have for the entire *Re-*

search Design and Methods section by the number of aims. (Although this guideline will generally hold true, we can envision — and have encountered — situations in which this approach isn't appropriate, i.e., in which the aims must be weighted differently.)

As you conceive this section, remember that you should *always* put the most interesting and important, i.e., conceptual, material up front. Then, *and only then*, should you follow with the details. This approach is designed to 'hook' the reviewer's interest and make him/her *want* to read what you have written. If you think of your presentation as an inverted pyramid, its apex should be the title of the specific aim, i.e., that eye-catching, interest-grabbing 'headline' that you have written earlier. That 'headline' should be repeated here, verbatim, as the title of the *Research Design and Methods* subsection that will describe the research associated with the first aim. The title (headline) should be followed by paragraphs that gradually increase the extent of detail. Use the following format (or a similar one):

Specific Aim #1: Title.
- 1.1 Introduction
- 1.2 Experimental (or Research) Design:
  - 1.2.1 Study #1 (write an explanatory title)
  - 1.2.2 Study #2 (write an explanatory title)
  - 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 all subsequent aims.

Timetable
Future Directions

The format for each aim begins with an introductory paragraph that summarizes for the reviewer all of the essential *conceptual* information that is associated with pursuit and successful completion of the aim. Detailed description of individual studies should next be presented under Experimental Design, one study per paragraph. (For applications that do not propose actual 'experiments' you should title this subsection 'Research Design.') A separate paragraph with the subheading 'Expected Outcomes' should briefly summarize anticipated results and their collective impact. Offering such a paragraph is reviewer friendly because, when the main outcomes are presented together, in one place, an evaluator can more easily appreciate that they collectively achieve the aim's overall objective – especially when the outcomes are accompanied with one or more integrating sentences. A concluding paragraph, Potential Problems and Alternative Strategies, should acknowledge problems that might arise, as well as your proposed solutions to them (i.e., alternative approaches). NIH reviewers are directed to determine whether applicants anticipate problems and provide alternative tactics / strategies for them. Thus, this last subsection is responsive both to this directive and the instructions that are contained in the text box on page 66. This same format should be used to develop each of your subsequent specific aims. Near the end of the *Research Design and Methods* section, i.e., after all of your specific aims have been developed, you should include a timetable that relates the important activities that are proposed during the requested period of support. This is required by the instructions (see text box on preceding page). The last paragraph in the section, which should be titled something like '*Future Directions,*' should be used to tell the reviewer where you expect the proposed research to lead. You want to reinforce that the work described in this proposal is part of

the continuum of research that will ultimately allow you to attain your long-term goal. This last paragraph in the Research Plan is where you project that vision.

As a final general point, we suggest again here that you formally schedule your writing of this section in discrete blocks, i.e., that you write a little every day at a scheduled time. For example, commit to writing an introductory paragraph for one of the aims or the experimental design subsection. If you do this, and do it consistently, you should have no trouble in completing a first-rate *Research Design and Methods* section over the course of approximately three weeks while, at the same time, you manage all of your competing commitments.

TIPS ON WRITING THE *RESEARCH DESIGN AND METHODS* 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 do so by first writing bullets, which you then convert to text.

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

Introduction. You should title the first subsection under each of your aims, 'Introduction.' This title should be indented and be presented in bold Italics, as it is in this paragraph. Continue with text on the same line, as has been done here, with subsequent lines returning to the left margin. This introductory paragraph should be an overview that will let the reviewer know what is to be detailed in the remainder of the subsection, and why it is important to do what will be proposed. Key words in this paragraph (e.g., *objective, working hypothesis, approach, expectations, etc.*) should be highlighted in non-bolded italics to allow reviewers to find these components easily.

Begin this paragraph by justifying why the work under this aim needs to be performed. In doing so you should call attention to the part of the overall problem that will be addressed.

Next, write the *objective* that you have for this aim. Your aim's objective should be stated in such a way that its attainment will resolve the problem / question that you highlighted with your justification, above. You might begin this component with something like, 'The *objective of this aim* is to ____(solve the problem/answer the question that the aim will address)____.

Now, tell the reviewer how you will attain the objective that you have written. You will do so by testing the aim's *working hypothesis.* You followed the statement of this aim in the *Specific Aims* section with a working hypothesis. It should be repeated here, verbatim. It is critical that you repeat the working hypothesis in this introductory paragraph, because you want to underscore for your reviewers that the work to be done will be hypothesis-driven. We suggest that you phrase your working hypothesis something like: 'To attain the objective of this section, we will test the *working hypothesis* that _____ etc.' [NOTE: If you are writing an aim that is better driven by a statement of need, substitute that for the working hypothesis.]

To test your working hypothesis (meet the need), you will employ an *experimental approach* (*strategy*). Briefly summarize the principal approaches / methods that will be used to attain the aim's objective, e.g.: 'We will test our working hypothesis by using the *experimental approach* of etc.

The *rationale* for the work to be proposed under this aim – why you want to undertake this part of the research – should be presented next. The litmus test to be applied here is the same one that you used for testing the overall rationale that you wrote for the *Specific Aims* section. Does what I have written tell the reviewer what will become possible after the research proposed in this aim is completed, which is not possible now? Write an enthusiastic sentence or two that describe(s) your rationale for this aim. This is an opportunity to convey some of your excitement about the research to your reviewers. Write something like, 'The *rationale* for this aim is that successful completion of the proposed research will contribute a missing, fundamental element to our base of knowledge, without which the metabolism of compound X cannot be understood. The acquisition of such knowledge is critical to the development of improved therapeutic strategies for disease Y.'

Finally, summarize what the overall outcome(s) of this aim is / are expected to be. Phrase the outcome without parroting the aim, i.e., the title of the subsection. Remember to stay at a general, not detailed, level. You might write something like, 'When the proposed studies for aim #1 have been completed, it is our *expectation* that the metabolic pathway identified will entail phosphorylation of key amino acids in compound X's cytoplasmic domain. Such a finding would be of importance, because it would allow, for the first time, the development of novel and much needed approaches to _____.'

When completed, the introductory paragraph should occupy no more than 0.25-to-0.5 page. As you read it, the flow of logic in this overview *must* be clear and compelling – it must 'hook' the reviewer's interest in this aim.

Experimental (or Research) Design. In this subsection, you will present and discuss the activities that will be undertaken to accomplish the objective of specific aim #1. These activities must grow logically out of the approaches / strategies that you have summarized in your introductory paragraph. Keep in mind that each paragraph in this subsection should be a conceptual unit, i.e., a related group of activities that address a single point. Begin by creating bullets that denote the planned activities. Accompany each with an informative, interest-attracting title — *headline* — that will be used to introduce the related paragraph in your Experimental (Research) Design subsection. As for the aims themselves, no one of the activities should be absolutely dependent on an expected outcome of an earlier one. Make certain that the range of activities is sufficiently comprehensive that the outcomes will collectively attain the aim's objective. If that isn't clear, then you should revise the Experimental (Research) Design subsection until it is.

TIP: Many applicants make the mistake of including too little meaningful experimental detail in their Experimental Plan

Your next step should be to outline what will be entailed under each of the activities that you have listed. Because there is a great range of what might be included, depending on the subject, it is not possible to provide an all-inclusive list here. *You need to provide detail*, but it must be meaningful detail. In other words, it should not be routine methodological detail. Consider each of the following, at the least. When something in the list is found to be relevant create a corresponding bullet. Embellish the list with other points that are relevant to your research.

Write the title of your first study:

Approach to be used.

Method(s) required.

Essential reagents needed.

Critical equipment required.

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

Statistical analysis needed.

Controls (VERY important).

Replicates that will be needed.

Detailed expectations (VERY important).

How results will be interpreted.

Time required to complete the studies.

Next, write the title of your second study:

Consider each of the headings listed above for study #2. Continue this process for other studies that are needed, until you have completed a full outline of the activities that will be undertaken for Specific Aim #1.

Begin writing the Experimental Design subsection for Aim #1 by expanding the bullets you have written. As you write, remember that you *must* engender maximal enthusiasm and acceptance of your proposal. Avoid cluttering the reviewer's mind with material that is tangential to the main point that you want to make in each of your paragraphs. Write in simple declarative sentences that are free of jargon and nonstandard abbreviations and acronyms. Whenever it is credible to do so, use strong words, like 'expect,' and 'can.' Avoid weak words, i.e., those that unnecessarily plant a seed of doubt in the reviewer's mind about what you are proposing (see chapter 4 for examples). Emphasize the conceptual, because that is what is exciting and likely to attract the interest of the reviewer. Make sure, however, that you provide enough experimental detail, e.g., methodological, statistical, and appropriate controls, so that the reviewer will know not only what you plan to do but also how the resultant data will be interpreted. Don't make the mistake of going to the other extreme, i.e., of including too much detail. Doing so usually causes the reviewer to become hopelessly bogged down in a morass of boring minutiae (e.g., how many milliliters of this are added to how many of that, etc).

If you are a little confused about how much methodological detail to include, don't feel like you alone have such a problem; there is *always* the question of how much methodological detail is enough. As a general rule, detail only those methods that are either new to you or that are unique to your group, i.e., that wouldn't otherwise be known by the reviewers. New Investigators should present more detail than established investigators do, keeping in mind that they must convey that what is proposed is feasible in their hands. Also, ask yourself, "Have I erred on the other side and presented so much routine detail that the conceptual aspects of the aim have been obscured?" In other words, the solution to the dilemma can often be found by asking:

"Have I offered just the right amount of detail to convey that what will be done is feasible in my hands?" In other words, put yourself in the position of the reviewer. If you still don't have a clear idea of how much detail to include, we suggest that you avoid *routine* methodology – the kind of stuff that could be copied from a methods manual. This is especially true if your *Biographical Sketch* shows that you have been trained to use the relevant methodology and/or that you have published experience with the methodology in question. As a reviewer, would you require that a formally trained or experienced investigator describe a routine method that is commonly employed in the field? We think not.

If parts of your Experimental (Research) Design subsections are common to two or more of your aims, consider including a Methods and Procedures sub-subsection. If you decide to use this approach, to avoid redundancy we suggest that you put it either at the beginning or end of the Experimental (Research) Design subsection. If you think that it is necessary for reviewers to have methodological detail before reading about what will be done, the Methods and Procedures subsection should be inserted at the beginning of the subsection. The problem with doing so is that reviewers will have to read about methods before getting to the more interesting parts of the Experimental (Research) Design subsection. As an alternative, if reviewers won't need to have methodological detail early on, you can put the sub-subsection at the end of Experimental (Research) Design subsection, where they won't need to read it until they know why it is necessary to do so. If you take this approach, include an introductory sentence at the beginning of the Experimental (Research) Design subsection that alerts reviewers to the fact that methods and procedures can be found at the end of the subsection. By putting it at the end of subsection you make methodological detail available to the reviewers, but you don't force them to wade through it to get to the interesting, experimental parts of what you present. An approach that we recommend AGAINST is inclusion of a Methods and Procedures appendix. Doing so is likely to cause the person who performs the compliance review at the Center for Scientific Review to decide that you have tried to circumvent the page limitation for the Research Plan. Should this happen, your application would be returned without review.

Expected Outcomes. *It is critically important that this subsection be included for each aim.* The summary of expected results that you write here highlights the 'return on investment' that reviewers will be seeking. You should pull together the detailed results that were included under each paragraph of the Experimental (Research) Design subsection. As noted earlier, this gives the reviewer an appreciation for how they *collectively* attain the aim's objective. This overview should be more extensive than the summary sentence (or two) that you wrote about expected outcomes in the introductory paragraph for the aim. What you write here can usually be presented in a single paragraph that does not need to be extensive in its length – 1/3-to-1/2 page, at most.

To create this kind of paragraph, first collect all of the detailed expectations from the preceding Experimental (Research) Design subsection in one place. By doing so, you can then see how they relate to each other and how the overall outcome and importance of these findings can be summarized. As an approach, we suggest that you copy/paste all of your detailed expected results into a new file. After making your analysis of this material, write the paragraph to: (1) summarize the expected outcomes, and (2) convey how they collectively achieve the aim's objective. The Expected Outcomes paragraph is another opportunity that you have to create excitement, so make every effort to underscore why the expected results are important. There are at least two reasons why they are. First, they collectively attain the aim's objective and, second, they contribute to attainment of the application's overall objective. Be enthusiastic when 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.

Potential Problems and Alternative Approaches. Your goal here is to anticipate (and then eliminate) justified concerns of your reviewers. You do so by presenting alternative approaches / strategies that will be used to overcome potential problems that you have identified. You are directed to include such information by the instructions for this section, which are repeated again here: "Discuss the potential difficulties and limitations of the proposed procedures and alternative approaches to achieve the aims." An additional indicator of the importance of this subsection is included in the 'APPROACH' review criterion: "Does the applicant acknowledge potential problem areas and consider alternative tactics?" You know – and the reviewers will know – that no matter how hard you plan and prepare, problems can develop. *Failure to address this fact of life by not including this subsection can seriously undercut the fundability of your proposal*, as is suggested by the following quote from NIDDK's website.

> TIP: "The typical successful R01 ... [has] proposed experiments [that] are clearly described in detail, with suggestions for proceeding with the work should they fail to produce the expected outcome." (see *www.niddk.nih.gov/fund/grants_process/grantwriting.htm*)

If you are doing hypothesis-driven research, first and foremost among problems that reviewers will expect you to address is the possibility that the working hypothesis for the aim will prove to be invalid when it is tested objectively. In that unlikely event, what would you do? To what alternative would you turn? Reviewers will also be concerned about critical reagents: Will they be available and will they perform as expected? Will sufficient patients be available, if a clinical research project is being proposed? And will assays be as discriminating as you say they will be? The problems presented here should *not* be major ones. Major problems should be addressed under the Experimental (Research) Design subsection, not here. Rather, the problems included here should be ones that are, for example, similar to your getting into your new car on a warm, sunny morning and finding that it won't start. Although this would be totally unexpected and highly unlikely, it *could* happen. Alternative strategies that would still allow you to reach your destination might include calling a taxi, renting a car, calling a friend, bicycling, etc. You would have no problem whatsoever convincing even the most critical reviewer of the fact that, should this *unlikely* possibility actually occur, you would overcome the problem and still reach your destination. You need to list equivalent kinds of problems and alternative strategies here for your first specific aim. You need to assure reviewers that, regardless of what might happen, you will still reach your scientific 'destination.' Begin with what you would do, should your working hypothesis for the aim prove to be invalid. Then list other potential problems.

Summarize these potential problems in a paragraph, making certain that you have chosen only the most important and probable problems that might occur. Also make certain that the solutions 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) / strategy(ies) you would employ, should the problem be encountered. Note that all of the studies (alternative strategies) proposed should be addressed in the conditional verb tense, because they all represent things that would be done if,

and only if, they became necessary due to unexpected difficulties (i.e. not 'If this happens, we will ....' but rather 'If this happens we would ....')

For example: 'Our working hypothesis for this aim is _____. Although our preliminary data (see *Preliminary Studies* section) and what is extant in the literature (refs) strongly support that this hypothesis 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. Another potential problem is the way in which we have proposed to determine whether _____ will result in _____. We expect this approach to work because _____. We acknowledge, however, that this new, rapid and inexpensive technology may not prove sufficiently sensitive to quantify X in up to 5% of the samples. Were this problem to arise, we would employ the labor-intensive, expensive 'gold standard' approach (ref) that is known to have the necessary level of sensitivity. We have used this alternative method successfully in the past (ref). Another possible problem that could arise is_____. etc." Note that your plans to address potential problems should be written using conditional sentences. These are not what you will do. They are what you would do, should the problem actually arise. This subsection should be no more than 1/3-to-1/2 page long. We cannot underscore enough the importance of including this subsection in your Research Design and Methods section. If you think that reviewers are reading your Experimental (Research) Design subsection looking for ways to fund you, you are dead wrong. They will be looking for problems. If you have thought of the same problems and offer the solutions to them here, it will make a very positive impression on your reviewers.

TIMETABLE

This important section of the *Research Design and Methods* section is not included by most applicants, in spite of the fact that they are explicitly directed to include it (see text box at the beginning of this chapter). Its inclusion can be extremely helpful to reviewers, and to the NIH. It is

TIMETABLE					
AIMS/TASKS	YEAR 01	YEAR 02	YEAR 03	YEAR 04	YEAR 05
Specific Aim #1	←	—	—	→	
Title, Study #1.1	←	→			
Title, Study #1.2		←	—	→	
Title, Study #1.3			←	—	→
Specific Aim #2		←	—	—	→
Title, Study #2.1		←	—	→	
Title, Etc.			←	—	→
Specific Aim #3			←	—	—
Title, Study #3.1			←	—	→
Title, Etc.			←	—	—

important to include one like that which is depicted below. A well-conceived timetable can give your reviewers perspective about your project that they would otherwise lack. It should not, however, 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 project. Enter the years requested as column headings and your specific aims / studies as labels for the rows. 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 tasks that will be required to accomplish the aim. If it would help make the timetable more understandable, enter the titles of specific tasks over the related arrows in the table.

FUTURE DIRECTIONS PARAGRAPH

This should be the final paragraph of your *Research Design and Methods* section. It is the paragraph in which you tell your reviewers what they can expect in the future, should they decide to fund your proposal. You should begin by *briefly* summing up where you expect to be at the conclusion of this project. In doing so, you want to leave no doubt that the results of this period of funding will complete a step along the continuum of research that you projected in the *Specific Aims* section with your long-term goal. You should conclude this paragraph by telling the reviewers what your next steps are expected to be, and why they will be important. Thus, this paragraph provides yet another opportunity to get across to reviewers that you are pursuing a continuum of research that is compatible with the overall mission of the NIH. This paragraph is especially important if you are a new applicant, because a significant consideration for the reviewers may be the extent to which you reflect vision in your application. The 'Future Directions' paragraph gives you an outstanding opportunity to assure the reviewers, without being obvious about it, that you have such vision. You want them to know that, if they invest in this project, they can expect it to continue to grow and evolve in important directions that will relate to prevention, diagnosis or treatment of disease.

DEVELOPMENTAL STEPS FOR CHAPTER TEN:

1. Understand the expected content of this section, as described in the PHS 398 instructions.
2. Understand the "APPROACH" review criterion and how it relates to this section.
3. Copy and paste your first specific aim from your *Specific Aims* section into a new document file.
4. Prepare a first draft of the "Introduction" paragraph for this first specific aim. Be certain that it provides a conceptual 'overview' for this subsection.
5. Write the "Experimental (Research) Design" subsection for this aim. Be certain that meaningful, but not excessive or mindless, detail is provided.
6. Summarize results that you expect to obtain for aim #1 in the "Expected Outcomes" subsection; integrate these to show that they collectively attain the aim's objective.
7. Review your research plan and identify problems that could develop – probably won't – but could. List these, together with your solutions, in the Potential Problems and Alternative Approaches subsection for aim #1.

8. Repeat 3-7, above, for each of the remaining specific aims in your *Specific Aims* section.
9. Prepare a timetable that summarizes when the major activities proposed in your Experimental (Research) Design subsections will occur.
10. Write a brief paragraph entitled "Future Directions." Briefly summarize what you expect the outcomes of the proposed research to be and relate them to where you expect your continuum of research will lead in the future.
11. After finalizing this section, covert the document into a PDF file and upload it into the PHS 398 Research Plan Component of the SF 424 (R&R) application package using the "Add Attachment" button on line 5 of section 2 (see next page).

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Expiration Date: 9/30/2007

PHS 398 Research Plan

2. Research Plan Attachments:

Please attach applicable sections of the research plan, below.

1. Introduction to Application			
(for RESUBMISSION or REVISION only)			
2. Specific Aims	Add Attachment		
3. Background and Significance	Add Attachment		
4. Preliminary Studies / Progress Report	Add Attachment		
5. Research Design and Methods	Add Attachment		

CHAPTER 11

BACKGROUND SUBSECTION of the BACKGROUND AND SIGNIFICANCE SECTION and the BIBLIOGRAPHY & REFERENCES CITED SECTION

BACKGROUND SUBSECTION

> Instructions for the Background Subsection of the PHS 398 Research Plan Component / Background and Significance Section: "Briefly sketch the background leading to the present application, critically evaluate existing knowledge, and specifically identify the gaps that the project is intended to fill. **Two to three pages are recommended."** [Including the significance paragraph that was formulated earlier.]

DEVELOPING THE BACKGROUND SUBSECTION

You are now ready to begin writing the background component of your *Background and Significance* section. This is one of the main ways, together with the significance paragraph, that you justify the need for the proposed research. It is a commonly misunderstood component, because most writers of grant applications think that it should be a comprehensive review of ALL of the literature. Nothing could be further from the truth. How could anyone possibly write a comprehensive review of his/her field in the few pages that are recommended? It's simply not possible. Thus, this important means of justifying what you propose must be viewed in a different light. Its real purpose is to provide a highly *selective* review that justifies the need for the proposed research.

We recommend that you not write this subsection until *after* you have written the *Research Design and Methods* section. Why? Because, if you think of the *Research Design and Methods* section as the 'plug' that will fill the gap in the knowledge base, you can now custom design the 'hole' into which the plug will exactly fit. Background subsections that are written before the *Research Design and Methods* section usually contain a great deal of extraneous information that is not necessary to justify the specific research that is proposed. That problem is avoided by writing the background component *after* the research plan has been written. We recommend that you title this section, ***Review of Relevant Literature***. Put this title in bolded, italicized letters and then continue to write on the same line with text that is not highlighted. The phrasing of the title anticipates, and is designed to deflect, any criticism by an inexperienced reviewer that your background subsection is not a comprehensive review of the field.

Because the background subsection will vary greatly application-to-application, our recommendations here will be general suggestions as to how you should write this subsection. For exam-

ple, this should be a *critical analysis* of what has been published, not a passive one (i.e., 'Smith did this, Jones did that.'). Without being overly critical of other workers, if there are relevant gaps in what has previously been published, those gaps need to be identified. You should not rely exclusively (or even primarily) on review articles and books when you write this subsection. Reviewers will want to know how complete your command is of the primary literature of your field. Your treatment of the relevant literature needs to be fully up to date. As noted earlier, we recommend that you cite previously published work using first author/year, rather than numbers.

PURPOSE OF THE BACKGROUND SUBSECTION

The purpose of the background subsection is to justify why the proposed research is necessary. It must substantiate all of the unsubstantiated assertions that you made in the first, introductory paragraph of the *Specific Aims* section. It should detail and expand upon the fact that there truly is an important gap in the knowledge base, and that such a gap represents a critical need or problem. You should begin the background subsection with a brief historical overview of that part of the literature that is directly relevant to the subject of your application. In the first paragraph, you should summarize the most important older accomplishments and observations.

You should follow this paragraph with one that details the most important recent contributions, i.e., the details that will bring your reviewers to the edge of current knowledge. If there are members of the targeted review panel who have been substantive contributors to your field, be certain to cite their work, as long as it does not appear contrived to do so (In other words, they must truly have made a contribution.). Your own published contributions to the field can also be briefly presented, either as a part of this paragraph or in a third, separate paragraph.

The next paragraph should begin identification of the gap in the knowledge base that will be addressed by your application. The more explicit you can be in identifying the gap, the better. Its identification should then be followed by evidence that supports your earlier assertion (in the *Aims* section) that the gap is an important problem, i.e., that it is preventing vertical advancement of the field.

At this point, you should begin a new paragraph by again presenting the central hypothesis that will be tested. You do so, because testing of it will fill the gap. You should immediately follow its presentation with strong support for how it was formulated. Remember the single sentence that you wrote in the *Specific Aims* section about how your central hypothesis was formulated? If it included reference to the work of others, this is where you back up that statement with supporting citations from the literature. Your reasons for selecting this particular hypothesis over alternatives should be given in detail, with discussion of the potential merits/demerits of alternative hypotheses, if there are any.

At the conclusion of this subsection, there should be a final sentence or two that bridges to your *Preliminary Studies* section. This last component of the *Background and Significance* section should make clear that you and your colleagues have already made progress toward filling the gap in the knowledge base that will be targeted. In particular, you want to underscore that your central hypothesis is supported by the results that you have obtained to date. This ending provides an excellent segue into the next, *Preliminary Studies* section.

Consider writing your background subsection as an outgrowth of the sample sentences that are provided below. Either modify them or write new ones that will accomplish the same objectives.

Introductory (historical perspective) paragraph(s). 'In 19??, _____ *et al.* made the seminal observation that_____. On the basis of these studies, it was concluded that _____. As a direct result, _____ *et al.* investigated _____, which led to the additional conclusion that _____. Etc.'

'Edge of Current Knowledge' paragraph. 'The evidence cited above has led workers in the field to appreciate that _____. The most recent findings in this area support and extend this concept by_____. Our own studies have contributed to this contemporary body of knowledge by showing that _____. Etc.'

'Gap in the Knowledge Base' paragraph. 'Although the work cited above provides convincing evidence that A and B interact, the precise mechanism by which this occurs is completely unknown. For example, the work of Santee and Armstrong (1998) showed very clearly that _____, but stopped short of identifying the related mechanism. Casey *et al.* (1999) were similarly frustrated in their attempts to discover the mechanism. Such lack of understanding has recently been highlighted as a problem by Gonzales and her colleagues (2000), as well as by Smith and Brown (2001). Each of these groups underscored that progress in the field is highly unlikely until the mechanism becomes known. We are in total agreement with these earlier investigators, because our own progress has been impeded by this gap in the knowledge base. To resolve this issue, we propose in this application a series of studies designed to identify the relevant interactions between A and B that will allow identification of the underlying mechanism. To do this, we will _____ , using approaches already developed in our laboratory (refs).'

'Central Hypothesis and How Formulated' paragraph (BRIEF). 'To identify the mechanism we will objectively test the central hypothesis that _____. Considerable published support for this hypothesis derives from the following: 1) _____ (citation[s]); 2) _____ (citation[s]); and 3)_____ (citation[s]). Although it might be argued that _____is the mechanism, we consider this alternative is unlikely, because_____. Etc.'

Concluding, transitional paragraph or sentences. In conclusion, the collective evidence reviewed in this section strongly supports the conclusion that there is a need to identify the mechanism by which _____ relates to _____,. Such information is important because it would ultimately allow the development of _____. Previous studies and our own preliminary data, which will now be presented under *Preliminary Studies*, support the need for such research and provide support for the central hypothesis that we have formulated.

Using this approach, your background subsection should consist of six-to-eight highly focused paragraphs. Refine the material by inserting additional information or transitional sentences needed to improve readability and the flow of logic from one point to the next. There should be no more than a total of three pages for the entire *Background and Significance* section, including the significance paragraph that you wrote earlier. Have you brought your reviewers fully 'up to speed' with respect to the problem that you want to address? Does the flow of information build logically and persuasively toward what your contribution will be? Is the final paragraph written in such a way that it is a good transition into your *Preliminary Studies* section? If your answers to these questions are affirmative, you have accomplished your goal for this subsection and are ready to go on to the next step.

BIBLIOGRAPHY & REFERENCES CITED SECTION

> PHS SF424 R&R Instructions: "Be especially careful to follow scholarly practices in providing citations for source materials relied upon ...This section should include any references cited in the Research Plan Component. The references should be limited to ***relevant and current literature*** [emphasis added]. While there is no page limitation, it is important to be concise and to select only those literature references pertinent to the proposal."

The *Bibliography & References Cited* section should be created as a separate PDF file and uploaded into the application using the "Add Attachment" button on line 8 of the SF 424 Other Project Information Component.

The choice and number of citations included in support of your proposal are important. In fact, the references that accompany your application say a lot about you as an investigator. They should mostly be citations of the primary literature, *not* reviews. They should be up to date, especially if you are resubmitting an application that wasn't funded on an earlier attempt. Forgetting to update the *Bibliography & References Cited* section in resubmitted applications is a relatively common mistake. Reviewers will often check this point to see whether or not an applicant has cared enough to update the literature that is presented in support of the proposal. Citations should be complete, i.e., all authors in their published order, title, accepted abbreviation for the journal, volume, year of publication and full pagination. Finally, it is reviewer friendly to present your references in alphabetical order, based on the name of the first (only) author. Do not open a line after each one is presented, because it unnecessarily increases the length of this part of the application. Set off each citation either by numbering it or by presenting it un-numbered in a 'hanging indent' format.

DEVELOPMENTAL STEPS FOR CHAPTER ELEVEN:

1. Assemble a file (either hard copy or electronic) of all of the key literature citations that you will plan to use in writing the background subsection.
2. Be certain that you have familiarized yourself with the information in these publications. This means reading more than the abstract.
3. Identify the most important early seminal publications for the field in which you will be writing your proposal. Use them to write the "Historical Perspectives" paragraph.
4. Decide what the most important issues are that need to developed and write a paragraph for each. Be critical in a positive sense, and make certain that each paragraph allows for a conclusion that justifies the need for what you will propose.
5. Write the "Gap in the Knowledge Base" paragraph that provides the driving force for the proposed activities.
6. Write the paragraph that provides the conceptual framework for the proposal's central hypothesis, together with the arguments that would support its validity.
7. Develop the concluding paragraph that provides a 'bridge' or transition to the next, *Preliminary Studies / Progress Report* section.
8. Combine the 'Review of Relevant Literature (Background subsection) with the previously prepared significance paragraph (chapter 9) to create one document. The significance paragraph should be first, even though the title of the section is Background and Significance.

9. Convert the Background and Significance section into a PDF file and upload in the PHS 398 Research Plan Component of the SF 424 (R&R) application kit using the "Add Attachment" button on line 3 of section 2 (see below).

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PHS 398 Research Plan

2. Research Plan Attachments:

Please attach applicable sections of the research plan, below.

1. Introduction to Application			
(for RESUBMISSION or REVISION only)			
2. Specific Aims	Add Attachment		
3. Background and Significance	Add Attachment		
4. Preliminary Studies / Progress Report	Add Attachment		
5. Research Design and Methods	Add Attachment		

10. Compile the citations that you have used in the Background and Significance section, as well as in other sections of the Research Plan into a separate, *Bibliography & References Cited* section.
11. Convert the *Bibliography & References Cited* section into a PDF file and upload it into the Other Project Information Component using the "Add Attachment" button on line 8 (see below).

7. * Project Narrative		Add Attachment		
8. Bibliography & References Cited		Add Attachment		
9. Facilities & Other Resources		Add Attachment		

CHAPTER 12

PRELIMINARY STUDIES SECTION / PROGRESS REPORT

If you are submitting a new application, you will prepare a *Preliminary Studies* section. If you are submitting either a renewal (competing continuation) or revised (supplemental) application, you should replace the *Preliminary Studies* section with a *Progress Report* that documents the advances you made during the current period of support. Because most users of this *Workbook* will be submitting new applications, we will address preparation of a *Preliminary Studies* section first.

TIPS ON WRITING THE *PRELIMINARY STUDIES* SECTION

> Instructions for *Preliminary Studies* Section of the PHS 398 Research Plan Component of the SF 424 (R&R) Application Kit: "For new applications, use this section to provide an account of the principal investigator/program director's preliminary studies pertinent to this application.... This information will also help to establish the experience and competence of the investigator to pursue the proposed project. Except for Exploratory/Development Grants (R21 & R21/R33), Small Research Grants (R03), and Phase I Small Business Research Grants (R41/R43), peer review committees generally view preliminary data as an essential part of a research grant application. Preliminary data often aid the reviewers in assessing the likelihood of the success of the proposed project. "

We are often asked the question, "How much preliminary data is enough?". The answer is: it depends on the granting mechanism that you are using. At the R01 level, it is essential that you have a lot of preliminary data, even if you are a New Investigator. The NIH-recommended length of this section is 6-to-8 pages – *one-quarter to one-third of the entire 25-page allocation* for the Research Plan of an R01 application. If you are proposing hypothesis-driven research, you should have data in support of the proposal's central hypothesis and each aim's working hypothesis. For either hypothesis- or need-driven proposals, the feasibility of each aim must also be supported. On the other hand, at the R03 level you can actually undercut the fundability of your application if you include a lot of preliminary data. Why? Because the purpose of most R03s is to produce preliminary data, if you already have it you shouldn't be using that granting mechanism. This is one reason why the length of the Research Plan in an R03 is limited to 10 pages. The R21 is somewhere in between, which is why its Research Plan is usually held to 15 pages. In spite of what is implied in the instructions (see text box, above), we recommend that you include some preliminary data in an R21 to help reassure reviewers that, although there is relatively high risk of failure associated with the project, the risk isn't so high that there is virtually no chance for success.

Given these points, you have probably concluded correctly that *the purpose of the* Preliminary Studies *section is to establish that the work proposed is feasible in your hands,* i.e., that you and your research team have the competence and experience needed to do what is proposed. We want you to write this section after you have written the three other sections of the Research Plan because this section must be supportive of them, especially of the *Research Design and Methods* section. Knowing what their contents are will help to inform the writing of the *Preliminary Studies* section, therefore.

As has already been mentioned, if you are a New Investigator reviewers will be instructed to place less emphasis on this section than they would put on it in the application of an experienced investigator. We want to emphasize that this does not mean that a New Investigator can get away with little or no preliminary data in an R01-level proposal. You must have substantial amounts of high-quality preliminary data – but not as much as would be expected from an established researcher. If you don't have data in support of all of your aims and/or formulation of your central hypothesis, rather than applying for an R01, you should consider submitting an R03 (providing, of course, that the NIH awarding component you are targeting supports that granting mechanism). Alternatively, use local or regional funds to develop the base of preliminary data that will be needed to make R01-level research feasible in *your* hands.

What to Include

This section is not meant to be an outpouring of raw data from your record books. Nor is it meant to be a section in which you extensively present the results of your own published work; most such data more appropriately belong in the *Background and Significance* section. And even though some recommend it, in our opinion, the *Preliminary Studies* section should never contain the results of work performed by others, i.e., by those outside of the research team. This section is meant to show reviewers that the proposed work is feasible in your hands, not the hands of others. If you want to include the unpublished work of other investigators in your application you should do so in the *Review of Relevant Literature* subsection of the Background and Significance section. Cite it as "unpublished" and accompany the proposal with a letter from the investigator that corroborates your claim. If you don't include such a letter, it is risky to present such data because reviewers would have nothing with which to confirm your claim.

Begin developing the *Preliminary Studies* section by collecting all of your team's *unpublished* work that might be relevant. Under your central hypothesis or statement of need, list which of the data support either its formulation or existence, respectively. In the case of a statement of need, the data should be the results of your own assessment of need, not the work of other investigators who have independently called attention to its existence. As noted earlier, such citations belong in the *Review of Relevant Literature* subsection, not here. Do the same under each of your aims – which data support feasibility of which aim? After each data listing, write a statement regarding what the data set shows and why the data are important. After you have completed this organizational step, begin to 'prune' the list, keeping only those sets of data that are complete and that persuasively contribute to the 'story' that you want to tell. Now, arrange the data sets in a logical and compelling order. Remember that your objective is to lead your reviewers to the conclusion that you are highly capable of accomplishing what will be proposed in the next, *Research Design and Methods* section.

Finally, review and carefully analyze your team's *published* work to determine whether any of it will be needed as the foundation for presenting your preliminary (unpublished) work. If so, inte-

grate it appropriately into the presentation sequence. This material will almost always appear at or near the beginning of the section.

Organizing and Presenting Your Preliminary Data

We suggest that you begin this section by providing a conceptual overview of your research interests in which you "introduce" the reviewer to the focus of your laboratory. This will allow you to segue from the general concept of your research to the specifics of what this application will be about, and once again, allow you to be proactive in promoting yourself.

Just as the *Research Design and Methods* section was organized along the lines of your specific aims, we also suggest that the remainder of this section be organized similarly, i.e., around your statement of need and/or central hypothesis and specific aims. Each should be a subheading. Using this approach will help reviewers appreciate more easily how the data presented support the feasibility of your central hypothesis and aims.

> TIP: It is critical that you present actual data, not summaries of data. Lead your reviewers through what you present, assuring that they make the connections that you want them to make.

Each set of data / figure should be designed to make a single point / be the basis for a single conclusion. As noted earlier (chapter 4), each paragraph that you write in your proposal should make a single point. Thus, in the *Preliminary Studies* section each data set / figure should be accompanied by a paragraph that discusses it and makes a point / leads to a conclusion. Strive for simplicity. Juxtapose the text and the related data as closely as possible. Ideally, the reviewer will only have to glance back and forth between the two.

Each paragraph should be given a heading – one that introduces reviewers to its content, much like the headline in newspapers introduces the content of the article that is related to it.

With respect to calling attention to what is important, we recommend that you include a fully italicized sentence in each paragraph that helps reviewers connect to how / why the related data support feasibility. For example, the sentence might read something like, *'These preliminary data are important, because they helped to narrow our focus to the approach that is proposed for specific aim #2.'* or *'Collectively, these data provide a key part of the foundation for this proposal, because they unequivocally confirm that XYZ occurs, which was the essential observation needed to propose specific aim #3.'*

Vary the means of presenting your data. Even if you can present everything in tabular format, table after table becomes boring. What you should do is change the format to make the data as appealing to reviewers as possible. So, for example, include a table. Then present a histogram. Then use a line drawing. Then a pie chart, etc.

Scan figures and embed them into the text. Wrap text around them if you have a space problem. If you are using full justification, auto-hyphenate the document to minimize spacing problems in relatively narrow areas of text that are adjacent to embedded figures.

In our opinion, *the most common error made in this section is failure to lead the reviewers through the data that are presented.* The usual approach is to provide a conclusion and then

refer the reviewer to a data set or figure so that s/he can determine how that conclusion was reached. That makes the reviewer do all of the work, which is not reviewer friendly. More important, it risks that s/he either won't make the effort or will misinterpret the data. A better approach, in our opinion, is to give the reviewers the conclusion, refer them to the data / figure, and then lead them through what you have referred them to. For example, after you introduce the concept for the study and provide some background as to how the data were generated, you could follow with: 'As can be seen from the data in Figure 1, we conclude that _____. Note that there is a band in column one that is missing in column two. This indicates _____.' By using this approach, you can be guaranteed that the reviewer will come down in the same place that you came down. Once there, s/he may disagree with your conclusion, but at least you will know that s/he got to the same point that you did.

A data set / figure should not be presented until after it is first referred to in the text. Thus, if there is no room at the bottom of a page after a table is first mentioned, it should not be moved to the top of that same page. Were you to do so, the reviewer would encounter the table before s/he would know why it has been included. Rather, it should be moved to the top of the next page with a note on the preceding page that specifies its location, e.g., '(see Figure 3, top of next page).'

Even though the electronic version of your application will contain faithful reproductions of figures that include color, you must anticipate that one or more of your reviewers will want to read and evaluate your application after first downloading and printing it using a black-and-white printer. Therefore, as noted earlier, you should choose colors used in figures to have distinct grayscale differences when reproduced in black and white. Then, note those grayscale shades in the accompanying figure legend (e.g., red [dark gray]). It used to be possible to overcome this problem by submitting color copies of the figure as appendix material, because appendices were distributed to reviewers in hard copy. In the SF 424 (R&R) approach, appendix material must be scanned and uploaded for electronic submission. Thus, the 'appendix' approach no longer circumvents the problem, necessitating that colors in figures be chosen to have readily identifiable grayscale differences.

It is important that every figure in this section have a detailed figure legend accompanying it, with a descriptive and informative title at its beginning. Indent your figure legends one tab left and right to distinguish them from the text. Figure legends should have two parts. The first of each legend should include whatever description is necessary to make the figure intelligible. The meanings of all symbols should be included. Don't forget to include information about statistical notations (e.g., error bars). The second part of the legend should briefly summarize the method(s) used to generate the data. This second part should be preceded by the title, 'METHODS.' The legend should be referred to in the text if a methodological point needs to be made there.

Avoid extensive descriptions of routine methods. If routine methodology – the kind that could be copied out of a methods manual – must be included, it should be located in figure legends and footnotes to tables, not in the text. There are two reasons for this. First, while there are strict guidelines on font size for text and form pages (at least 11 point and 15 or fewer characters and spaces per linear inch), these restrictions are relaxed for legends and footnotes. The only requirement for figure legends and footnotes to tables is that "it must be ... readily legible" and in one of the four approved typefaces (see quote of instructions at the top of the next page).

SF 424 (R&R) Format Specifications for Text (PDF) Attachments: **Figures, Graphs, Diagrams, Charts, Tables, Figure Legends, and Footnotes:** You may use a smaller type size but it must be in a black font color, readily legible, and follow the font typeface requirement.

Second, if routine methodology is 'buried' in figure legends and footnotes to tables, it is accessible to reviewers but they don't have to read it unless they want to do so.

Based upon these preceding points, we recommend that you use either 9- or even 8-point type, with the first part of the legend or footnote bolded, as is illustrated in the text box, below. To allow you to compare them, the first part of the legend in the text box is in 9-point Arial and the second, "Methods" part is in 8-point. We prefer the 9 point.

Figure 3 Enhanced expression of TLR4 on macrophages from *B. anthracis* infected mice. The data show the level of surface expression of TLR4 in alveolar macrophages at 24 and 48 hours post infection of C57/Bl6J mice with a virulent strain of B. anthrasis spores (open bars) is markedly elevated relative to the avirulent strain (shaded bars) or B. subtilis (filled bars), indicating that virulence is associated with rapid induction of innate host immunity. Methods: Mice were infected via inhalation with 10 million spores as indicated. At 24 and 48 hours post-infection, five mice from each group were euthanized and pulmonary lavage fluids were obtained. Macrophages were isolated by magnetic bead adherence using anti CD11b monoclonal antibodies, stained with fluorescein conjugated polyclonal rabbit anti-mouse TLR4 antibody and analyzed by flow cytometry. Data are averages of triplicate determinations ± S.E.M.

TIPS ON WRITING THE *PROGRESS REPORT* FOR RENEWALS & REVISIONS

Instructions for *Progress Report* Section of the PHS 398 Research Plan Component of the SF 424 (R&R) Application Kit: "A Progress Report must be provided for renewal [competing continuation] and revision [supplemental] applications. Provide the beginning and ending dates for the period covered since the project was last reviewed competitively. Summarize the previous application's specific aims and the importance of the findings. Discuss any changes in the specific aims as a result of budget reductions. Include the complete references to appropriate publications and manuscripts accepted for publication (not part of the page limitations). ... Provide a succinct account of published and unpublished results, indicating progress toward their achievement. List the titles and complete references to all publications, manuscripts accepted for publication, patents, and other printed materials that have resulted from the project since it was last reviewed competitively. Up to 10 such publications may be included in the appendix attachment."

If you are applying to renew an existing grant, as noted earlier, you must write a *Progress Report* rather than a *Preliminary Studies* section.

Many of the principles covered in the subsection on *Preliminary Studies* paragraphs apply here equally. However, there are some important differences. First, the section should begin with the duration of time that the *Progress Report* covers. That is not the duration of the grant. It is the period from the date of award to the time that the renewal application is submitted.

Second, you need to present the specific aims that directed the research that will be summarized in the Progress Report. They may not be the ones that were submitted in the previous application. For example, if a reduction in your budget of ≥10% made it impossible to address all of the aims that you originally offered, you should have made that fact known in an official letter sent through your Research Office. If you did so and you letter was approved by NIH, you are responsible for the smaller scope of work, not the original aims. You should present the revised aims at the beginning of your *Progress Report*, not the aims that constituted your original scope of work. If the cut was less than 10% and you did not change the scope of work but were impacted negatively by the cut, you should detail that circumstance at the beginning of your *Progress Report*.

As another example, you might have found that, in spite of your best projections, one or more of the original aims had to be changed during the course of the research. You should have noted the need to make that change in one or more of your annual, non-competing Progress Reports. If there was no objection to the proposed change (and there almost never is), the revised set of aims would become what you would present at the beginning of the *Progress Report* in your competing renewal. As with the *Preliminary Studies* section, you should organize and present your *Progress Report* in a competing renewal application using the former and/or revised aims as subsection headings. Third, each paragraph in the *Progress Report* should be devoted to one discovery that you made. As in the *Preliminary Studies* section, you should include an italicized sentence in each paragraph. The difference here is that you should highlight for reviewers why each discovery was important and how it contributed to attainment of the grant's overall objective. Fourth, at the end of the section, you need to list every product that came from the prior funding. The space occupied by this list is *not* counted against the 25 pages to which your *Research Plan* is limited. It is important to realize in constructing this list that, in addition to evaluating quality, reviewers count. Therefore, we recommend that you approach the creation of this list in the following way. Identify everything that could be construed as a product of your current funding. Prioritize these products from most-to-least important. Publications in peer-reviewed journals will almost always be your most important product. Therefore, begin your list with a subheading, 'Publications in Peer-Reviewed Journals,' excluding submitted and 'in-preparation' entries. List them, for example, 1-through-12. The next most important product might be three invited monographs. To include them, you would insert another subheading, 'Invited Monographs.' However, instead of numbering them 1-through-3, you would continue the sequence of numbers from above, i.e., they would be 13-through-15. You would continue with patents, and any "other printed materials" (e.g., reviews, book chapters, published conference proceedings and the least important, abstracts, which would be last).

> TIP: If you decide to present abstracts, make sure that most of the earlier ones are reflected as later, full-length publications in peer-reviewed journals. If you present numerous abstracts that do not give rise to subsequent peer-reviewed publications, it will give reviewers the impression that your discoveries either cannot pass the test of rigorous peer review, or that you aren't sufficiently motivated to publish in respected journals.

When you have completed this list, the total number at the end will be large and much more impressive than a series of smaller totals for the various subsections that are included in your list. Fifth and finally, it is important for you to appreciate that progress made with existing funding is a major criterion that is used by reviewers to determine whether or not a competing renewal ap-

plication will be funded. If you (and colleagues who you consult) recognize that insufficient progress has been made to merit a fundable priority score, you would probably be unwise to submit a competing renewal application unless there were highly convincing mitigating circumstances to explain the relative lack of progress. You would most likely be preordained to fail. *In such a case, you should change the proposal enough to convert it into a new application.* Change the title. Change the principal investigator. Substantively revise the orientation of the research. Do whatever is necessary to make the application sufficiently different that it could not be recognized as a competing renewal. By making such changes, you would be able to submit a *Preliminary Studies* section, not a *Progress Report*.

If your research with the current funds involved clinical studies, you must include Target and Enrollment Reports / Tables as part of your *Progress Report*. They do not count against the 25-page limit for the Research Plan, however.

TRANSITION TO THE NEXT SECTION

Whether you are writing a *Preliminary Studies* section or a *Progress Report*, you will need to include a short paragraph at the end of the section that will carry the reviewers' concentration seamlessly into the next one, which is *Research Design and Methods*. For example, you could effectively segue into presentation of your research design with something like, 'In conclusion, these preliminary studies have: 1) confirmed that such-and-so is operative; 2) shown that the XYZ approach is feasible in our hands; and 3) provided strong clues as to which mechanism of action is responsible for ABC. Collectively, these results position us well to undertake the studies that we will now propose in the next section.' Particularly if you are a New Investigator, you can also use this final paragraph to underscore your qualifications and competence to do the work that is proposed, i.e., that it is feasible in your hands.

DEVELOPMENTAL STEPS FOR CHAPTER TWELVE:

New Applications

1. Collect and analyze all of your unpublished work that supports the formulation of your central hypothesis, the existence of the need, and/or the feasibility of your aims.
2. Prepare a bulleted list of any of your published work that is needed to serve as a foundation for the unpublished material.
3. Write subheadings that reflect your central hypothesis / statement of need, as well as your specific aims.
4. Organize the published and unpublished data under each of the subheadings.
5. Write a paragraph to complement each set of data and that makes a single point or conclusion.
6. Write a fully italicized sentence for each paragraph that tells how it supports the feasibility of what is proposed in the *Research Design and Methods* section.
7. Arrange the paragraphs in a logical progression

Renewal or Revision Applications

1. If you are writing a Progress Report, summarize the specific aims for the current period of support.
2. Follow the same approach described for new applications, except concentrate on both published and unpublished results that have been produced with the current funds.

3. Write a fully italicized sentence for each paragraph that highlights the importance of the particular discovery described and how it supports what is proposed in the renewal / revision.
4. Complete your *Progress Report* by listing the products – peer-reviewed publications, patents, monographs, reviews, book chapters, published abstracts, and any other published or in-press material – that could be construed as a product of the current funding. Do not include submitted or 'in-preparation' manuscripts.

***Steps Common to* Preliminary Studies *Sections and* Progress Reports**

1. Write a concluding paragraph that summarizes the relevance the presented data collectively have to the proposed work. This paragraph should provide a 'bridge' to the next, *Research Design and Methods* section.
2. When you have completed the section, re-examine each figure / table, including legends / footnotes, to ensure that *everything* is fully legible. This is particularly important for figures or tables that have been reduced in size to make them fit into a small space.
3. Convert the document to a PDF file and upload into the *PHS 398 Research Plan* component of the SF 424 (R&R) application kit using the "Add Attachment" button on line 4 of section 2(see below).

OMB Number: 0925-0001
Expiration Date: 9/30/2007

PHS 398 Research Plan

2. Research Plan Attachments:

Please attach applicable sections of the research plan. below.

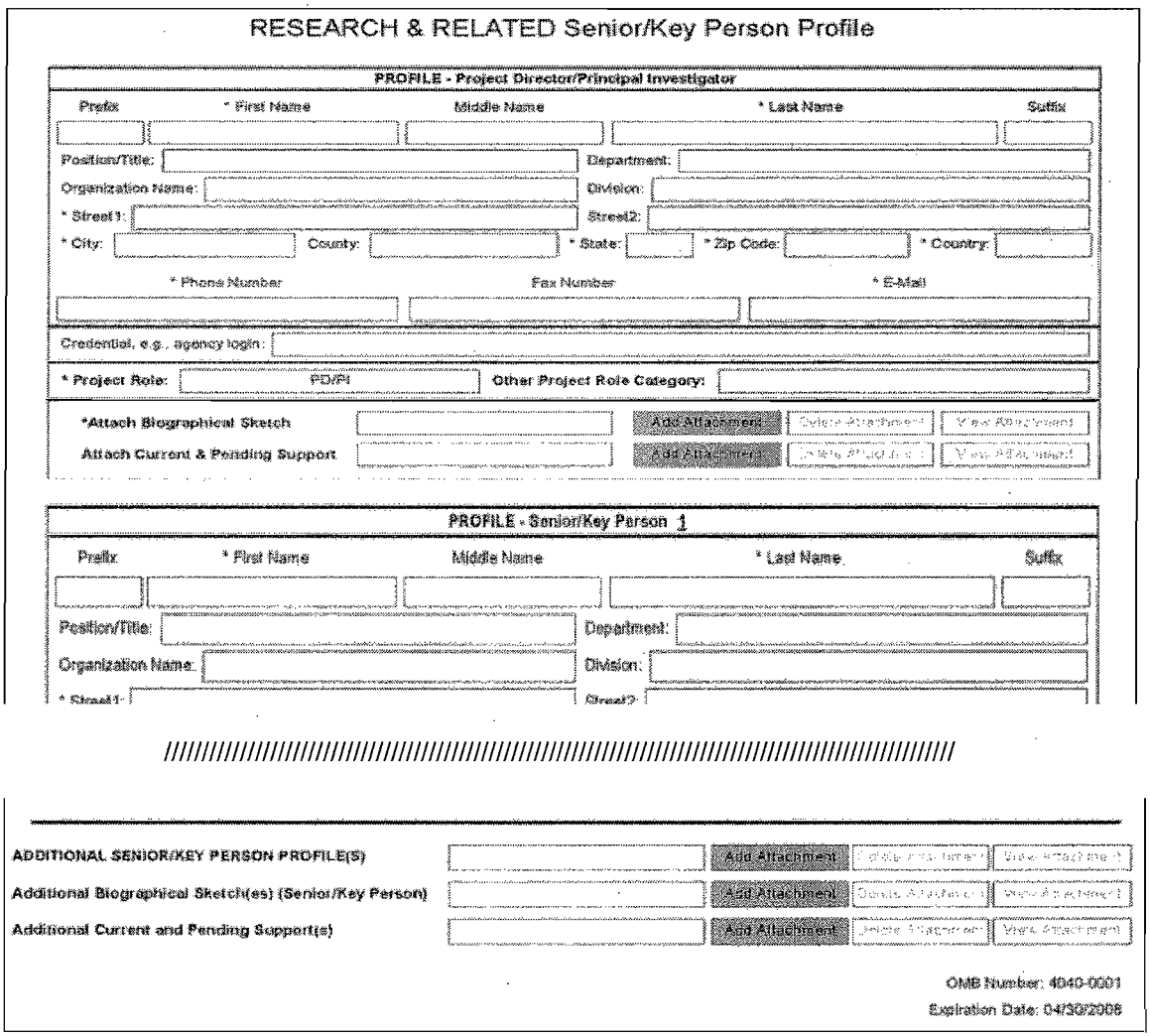
1. Introduction to Application (for RESUBMISSION or REVISION only)	
2. Specific Aims	Add Attachment
3. Background and Significance	Add Attachment
4. Preliminary Studies / Progress Report	Add Attachment
5. Research Design and Methods	Add Attachment

CHAPTER 13

SENIOR/KEY PERSON PROFILE(S) COMPONENT and BIOGRAPHICAL SKETCHES

GENERAL CONSIDERATIONS

Biographical Sketches are prepared and included in the application using the *PHS SF424 (R&R) Senior/Key Person Profile(s)* component (section 4.5 of Part I of the *PHS SF424 [R&R] Application Guide*), parts of which are reproduced, below.


RESEARCH & RELATED Senior/Key Person Profile

PROFILE - Project Director/Principal Investigator

Prefix | * First Name | Middle Name | * Last Name | Suffix

Position/Title: | Department:

Organization Name: | Division:

* Street1: | Street2:

* City: | County: | * State: | * Zip Code: | * Country:

* Phone Number | Fax Number | * E-Mail

Credential, e.g., agency login:

* Project Role: PD/PI | Other Project Role Category:

*Attach Biographical Sketch | Add Attachment | Delete Attachment | View Attachment

Attach Current & Pending Support | Add Attachment | Delete Attachment | View Attachment

PROFILE - Senior/Key Person 1

Prefix | * First Name | Middle Name | * Last Name | Suffix

Position/Title: | Department:

Organization Name: | Division:

* Street1: | Street2:

//

ADDITIONAL SENIOR/KEY PERSON PROFILE(S) | Add Attachment | Delete Attachment | View Attachment

Additional Biographical Sketch(es) (Senior/Key Person) | Add Attachment | Delete Attachment | View Attachment

Additional Current and Pending Support(s) | Add Attachment | Delete Attachment | View Attachment

OMB Number: 4040-0001

Expiration Date: 04/30/2006

Biographical sketches must be prepared for all Senior/Key Personnel and Other Significant Contributors. Generically, these are individuals without whom completion of some part of the project would become problematic. The distinction between these two personnel categories relates to time committed to the project: Senior/Key Personnel "contribute in a substantive, measurable way to the scientific development or execution of the project, whether or not salaries are requested." Other Significant Contributors "have committed to contribute to the scientific development or execution of the project, but are not committing any specified measurable effort to the project." Thus, the distinction between the two comes down to measurable effort. Senior/Key Personnel include the Principal Investigator, Co-Investigator(s), and can include Collaborators and Consultants if their effort is measurable. Other Significant Contributors are usually collaborators (e.g., someone who provides a critical reagent or technology) and consultants who have such a limited role that their effort is not quantifiable. Even though post-doctoral research fellows, graduate students and technicians may have measurable effort on your project, they rarely qualify as Senior/Key Personnel because their expertise can usually be replaced. Thus, they usually will not be represented with a Biographical Sketch. The credentials of such members of the personnel set should be described, along with their roles in the project, only in the Budget Justification.

Biographical sketches are important components of the application, because they are additional means of establishing feasibility: Can the proposed work be accomplished by these applicants? As you know, the investigators' credentials constitute a specific focus for the review of NIH grant applications (mandatory INVESTIGATOR review criterion). Therefore, extensive thought should be given to the preparation of this part of the application. *Under no circumstances should you simply photocopy biographical sketches from other applications.* To do so is a serious strategic error, in our opinion. Those biographical sketches were prepared to support the applications for which they were written, not yours. Another reason to prepare the biographical sketches for your application freshly is to ensure that they all look alike, i.e., that they all have the same font and formatting as the Principal Investigator's. You are trying to project that this is an integrated research team, not a bunch of disparate parts that have been cobbled together to get the money. The approach that we recommend to assure that each Biographical Sketch maximally supports your proposal while, at the same time, it contributes to the image of integration is described later in this chapter, under the 'Preparation' subsection.

PERSONNEL PROFILES

Each Senior/Key Person and Other Significant Contributor must have a profile prepared for him/her. Such profiles are created using the series of blocks on the SF424 Senior/Key Person Profile(s) Component. There is a separate profile at the beginning of the Component for the Principal Investigator ("PROFILE - Project Director/Principal Investigator"), which is followed by another part that is used to create the profiles of other Senior/Key Personnel and Other Significant Contributors are created ("PROFILE – Senior/Key Person"). In this latter part of the Component, Senior/Key Personnel should be presented first, in alphabetical order. Other Significant Contributors should be presented after Senior/Key Personnel, again in alphabetical order. The profile for each member of the Senior/Key Personnel and Other Significant Contributors group after the first is created by clicking the "Next Person" button at the lower right of the "PROFILE - Senior/Key Person" form. If there are more than eight such persons, their profile of each must be uploaded as a separate PDF file using the "Add Attachment" button that is adjacent to the

"ADDITIONAL SENIOR/KEY PERSON PROFILE(S)" field at the bottom left of the SF424 Senior/Key Person Profile(s) Component.
The "Project Role" field of the Senior/Key Person profile offers a list of roles, one of which is "Other." The "Other" role should be selected for Other Significant Contributors. Then, "Other Significant Contributor" should be typed into the "Other Project Role Category" field.

There is a field in the series of profile blocks for the Principal Investigator, as well as in the series of profile blocks for Senior/Key Persons, which is titled "Attach Current & Pending Support." This attachment upload should not be included in NIH and other PHS agency proposals.

BIOGRAPHICAL SKETCH ATTACHMENT

In addition to the profile that is created for each Senior/Key Person and Other Significant Contributor, a Biographical Sketch must be provided. Each is uploaded as a PDF file using the "Add Attachment" button that is related to the "Attach Biographical Sketch" field on the person's SF424 profile. Biographical sketches in excess of eight must be added using the "Add Attachment" button to the right of the "Additional Biographical Sketch(es) (Senior/Key Person)" heading at the lower left of the SF424 Senior/Key Person Profile(s) Component. An additional format page for Senior/Key Personnel in excess of eight is provided at http://grants.nih.gov/grants/funding/424/index.htm.

Format of the Biographical Sketch

The generic SF424 (R&R) instructions regarding what to include in your Biographical Sketch should be disregarded. The NIH/PHS-specific instructions should be substituted. These are offered under the title, "Additional NIH and Other PHS Agencies Instructions for a Biographical Sketch." They are provided in the text box, below.

> General Instructions for NIH and Other PHS Agency Applications: "Use the sample *format* on the Biographical Sketch Format Page to prepare this section for **all** (modular *and* other) grant applications. Include biographical sketches of all **Senior/Key Personnel and Other Significant Contributors**. The Biographical Sketch may not exceed four pages per person. This 4-page limit includes the table at the top of the first page."

A Biographical Sketch Format Page is supplied for all NIH and other PHS agency applications at http://grants.nih.gov/grants/funding/424/SF424R-R_biosketch.doc. It must be used to prepare the biographical sketches for your proposal. If it is 'protected' when downloaded you can 'unprotect' it to allow you to make changes in its formatting. To do so, download the Word version of the Format Page, click on "Tools" in the toolbar and then on "Unprotect Document" on the drop-down menu. After completing each Biographical Sketch, convert it to a PDF file to preserve its formatting before uploading it into your application using the "Add Attachment" button to the right of the "Attach Biographical Sketch" subheading. An example of a Biographical Sketch, which is adapted from the sample that is provided by NIH (see http://grants1.nih.gov/grants/funding/424/SF424R-R_biosketchsample.doc) is included at the end of this chapter. Despite these instructions and examples, even when complemented by the additional information that is contained in this chapter of *The Grant Application Writer's Workbook – NIH,* our experience is that most applicants make numerous small mistakes in the preparation of their biographical sketches. These are completely avoidable. Simply read and follow-

ing the instructions carefully. It is important to do so, because many small mistakes that are clearly attributable to not reading and following instructions say something very negative about your attention to detail – and what is research about other than attention to detail.

The same typeface used for the rest of the application should be used to complete the biographical sketches. The font size should be 11 points or larger.

You are allowed up to four pages for each biographical sketch. A significant change with the SF424 application kit is that all biographical information, including publications, is no longer restricted to the first two pages, as it was with the PHS 398 application kit.

Education/Training Table. This part of the Biographical Sketch should begin with the baccalaureate and conclude with post-doctoral training, i.e., the entries should be in chronological order. A common mistake is to put post-doctoral training under Positions and Honors, rather than in this table. Include enough information that it is clear which institutions were involved and when. If additional rows are needed in the Word version of the Format Page go to "Table" in the toolbar and then use the dropdown menu to manipulate the layout of the table, as needed. Vertical lines can be moved left and right by clicking on the line and then dragging it to the desired location. If you don't need all of the rows in the preset table, use the "Delete – Rows" function under "Table" to remove them.

Section A. Positions and Honors. Make these entries chronologically, concluding with your present position. Refer to the Sample Biographical sketch for an example of how this subsection should be configured. As will be seen, it is permissible to subdivide this part of the Biographical Sketch into subsections that are pertinent to the title of Section A.

Section B. Selected Peer-Reviewed Publications. These also should be presented chronologically. Only peer-reviewed publications that are published or in press should be included. That means no reviews, book chapters or published abstracts. Submitted and 'in-preparation' manuscripts are not allowed.

Section C. Research Support. This section should be divided into two subsections: (1) Ongoing Research Support, and (2) Research Support Completed During the Last Three Years. Use the format for this section that is shown in the sample Biographical Sketch at the end of this chapter / on the NIH Web site. The cutoff date for deciding whether completed support is older than three years is the deadline date for submission of the proposal.

Research support should be presented from most to least relevant to the subject of the current proposal. In other words, it is not meant to be chronological, reverse chronological, or in order of the most to least important role (e.g., PI, Co-I, Consultant).

The purpose of the Research Support section of each Biographical Sketch is to contribute additional information about each participant's expertise and scientific accomplishments. If it is possible to do so, the scientific focus of each source of support and the investigator's role in it should be related to your project. In other words, such support should be used to help reviewers better understand why the investigator in question has been asked to fill the specific role that you are proposing for him/her in your project.

A common error made in this section is failure to include all funding. All federal AND non-federal support should be included. For example, we are often asked if New Investigators should include their start-up funds. The answer is YES – absolutely YES – because such de-

partmental or institutional funding is a tangible mark of institutional support. Remember that reviewers are told to look for evidence of institutional commitment when reviewing the applications of New Investigators. Another common error is to confuse this section with Other Support, where amounts and percentage effort associated with each source of support must be given. The purpose of Other Support information is to check for overlap with other projects, which is very different from the purpose of Research Support section of the Biographical Sketch. Other Support information is submitted only after an applicant has been notified that his/her application is being considered for funding. In other words, it is not submitted at the time the proposal is submitted.

Tips on Preparation of the Biographical Sketch

To ensure that all of the biographical sketches are identical in format and typeface to the Principal Investigator's, we recommend the following approach. The PI should ask each member of the Senior/Key Personnel group, including Other Significant Contributors, to provide an electronic copy of the Biographical Sketch from his/her most recent grant application, as well as an updated copy of his/her *curriculum vitae*, to include research support. The PI should review the Biographical Sketch and remove anything from it that is not relevant to the project being proposed. S/he should next go through the *c.v.* and add to the Biographical Sketch any relevant information that was missing from the original, e.g., honors, relevant experience, and/or recent publications. After revisions have been completed, the biographical sketches should be retyped in the same format as the Principal Investigator's. An example of the format we recommend for the Biographical Sketch, which is adapted from the sample provided by NIH at http://grants.nih.gov/grants/funding/424/SF424R-R_biosketchsample.doc, appears at the end of this chapter.

Principal Investigator, Co-Investigators and Collaborators. The Principal Investigator is, of course, a member of the Senior / Key Person set. Co-Principal Investigators are being phased in at NIH and other PHS agencies. At the moment, this category can be included only if the FOA to which you are responding allows it.

Co-investigators will always be included in the application with measurable percentage effort. Thus, they will be members of the Senior/Key Person set. Collaborators, on the other hand, will seldom have measurable effort associated with their participation. Therefore, they should almost always be included as Other Significant Contributors – those who have a key role but no measurable effort. Any individual without measurable effort must provide a letter of support with the application, which will be included by uploading it into sub-subsection 16 of subsection 2 of the PHS 398 Research Plan component. *You should draft all letters of support yourself*, because you know better than anyone else why the related investigators have been asked to participate in your research project. Your 'example' should be given to the Other Significant Contributor(s) with the understanding that a letter 'like' the one you have prepared is needed. This usually will result in the Other Significant Contributor embellishing what you have written and, therefore, a final letter of support that is even stronger than the draft that you provided. This approach is almost always appreciated, because it saves the Other Significant Contributor's time.

No one should be included as a member of the research team unless s/he is proposed for a readily identifiable purpose. Thus, including someone senior as a mark of respect or including an established investigator who duplicates the credentials of a junior member of the team is usually inappropriate. In the latter case, inclusion of the senior person could undermine the

perception that the junior person is truly an independent investigator, especially if s/he is the Principal Investigator.

In preparing the publication lists of co-investigators/collaborators, remember that *three things are relevant*: (1) has the person been regularly productive in the recent past; (2) what is the quality of his/her publications; and (3) are they relevant to what the investigator has been recruited to do in the proposed research program? A member of your research team who has few or no publications relevant to your proposal should be considered as a 'weak link' and, therefore, someone who you may want to remove/replace. If a participant has two or more different kinds of publications, e.g., research and clinical or research and technical, we recommend that they be grouped under separate subheadings, not intermingled.

A New Investigator should be particularly diligent in completing his/her Biographical Sketch, because the INVESTIGATOR review criterion is a particularly high bar for him/her to clear. In particular, the extent and quality of the New Investigator's background and training should be highlighted, because there isn't yet much of a record of productivity to use as a gauge of past performance. Thus, a New Investigator should consider including his/her dissertation as a publication and a copy of the related dissertation abstract as one of the ten publications allowed as appendix material. The latter gesture will be seen as considerate of reviewers because of the time and effort that would otherwise have to be invested to obtain the dissertation abstract. In addition, using a few sentences under the "Education/Training" table at the beginning of the Biographical Sketch to elaborate on graduate/post-doctoral training (e.g., who the mentor was, and how the research conducted at those times relates to what is being proposed in the current application) is a good idea. An additional strategy is to accompany particularly strong or relevant publications listed in the bibliography of a New Investigator with a sentence or two that highlights for the reviewer why those publications are relevant to the current proposal and, especially, how the work that produced those papers has helped to prepare the applicant to undertake the work being proposed. Reprints of such papers should accompany the application as appendix material, if at all possible.

Include in the Biographical Sketch only information that is specifically relevant to the project being proposed. Never 'pad' a Biographical Sketch with extraneous entries, such as being included in 'Who's Who in American Biological Science in New England, 2005', or trivial ones, such as hobbies. This is especially important with respect to New Investigators, who sometimes try to increase the length of their biographical sketches with such non-relevant entries. Instead, as mentioned above, find legitimate ways to highlight the quality of training, productivity during training, and the quality of material that has been produced to date. These are highly relevant ways for a New Investigator to 'flesh out' his/her Biographical Sketch.

If a member of the research team has had a gap in productivity, as reflected by absence of grant support, employment, and/or publications for a period of time, we strongly recommend that the cause be addressed in his/her Biographical Sketch. For example, if the person had an extended illness, took time from his/her professional career to raise children, or had a term of military duty, the vast majority of reviewers will understand and be sympathetic. Simply explain the cause without being defensive about it. If this is not done, reviewers will wonder about the gap in productivity and, as a result, could potentially discount the person's value to the research team.

Consultants. These are individuals who have exceptional credentials in support of their projected role in the research program but will have only a limited commitment (usually intellectual). They can either be members of the Senior/Key Person set, if the extent of their effort is measur-

able in person months (http://grants1.nih.gov/grants/policy/person_months_faqs.htm) or as an "Other Significant Contributor" if no person months are included in the Budget Justification. A consultant's Biographical Sketch should be written to emphasize specific qualifications that are relevant to what s/he will do — for example, to act as an external advisor to a program project or as the provider of a specific kind of critical expertise that will be needed for such a short time that it would be impractical and cost-ineffective for the Principal Investigator to develop it in his/her own laboratory. As noted above, do not simply copy the Biographical Sketch from the consultant's last grant application for inclusion in your proposal. Ask for the consultant's entire *curriculum vitae*, from which you should then pick and choose those items that specifically support *your* need for him/her. Thorough documentation of the specific need for the consultant is critical in the Budget Justification, even if s/he has no measurable effort. If the consultant is included as an Other Significant Contributor, you will need to draft a letter of commitment for him/her, as described above.

DEVELOPMENTAL STEPS FOR CHAPTER THIRTEEN:

1. Understand the instructions that guide preparation of biographical sketches.
2. Prepare your own Biographical Sketch exactly as instructed using the format suggested by the example at the end of this chapter.
3. Obtain an electronic copy of the most recent Biographical Sketch and updated *curriculum vitae* from each member of the Senior/Key Personnel and Other Significant Contributors set.
4. Revise, update and retype each Biographical Sketch to appear like the PI's.
5. For each member of the Other Significant Contributors group (i.e., participants without measurable effort on the project), draft a letter of specific commitment / contribution (see creating Letters of Support, chapter 21).

BIOGRAPHICAL SKETCH FORMAT PAGE

(Downloadable from http://grants1.nih.gov/grants/funding/424/SF424R-R_biosketch.doc)

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
eRA COMMONS USER NAME	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY

We recommend that New investigators who have recently completed postdoctoral training relevant to their proposal should consider writing a brief paragraph here to describe their project and mentor(s) more fully. This approach helps reviewers better assess the extent and quality of the applicant's background and training – critically important considerations in the review of New Investigator applications.

NOTE: This form is not 'protected' when it is downloaded. The Word version of the table, above, can be expanded or contracted by going to "Table" in the toolbar. Use either "Insert" or "Delete" in the drop-down menu to add or remove rows / columns, respectively. Column width can be optimized by clicking on and dragging vertical lines in the table to the left or right.

If for some reason the form arrives 'protected,' you can 'unprotect' it by clicking on "Tools" in the toolbar. Then, click on "Unprotect Document" in the drop-down menu.

See the pages that follow for an example that is adapted from the sample that is provided by NIH at http://grants1.nih.gov/grants/funding/424/SF424R-R_biosketchsample.doc.

SAMPLE OF BIOGRAPHICAL SKETCH

(Adapted from http://grants1.nih.gov/grants/funding/424/SF424R-R_biosketchsample.doc)

Principal Investigator/Program Director (Last, First Middle): Carlucci, Joseph Louis

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Carlucci, Joseph Louis	Professor of Pediatrics and Microbiology
eRA COMMONS USER NAME	
Carluccij	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
University of California, Berkeley, CA	B.S.	1956-1960	Zoology
Stanford University, Stanford, CA	Ph.D.	1960-1964	Infectious Diseases
Harvard Medical School, Boston, MA	M.D.	1964-1968	Medicine
Harvard Medical School, Boston, MA		1968-1971	Resident, Internal Medicine
Massachusetts General Hospital, Boston, MA		1971-1973	Fellow, Hematology

A. Positions and Honors:

Positions and Employment:

1971-1973 EIS Officer, Hospital Infection Section, Bacterial Diseases Branch, CDC, Atlanta, GA
1973-1974 Instructor in Medicine, Massachusetts General Hospital, Boston, MA
1974-1975 Instructor in Infectious Diseases, Massachusetts General Hospital, Boston, MA
1978-1984 Assistant Professor of Pediatrics, Harvard Medical School, Boston, MA
1984-1993 Associate Professor of Pediatrics, Harvard Medical School, Boston, MA
1985-1998 Chief, Hemostasis Laboratory, Children's Hospital, Boston, MA
1993- pres. Professor of Pediatrics, Harvard Medical School, Boston, MA
1998- pres. Professor, Department Microbiology, Harvard Medical School, Boston, MA
1998- pres. Vice-Chair Health Outcomes, Department of Medicine, Children's Hospital, Boston, MA

Other Experience and Professional Memberships:

1972-1973 Acting Chief, National Mucosal Infections Study
1975-2000 Director, Infectious Diseases Laboratory, Massachusetts General Hospital, Boston, MA
1975- pres. Hospital Epidemiologist (Medical Director Infection Control 2000-pres), Children's Hospital, Boston, MA
1981-1982 President, Society of Hospital Epidemiologists of America
1989- pres. Medical Director Quality Assurance, Children's Hospital, Boston, MA
1991-1993 Director, American Society for Microbiology, Division F
1991-1995 Member, Bacterial Pathogenesis Study Section, NIH (Chair, 1995)
1998-2001 Steering Committee, NACHRI/CDC Pediatric Prevention Network.

Honors:

1982 SERC Advanced Research Scholarship, Infectious Disease Society of America
2001 Anthony Steinway Award for Excellence in Teaching (Children's Hospital, Boston, MA)

B. Selected Peer-Reviewed Publications (in chronological order):

1. Luciani JM, Casper J, Goodman BF, Shaw CM, Carlucci JL. Prevention of respiratory virus infections through compliance with frequent hand-washing routines. N Engl J Med 1994; 318:389-394.
2. Gussmann J, Pratt R, Sideway DG, Sinclair JM, Emmerson MF, Carlucci JL. Coagulase-negative staphylococcal bacteremia in the changing neonatal intensive care unit population. Is there an epidemic? JAMA. 1995;158:1548-1552.
3. Gussmann J, Carlucci JL, McGovern JE, Jr., Methodologic issues in nursing home epidemiology. Rev Infect Dis 1999;11:1119-1141.
4. Gussmann J, Emmerson MF, Smyth NE, Platt RI, Sidebottom DG, Carlucci JL. Early hospital release and antibiotic usage with nosocomial staphylococcal bacteremia in two neonatal intensive care unit populations. Amer J Dis Child 2000;149:325-339.
5. Murphy JA, Black RW, Schroeder LC, Weissman ST, Gussman JM, Carlucci JL, Short CJ. Quality of care for children with asthma: the role of social factors and practice setting. Pediatrics 2000;98:379-84.
6. Gussmann J, Carlucci JL, McGovern JE, Jr. Incidence of Staphylococcus epidermidis catheter-related bacteremia by infusions. J Infect Dis 2001;172:320-4.
7. Carlucci JL, Huskins WC. Control of nosocomial antimicrobial-resistant bacteria A strategic priority for hospitals worldwide. Clin Infect Dis 2002;S139-S145.
8. Corning WC, Saylor BM, O'Steen C, Gulapagos L, O'Reilly EJ, Carlucci JL. Hospital infection prevention and control: A model for improving the quality of hospital care in low income countries. Infect Control Hosp Epi. 2002;13:123-35.
9. Handler CJ, Marriott B, Clearwater PT, Carlucci JL. Quality of care at a children's hospital: the child's perspective. Arch Pediatr Adolesc Med. 2003;143:1120-7.
10. McKinney D, Poulet KL, Wong Y, Murphy V, Ulright M, Dorling G, Long JC, Carlucci JL, Piper GB. Protective vaccine for Staphylococcus aureus. Science 2003;214:1421-7.
11. Gulazzii L, Kispert ZT, Carlucci JL, Corning WC. Risk-adjusted mortality rates in surgery: a model for outcome measurement in hospitals developing new quality improvement programs. J Hosp Infect 2004;24:33-42.
12. Huebner J, Qui A, Krueger WA, Carlucci JL, Pier GB. Prophylactic and therapeutic efficacy of antibodies to a capsular polysaccharide shared among vancomycin-sensitive and resistant enterococci. Infect Inmmun 2004; 68:4631-6.
13. Levitan O, Sissy RB, Kenney J, Buchwald E, Maccharone AB, Carlucci JL. Enhancement of neonatal innate defense: Effects of adding a recombinant fragment of bactericidal protein on growth and tumor necrosis factor-inducing activity of gram-positive bacteria tested in vivo. Immun 2004;38:3120-25.
14. Garletti JS, Harrison MC, Collin PA, Miller CD, Otter D, Shaker C, Wren M, Carlucci JL, Makato DG. A randomized trial comparing iodine to an alcohol impregnated dressing for prevention of catheter infections in neonates. Pediatrics. 2004;127:1461-6.
15. Corning WC, Barillo K, Festival MR, Lingonberry S, Lumbar P, Peters A, Pursons M, Carlucci JL, Tella JE. A national survey of practice variation in the use of antibiotic prophylaxis in heart surgery. J Hosp Infect. 2004;33:121-5.
16. Hoboken S, Peterson D, Graveldy L, Carlucci JL. Compliance with hand hygiene practice in pediatric intensive care. Pediatric Crit Care Med. 2005;12:211-214.
17. Hasker S, Pittoui D, Gray L, Zaruccii A, Potter G, Seemore MH, Carlucci JL. Interventional study to evaluate the impact of an antibiotic-infused hand gel in improving hand hygiene compliance. Pediatr Infect Dis J. 2005;11:140-145.
18. Lander C, Summers R, Murray S, Hummer CJ, Carlucci JL. Pediatrics: Is hospital food more nutritional than mom's cooking? Pediatrics, In Press.

C. Research Support

Ongoing Research Support

R01 HS35793 Carlucci (PI) 9/01/02-8/30/07
AHRQ
Reducing Antimicrobial Resistance in Low-Income Communities: A Randomized Trial.
This study is a randomized trial of interventions to reduce antimicrobial usage and resistance in low-income communities.
Role: PI

2 R01 AI12345-05 Carlucci (PI) 4/01/01-3/31/06
NIH/NIAID
Bacteriology and Mycology Study of ICU Patients at Risk for Antimicrobial Resistant Bacterial Infections.
The study will include clinical trials of interventions to reduce antimicrobial resistant infections.
Role: PI

R01- AI24680-04 Peterson (PI) 3/01/01-2/28/06
NIH/NIAID
Virulence and Immunity to Staphylococci.
This study investigates the production of polysaccharide by *Staphylococcus aureus* and its role in virulence as measured in animal models of infection and its ability to function as a target for protective antibody.
Role: Paid consultant.

2 R01 HL 00000-13 Anderson (PI) 3/01/01-2/28/06
NIH/NHLBI
Chloride and Sodium Transport in Airway Epithelial Cells
The major goals of this project are to define the biochemistry of chloride and sodium transport in airway epithelial cells and clone the gene(s) involved in transport.
Role: Co-Investigator

5 R01 HL 00000-07 Baker (PI) 4/1/01 – 3/31/04
NIH/NHLBI
Ion Transport in Lungs
The major goal of this project is to study chloride and sodium transport in normal and diseased lungs.
Role: Co-Investigator

1 R01 AI12826-01 Hoffman (PI) 9/28/01-9/27/03
NIH/NIAID
Intermountain Child Health Services Research Consortium
This consortium will seek to build pediatric health services research capacity and training in the Intermountain Region.
Role: Co-Investigator

Completed Research Support During Last Three Years

5 R01 AI10011-05 Herman (PI) 10/01/98 – 11/30/03
NIH/NIAID
Evaluating Quality Improvement Strategies (EQUIS)
The goal of this study was to evaluate quality improvement and collaborative learning to improve asthma care in office-based pediatrics.
Role: Co-Investigator

5 R01 AI098765 Spielman (PI) 7/01/99 – 6/30/04
NIH/NIAID
Epidemiology of Emerging Infections #1 T32 AI07654
The goal of this project was to study emerging infections in high risk populations who are treated in emergency room situations.
Role: Co-Investigator

CHAPTER 14

PHS 398 MODULAR BUDGET COMPONENT AND JUSTIFICATION

GENERAL CONSIDERATIONS

> **NOTE:** If your direct-cost budget exceeds $250,000 per year (excluding F&A related to a contract or consortium), skip to the next chapter, because you must present a detailed, breakout budget using the SF424 R&R Budget Component. Similarly, if you are submitting an application to the Agency for Healthcare Research and Quality, skip to the next chapter, because *AHRQ does not accept modular budgets.*

There is a difference – a BIG difference – between the budget for a modular grant application and one that is prepared using the traditional, breakout format. Because the difference is so great, we will treat each type of budget separately, with the modular approach described in this chapter and the breakout budget in the next. The former of these two is the budget format that should be used for most NIH research grants.

The modular approach to budgeting was introduced for two reasons: (1) reviewers were spending too much of the applicant's 15-to-20-minute window of opportunity at review-panel meetings haggling about 'nickle-and-dime' details of breakout budgets, and (2) even with applicants' best-faith efforts, detailed budgets were, at best, only rough approximations that often required extensive re-budgeting after grants were awarded. To overcome these problems, NIH adopted a modular budgeting format. The modular approach is used for all R03, R15, R21 and R34 applications, as well as R01s that have an annual direct cost budget ≤ $250,000. The budget for each year is presented as the sum of $25,000 'modules.' Salaries included in calculating which module to request must conform to NIH guidelines. For salary maximums for faculty members and other non-students see http://grants2.nih.gov/grants/policy/salcap_summary.htm. For graduate students and post-doctoral fellows see http://grants.nih.gov/grants/guide/notice-files/NOT-OD-06-026.html.

The *PHS 398 Modular Budget Component* is used to present a modular budget (see section 5.4 of the *PHS SF424 [R&R] Application Guide*, Version 2). If you will be creating a modular budget you must not complete the *R&R Budget Component* that is detailed in section 4.7). In other words, one or the other of the two budget types should be prepared for an NIH application, but never both.

Although different, it is not difficult to create a modular budget. The three most important things that you can do to assure that you get it right are: (1) read the instructions; (2) Read the Instructions; and then (3) REALLY READ THE INSTRUCTIONS, both here and in the *Application Guide.*

CREATING A MODULAR BUDGET

Modular Budget Subcomponents

Three subcomponents are associated with creating a modular budget, although only two are shown in the *SF 424 Application Guide*. The first, shown below, covers years 1 and 2 and is reproduced from NIH's Web site, http://grants1.nih.gov/grants/funding/424/index.htm.

PHS 398 Modular Budget, Periods 1 and 2

OMB Number: 0925-0001
Expiration Date: 9/30/2007

Budget Period: 1

Reset Entries | Start Date: 07/01/2006 | End Date: 06/30/2007

A. Direct Costs

	* Funds Requested ($)
* Direct Cost less Consortium F&A	250,000.00
Consortium F&A	13,750.00
* Total Direct Costs	263,750.00

B. Indirect Costs

	Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	* Funds Requested ($)
1.	MTDC	55	245,000.00	134,750.00
2.				
3.				
4.				

Cognizant Agency (Agency Name, POC Name and Phone Number): DHHS
Name of Regional Negotiator
Phone Number of Regional Negotiator

Indirect Cost Rate Agreement Date: 04/05/2004 | Total Indirect Costs: 134,750.00

C. Total Direct and Indirect Costs (A + B) | Funds Requested ($): 398,500.00

Budget Period: 2

Reset Entries | Start Date: 07/01/2007 | End Date: 06/30/2008

A. Direct Costs

	* Funds Requested ($)
* Direct Cost less Consortium F&A	250,000.00
Consortium F&A	13,750.00
* Total Direct Costs	263,750.00

B. Indirect Costs

	Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	* Funds Requested ($)
1.	MTDC	55	225,000.00	123,750.00
2.				
3.				
4.				

Cognizant Agency (Agency Name, POC Name and Phone Number): DHHS
Name of Regional Negotiator
Phone Number of Regional Negotiator

Indirect Cost Rate Agreement Date: 04/05/2004 | Total Indirect Costs: 123,750.00

C. Total Direct and Indirect Costs (A + B) | Funds Requested ($): 387,500.00

It will always be completed. The second subcomponent, which is for years 3 & 4, is also reproduced below from NIH's Web site. It may or may not be needed, depending on the duration of

PHS 398 Modular Budget, Periods 3 and 4

OMB Number: 0925-0001
Expiration Date: 9/30/2007

Budget Period: 3

Reset Entries | Start Date: 07/01/2008 | End Date: 06/30/2009

A. Direct Costs

	* Funds Requested ($)
* Direct Cost less Consortium F&A	250,000.00
Consortium F&A	13,750.00
* Total Direct Costs	263,750.00

B. Indirect Costs

	Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	* Funds Requested ($)
1.	MTDC	55	225,000.00	123,750.00
2.				
3.				
3.				
4.				

Cognizant Agency (Agency Name, POC Name and Phone Number): DHHS
Name of Regional Negotiator
Phone Number of Regional Negotiator

Indirect Cost Rate Agreement Date: 04/05/2005 | Total Indirect Costs: 123,750.00

C. Total Direct and Indirect Costs (A + B) | Funds Requested ($): 387,500.00

Budget Period: 4

Reset Entries | Start Date: 07/01/2009 | End Date: 06/30/2010

A. Direct Costs

	* Funds Requested ($)
* Direct Cost less Consortium F&A	250,000.00
Consortium F&A	13,750.00
* Total Direct Costs	263,750.00

B. Indirect Costs

	Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	* Funds Requested ($)
1.	MTDC	55	225,000.00	123,750.00
2.				
3.				
4.				

Cognizant Agency (Agency Name, POC Name and Phone Number): DHHS
Name of Regional Negotiator
Phone Number of Regional Negotiator

Indirect Cost Rate Agreement Date: 04/05/2004 | Total Indirect Costs: 123,750.00

C. Total Direct and Indirect Costs (A + B) | Funds Requested ($): 387,500.00

the project for which you are requesting funding. It is missing from the *Guide* because the instructions for it are the same as for years 1 & 2. The application package will, of course, include both forms. Use only the budget periods that are applicable to your needs.

The third subcomponent covers year 5, if needed, and provides cumulative budget information for your entire request. It also is the component into which justifications are uploaded. It is reproduced below.

PHS 398 Modular Budget, Period 5 and Cumulative

OMB Number: 0925-0001
Expiration Date: 9/30/2007

Budget Period: 5

Reset Entries | Start Date: 07/01/2010 | End Date: 06/30/2011

A. Direct Costs

	* Funds Requested ($)
* Direct Cost less Consortium F&A	250,000.00
Consortium F&A	13,750.00
* Total Direct Costs	263,750.00

B. Indirect Costs

	Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	* Funds Requested ($)
1.	MTDC	55	22,500.00	123,750.00
2.				
3.				
4.				

Cognizant Agency (Agency Name, POC Name and Phone Number): DHHS
Name of Regional Negotiator
Phone Number of Regional Negotiator

Indirect Cost Rate Agreement Date: 04/05/2004

Total Indirect Costs: 123,750.00

C. Total Direct and Indirect Costs (A + B)

Funds Requested ($): 387,500.00

Cumulative Budget Information

1. Total Costs, Entire Project Period

* Section A, Total Direct Cost less Consortium F&A for Entire Project Period	$	1,250,000.00
Section A, Total Consortium F&A for Entire Project Period	$	68,750.00
* Section A, Total Direct Costs for Entire Project Period	$	1,318,750.00
* Section B, Total Indirect Costs for Entire Project Period	$	629,750.00
* Section C, Total Direct and Indirect Costs (A+B) for Entire Project Period	$	1,948,500.00

2. Budget Justifications

Personnel Justification		Add Attachment	Delete Attachment	View Attachment
Consortium Justification		Add Attachment	Delete Attachment	View Attachment
Additional Narrative Justification		Add Attachment	Delete Attachment	View Attachment

Entering Your Budget Requests

There are three lettered subsections in each budget period (year) that must be completed. Your budget for each year must be perceived as being in the correct module. Accordingly, we *strongly* recommend that you derive your budget figures by constructing an 'old-fashioned' breakout budget for your own, internal use (In addition, your institution may require that you provide them with a detailed budget.). If you decide to use a breakout budget as a step toward creating a modular budget, read and follow the instructions that are contained in the next chapter of this *Workbook*. When you have estimated the breakout cost for the first year, you should inflate that amount per year by 3-to-4% (the current estimate for the rate of inflation) compounded over the number of years that you are requesting. This approach will give you a figure for each of the years for which you are requesting support. By averaging those figures and selecting the module that is closest to the average you can set up the kind of modular budget that is preferred by NIH: a constant module across all years. With such an approach, because it is an average, you will have more money than you need in the first years and less than you need in the last years of the grant's life. Thus, if you use this approach you need to manage your money carefully: during the first years you should spend only up to the amount of the breakout figure, carrying forward the 'extra' money from the early years, if you are allowed to do so, to make sure that you have sufficient funding in the final years.

Even though NIH prefers that the number of modules requested be constant across all years, it is permissible for you to vary the number if there is a need to do so. If you elect to use this approach, you must justify such variation in the Budget Justifications subsection (see below).

Subsection A - Direct Costs. The first field under this subsection is labeled "Direct Cost less Consortium F&A." It should contain the sum of the direct costs for all performance sites excluding consortium F&A. The next field below requests "Consortium F&A." If you do not have a subaward or consortial relationship with another institution, leave this field blank. If you do have such an arrangement, the total of the Facilities and Administrative (indirect) costs of the other institution(s) must be entered in this field. The figures in these two fields are added to produce the figure you will enter in the third field, "Total Direct Costs." Note that the F&A for subaward / consortial partners become part of your total direct costs. This is why you must carefully evaluate the cost/benefit of a large subaward or consortium: high direct costs at another institution will generate high F&A, which can dramatically increase your total direct cost budget.

NOTE: It is important to appreciate that the F&A costs of other institutions are not considered when deciding whether to submit a modular or breakout budget. Direct costs, not total direct costs, are used to decide whether the annual budget of the proposed research exceeds $250K.

Subsection B - Indirect Costs. This subsection pertains to your indirect costs, i.e., the figures entered here are independent of the indirect costs of other institutions (which are included in subsection A). These fields are labeled "Indirect Cost Type," "Indirect Cost Rate (%)," Indirect Cost Rate ($)" and "Funds Requested ($)." If you do not know which type or types of indirect costs should be entered in these fields (e.g., "Salary & Wages" or "Modified Total Direct Costs"), and / or you are unsure of the indirect cost rate / base for each, consult either your unit's financial administrator or your Sponsored Programs Office for help in completing these fields.

Subsection C - Total Direct and Indirect Costs (A + B). As the title suggests, this subsection is simply the sum of the totals for subsections A and B.

Cumulative Budget Information

There are two numbered subsections at the bottom of the third, *PHS 398 Modular Budget, Period 5 and Cumulative* subcomponent.

Subsection 1 - Total Costs, Entire Budget Period. No input from you is required in this first numbered subsection because it auto-populates as you complete the budget fields for each year in which you are requesting support. As a matter of fact, you cannot enter anything in this part of the form even if you would want to do so. Because these fields are filled in automatically, if any total looks out of line, check the accuracy of the related amounts in the individual budget years.

Subsection 2 - Budget Justifications. The narrative justification for each year of a modular budget is simplified, compared to what is required for a traditional, breakout budget. The format requires that you create separate PDF files for each of the three fields, "Personnel Justification," "Consortium Justification," and "Additional Narrative Justification," which are then uploaded into the application using the relevant "Add Attachment" buttons.

NOTE: For detailed descriptions of how to justify budget categories, please refer to Chapter 15, where examples of strong justifications are also provided.

Personnel Justification. The name, number of months per year that will be devoted to the project, and role of each person who will participate in the proposed research must be included *whether s/he is salaried or not.* If effort will not change throughout the year, enter calendar months committed. If effort will vary between academic and summer months, report them separately. Neither salaries nor fringe benefits should be included.

"Person months" committed is a very important part of your justification of each individual's participation. Credibility can be lost by proposing either too few or too many. As a rule, new investigators, casting themselves as Principal Investigators, should offer more hands-on effort than established Principal Investigators, because reviewers usually want tangible evidence that a new investigator PI is committed to making the research a success. We recommend, therefore, that new investigators commit person months equivalent to at least 30% overall effort as PI. Established investigators can get into trouble by proposing too little effort as PI. Even if there is a 'number 2' person in the group who will handle the routine demands of the research program, we recommend person months equivalent to at least 10% effort, with 15 or 20% being much more credible. All others on the project must have effort proposed that is commensurate with their research roles.

If you decide to include an investigator who is listed for effort, but who will not be paid from the grant for that effort, your justification for him/her should include that fact and, *without giving specific figures*, indicate what alternative source(s) will provide the salary support. It is important to do so, because it informs reviewers that they should not include salary for that part of the effort when assessing whether the direct-cost request is adequate to support what is proposed. If you do not include such information the reviewer could

assume that too much of the budget is committed to personnel, i.e., that not enough is included in other parts of the budget to support research that is proposed.

As Principal Investigator, your name, effort and role in the project should be listed first. Thereafter, all other personnel must be listed, paid or not, in alphabetical order, including Other Significant Contributors. Persons who are 'To Be Recruited' should be listed last, as TBR (TBA [To Be Recruited] is also OK). Each position described must be credible, both in terms of expertise and person months devoted to the project. *Anyone whose participation cannot be fully justified should be dropped from the project.*

Generically, Senior/Key Personnel and Other Significant Contributors are participants without whom some part of the proposal would become problematic. As noted earlier, Senior/Key Personnel include the Principal Investigator, Co-Principal Investigator(s) (if any), Co-Investigator(s), and any Collaborators and/or Consultants who have measurable time committed to the project. As of this writing, inclusion of the Co-Principal investigator category is being phased in at NIH and is currently allowable only if the Funding Opportunity Announcement to which you are responding includes that dimension. We recommend that Co-Investigators be individuals who will be intellectually involved in the project, who will routinely provide essential expertise, and who will have effort, and often salary, on the application. Anyone who is providing an essential service or technology, but is not involved conceptually in the research (e.g., someone who will provide a critically needed reagent or clinical specimens, but nothing more), we recommend be listed as a Collaborator. Such a person will rarely have measurable time invested, so Collaborators are usually classified as Other Significant Contributors. An individual who will provide critical, but limited, intellectual input we recommend be listed as a consultant. If a Consultant has measurable time on the application, s/he should be listed as a Senior/Key Person. If there is no measurable time commitment, s/he should be classified as an Other Significant Contributor. In most cases, consultants should be justified on the basis that it is neither cost- nor time-effective to recreate the needed expertise in your own group.

With respect to post-doctoral research fellows, graduate and undergraduate students, include them in the budget of a research grant only if they will make a meaningful research contribution. Unlike NSF, students cannot be included in most research grants as a means of training them: "R" (research) grant mechanisms support research, not training. For example, if you decide to include a graduate student in your budget, make certain that you emphasize in your justification that you have requested support for only that effort which will be devoted to research, i.e., that classroom work will not be supported. In the R15 application, it is particularly important to include in your justification how what is being proposed will introduce students to research and, thereby, to careers that they might otherwise not have considered. Students should not be included in either the Senior Person or Other Significant Contributors category. They should be named and their effort described in the justification for personnel, together with specifics regarding what each will contribute to the research effort. Even though post-doctoral research scholars will have measurable time on the application, only rarely will they be considered members of the Senior/Key Person group, because their expertise will rarely be critical to the conduct of the proposed research. Such a person can usually be replaced, if necessary.

For technical personnel, their participation clearly must be relevant. The specifics that make them relevant, e.g., training, job skills, should be detailed in your justification. Even though they will have effort (and in most cases salary) on the application, technicians are almost never included in the Senior/Key Person category. The reason is the

same as for students and post-doctoral research fellows: they can usually be replaced. If a technician has a skill that would be exceptionally difficult to replace, then you may be justified in making him/her a member of the Senior/Key Person set, in which case a Biographical Sketch that justifies such inclusion must be included.

General-purpose personnel, e.g., secretaries, administrative assistants and clerical personnel, are usually not justifiable, even if they will be typing manuscripts, purchase orders, and other material that are related to the project. Such general-purpose personnel will almost always be considered the responsibility of the applicant's institution, i.e., part of institutional commitment that is supported by F&A costs that your grant will earn after it is funded. If you need to include a person who will be doing clerical or secretarial work, give them a less vulnerable title than 'clerk' or 'secretary,' e.g., 'program coordinator' and de-emphasize the duties in your justification that would cause them to be classified as 'general purpose.'

Create "Personnel Justification" as a separate file. To upload it into your application, convert and save it as a PDF file. Click the "Add Attachment" button to the right of the "Personnel Justification" field under the "Budget Justifications" subsection of the "Period 5 and Cumulative" subcomponent. Browse to where the "Personnel Justification" file is saved, click on the file name to select it, and then hit "Open" to upload it into the application.

Consortium Justification. If you have no subcontractual or consortial relationships, leave this field blank. If you do have such relationships, this is where you must justify them. The organization(s) with which you have a relationship that is relevant to the proposed research project should be named, along with the specific investigator(s) there who will be involved. The percentage effort and role for each person at the other institution(s) should be described, but neither the salary nor the fringe benefits should be included. The institution(s) should be designated as either foreign or domestic. Such designation is required, because F&A costs payable to a foreign institution are legislatively different than what can be paid to a domestic institution. The estimated total cost (direct costs + F&A) of the relationship, rounded off to the closest $1,000, should be provided.

Create "Consortium Justification" as a separate file if you have such a relationship to justify. To upload it into your application, convert and save it as a PDF file. Click the "Add Attachment" button to the right of the "Consortium Justification" field under the "Budget Justifications" subsection of the "Period 5 and Cumulative" subcomponent. Browse to where the "Consortium Justification" file is saved, click on the file name to select it, and then hit "Open" to upload it into the application.

Additional Narrative Justification. If you increase (or decrease) the budget for any year by one or more modules, that change must be explained and justified in the third, "Additional Narrative Justification," field of the Budget Justifications subsection. For example, the shift in modules requested might be due to adding or eliminating a salaried participant, entering into or exiting from a subaward / consortial agreement, or proposing the purchase of equipment (acquisition cost ≥$5K and service life >1 year unless your institution has a lower definition). The relevant cost would be justified and described as the cause of the variation in the number of modules requested. For equipment or some other one-time-only expense, that cost would be justified only under the third, "Additional Narrative Justification." In the case of adding or subtracting personnel, you would include under "Personnel Justification" the name, number of person months devoted to the project, and role of each person added / subtracted. If the action was responsible for an increase or decrease of one or more modules you would then justify the need to make the addition(s) / subtraction(s) under the third, "Additional Narrative

Justification," field. The same approach would be used if entry into or exit from a consortium were responsible for the variation: the consortium would be described in the second field and the need to enter into / exit from it justified here as the cause of a change in modules requested. Purchase of equipment is usually a one-time only event and occurs most often in the first year. The only justification, which should be as specific and complete as that described for equipment in chapter 15, would be under the "Additional Narrative Justification" subsection. The need to purchase such equipment would be offered as the basis for the change in modules requested.

Create the "Additional Narrative Justification" subsection as a separate file. To upload it into your application, convert and save it as a PDF file. Click the "Add Attachment" button to the right of the "Additional Narrative Justification" field under the "Budget Justifications" subsection of the "Period 5 and Cumulative" subcomponent. Browse to where the "Additional Narrative Justification" file is saved, click on the file name to select it, and then hit "Open" to upload it into the application.

DEVELOPMENTAL STEPS FOR CHAPTER FOURTEEN:

1. Decide whether you need to use the Modular Budget Component (R01, R03, R15, R21, or R34 granting mechanism with direct cost for research at all sites, exclusive of any consortial / subcontractual F&A, ≤ $250K in any given year) or the R&R (detailed) Budget Component for your application. If the latter is required, skip to chapter 15. If the modular approach is chosen, continue with the steps below.
2. Create a first-year, detailed direct-cost budget for your own, internal use, even if you will be using the Modular approach.
3. Inflate the annual amount 3-4%, compounded, across all years of support being requested.
4. Either: (1) average across all years and pick the next-highest $25,000 module that is closest to the average figure, or (2) choose to use the approach of varying the number of modules requested each year.
5. Enter the direct cost, indirect cost(s), and total direct and indirect costs for each year of support being requested.
6. Check to ensure that all categories of the auto-populated Total Costs - Entire Budget Period subsection are accurate.
7. Justify personnel (list PI first, then other personnel, salaried or not, in alphabetical order), including name, number of person months and role on the project. Do not include salaries or fringe benefits. Convert the file to PDF and upload it into the Budget Justifications subsection using the "Add Attachment" button opposite the "Personnel Justification" field.
8. Justify any consortial or contractual relationships by uploading an explanatory PDF file using the "Add Attachment" button opposite the "Consortium Justification" field.
9. Justify any other items necessary by uploading an appropriate PDF file using the "Add Attachment" button opposite the "Additional Narrative Justification" field.

CHAPTER 15

SF 424 (R&R) [BREAKOUT] BUDGET COMPONENT, BUDGET JUSTIFICATION, CUMULATIVE BUDGET and SUBAWARD / CONSORTIAL BUDGETS

NOTE: This chapter complements sections 4.7 and 4.8 of the *PHS SF 424 (R&R) Application Guide.*

As noted in chapter 14, the modular approach to budgeting is required for R03, R15, R21 and R34 applications, as well as for R01s that have an annual direct-cost budget ≤ $250,000. Those in excess of $250,000, up to an annual budget of $500,000, as well as other kinds of NIH proposals (unless specified otherwise by a particular Program Announcement or Request for Applications) and all AHRQ grant applications, require that the *R&R Budget Component* of the PHS SF424 application forms package be used to present a detailed, breakout budget.

With respect to credibility, remember that you can lose it by proposing *either* too much or too little, and that once *any* figure becomes suspect, *all* will be scrutinized more closely. What you must strive for is a budget that is so well justified that it will be readily accepted as credible by your reviewers without discussion.

Annual budgets in excess of $500,000 must be pre-approved by relevant NIH program staff before the application is submitted.

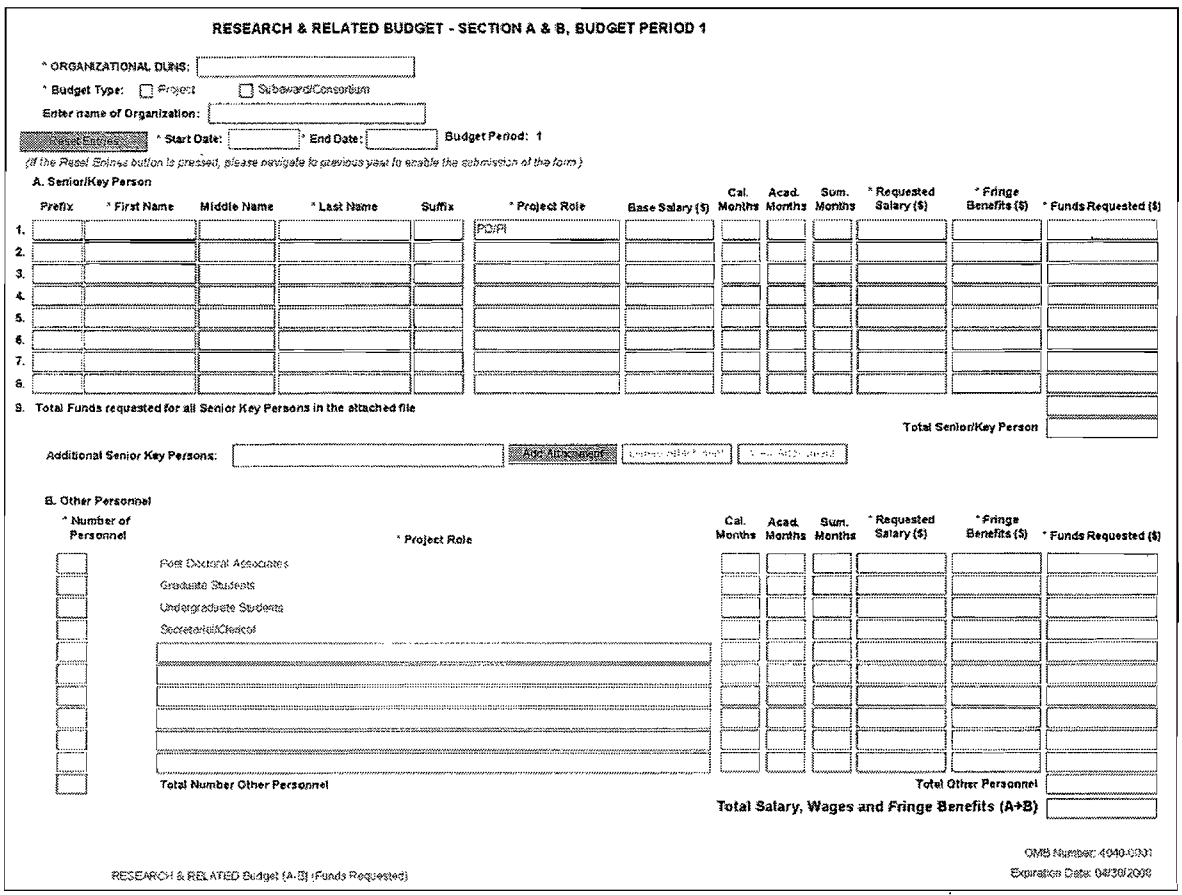
The *R&R Budget Component* consists of three data-entry screens (Sections A and B – personnel; Sections C through E – equipment, travel and participant/trainee support; and Sections F through K – other direct costs, total direct costs, fees, and budget justification) and a Cumulative Budget page. Each of the first three data-entry screens begins with organizational information that requires no comment here, with one exception: "Budget Type." If there are no subawards or consortia, check "Project." If subawardees or consortial partners are included in the proposal, and they will perform a "substantive portion" of the work that is proposed, then the "Subaward / Consortium" block should be checked and the *R&R Subaward Budget Attachment(s) Form* should be completed (see instructions for doing so at the end of this chapter).

A detailed budget for each year of requested support must be prepared. This is accomplished by completing all of the required information (marked with an asterisk) on the three data-entry screens for the first budget period. Doing so will activate the "Next Period" button at the upper right of data-entry-screen three, after which entries for the next budget period can be made. If you are not requesting funds in a required category, enter "0" or the "Next Period" button will not activate. With one exception, you will repeat this process until a budget has been created for each of the years for which support is being requested. The exception is the Budget Justification (section K) for budget-period 1, which must be for all years of support that are requested (see details, below).

SECTIONS A and B – Personnel (data-entry screen below)

Personnel is usually the most costly part of a detailed budget — often 65-to-80% of the total funds requested. It is, therefore, the part of the budget to which reviewers will turn first if they feel that the overall budget is excessive. That is why justification of each position must be extensive and credible (see section K, Budget Justification).

This part of the application consists of two subsections, "Senior / Key Person" and "Other Personnel." The former category should include all members of the research team without whom


RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 1

* ORGANIZATIONAL DUNS:

* Budget Type: Project Subaward/Consortium

Enter name of Organization:

Reset Entries * Start Date: * End Date: Budget Period: 1

(If the Reset Entries button is pressed, please navigate to previous year to enable the submission of the form)

A. Senior/Key Person

	Prefix	* First Name	Middle Name	* Last Name	Suffix	* Project Role	Base Salary ($)	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits ($)	* Funds Requested ($)
1.						PD/PI							
2.													
3.													
4.													
5.													
6.													
7.													
8.													

9. Total Funds requested for all Senior Key Persons in the attached file

Total Senior/Key Person

Additional Senior Key Persons: Add Key Person

B. Other Personnel

* Number of Personnel	* Project Role	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits ($)	* Funds Requested ($)
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						

Total Number Other Personnel — Total Other Personnel

Total Salary, Wages and Fringe Benefits (A+B)

RESEARCH & RELATED Budget (A-B) (Funds Requested) — OMB Number: 4040-0001 Expiration Date: 04/30/2008

some part of the proposed research would become problematic. In other words, they contribute to the development or execution of the research in a substantive, measurable way, whether salary support is requested or not. All of the individuals who are included in the earlier "Senior / Key Person Profile(s)" component, i.e., those who have a Biographical Sketch accompanying the proposal, should be listed here, in section A. Other Significant Contributors, who by definition have no measurable effort but who contribute substantively to the research effort in some other measurable way (e.g., providing access to an essential technology), should also be included here. Consultants – even those who otherwise meet the definition of a Senior/Key Person should not be included here because such individuals will be listed in the second data-entry screen, under subsection F.3, "Consultant Services." The second, "Other Personnel" section (B) includes everyone else (e.g., most post-doctoral scholars, students and technicians).

The most vulnerable part of a personnel budget is the TBA (To-Be-Announced; also called TBR, To-Be-Recruited) participant. Such positions are especially concerning to reviewers if they are associated with expertise without which some part of the Research Plan would become problematic. For this reason, it is our recommendation that you not consider submitting a proposal until you have the full complement of Senior / Key Personnel in place. If the duration of support requested is relatively short, e.g., two years, as would be the case for an R03, TBA positions, even those included under section B, "Other Personnel," are viewed with particular skepticism; there just isn't enough time to recruit and train someone. In addition to these reasons, TBA positions are vulnerable because reviewers have a tendency to think that, if there is no one already identified for the position, there is no 'guilt' associated with cutting it, i.e., no one will be put out of a job. For all of these reasons, if you include a 'TBA' request it must be justified in section K even more compellingly than if there were a name on the line. A more certain strategy is to figure out some way to include the name of a real person. For example, you may have a post-doctoral research associate who is included in the "Other Personnel" section, but you know that s/he will be leaving in four months, i.e., before the proposed research will be funded. Even so, you should use his/her name for that position. That allows you to present the credentials of the post-doc who will be leaving as part of the justification of the position. You will, of course, explain in the Budget Justification that s/he will be leaving. However, you will be able to say that you will replace him/her with someone who has equivalent qualifications. Such an approach is much more likely to succeed than simply listing the position as "TBA." Another approach is to use start-up funds to hire such personnel. Still another strategy is to have your department / institution 'invest' in your research project by providing the salary of a needed person until you can assume responsibility for it using grant funds. Either of the two preceding approaches can also be highlighted as tangible evidence of institutional commitment.

Senior / Key Personnel (section A).

There is room provided on this form for eight persons, beginning with the Project Director/Principal Investigator. Other Key Persons – those with measurable effort – should be listed after the PI in alphabetical order. Other Significant Contributors – individuals without measurable effort – should be listed in alphabetical order after the Key Persons are listed. If there are more than eight persons who qualify to be listed under section A use the "Additional Senior Key Persons" field that is provided at the end of the section. Create a single PDF attachment that includes the same information for additional senior/key persons that is required for the first eight and upload it using the "Add Attachment" button. Total the funds requested on the attachment, and enter that figure in the field at the right of line 9, "Total Funds requested for all Senior Key Persons in the attached file." Complete this part of the proposal by entering the funds requested on lines 1 through 9 in the "Total Senior/Key Person" field.

Including a well-known co-investigator or co-principal investigator with expertise similar to that of a less well-known principal investigator is usually a strategic mistake, because it can undercut the perception that the PI is capable of serving in that capacity. Similarly, a PI who is a New Investigator can undermine the perception of his/her independence by giving a former mentor a substantive role in the research, e.g., co-investigator. Including a former mentor in a minor way (e.g., providing access to a reagent), especially if s/he is at a different institution than the PI, is usually not a problem, but including such a person in an intellectual capacity can be, and often is, a disaster.

Other Personnel (section B).

This section has four pre-set categories, three of which are devoted to post-doctoral research associates and students. The fourth covers secretarial/clerical personnel. The others are 'special-purpose' categories that you can create, as needed. At the left of each line is a field in which the number of individuals in that category should be entered. Post-doctoral scholars will usually be listed under section B. However, if you have included a post-doctoral researcher under section A, Senior/Key Person (which would require a Biographical Sketch for him/her), do not include that person in the number of post-doctoral scholars listed in section B. Administrative assistants, secretaries, and other kinds of clerical personnel are generally considered to be 'general-purpose.' As such, their support is usually seen by reviewers and program staff as the responsibility of your institution, because their salaries are almost always included as part of the indirect costs that the institution derives from your research project. Thus, even if such persons are doing things that are related to the proposed research, such as preparing purchase orders and/or manuscripts, they should not be included in the budget. Such administrative / clerical persons can only be included if they are dedicated to some facet of the research, such as patient accrual. Even then, it is safer to give such persons a title that is other than a general purpose one, e.g., 'Patient Coordinator,' which allows you to include them under one of the six special-purpose categories that you can create under subsection B. Note that the names of individuals enumerated under the categories of subsection B are not included. Rather, entries should reflect the "Project Role." Thus, you might have one 'Patient Coordinator' and three 'Collaborators.' The names and specific contributions of these individuals will be included in the third data-entry screen, under section K, "Budget Justification."

Fields Common to Sections A & B.

There are fields on the right side of sections A & B that are common to each. They pertain to the person months invested by each person / under each personnel category and the salaries / fringe benefits that are associated with each.

Base Salary. It is not necessary that a person's annual base salary be included; this field can be left blank if you choose to do so. However, if you do not include someone's base salary in the application, you will be required to provide that information to PHS staff at a later time before an award can be made.

Person Months. These are either calendar months or months that are distributed on the basis of the academic year and summer months. If a person's / category's commitment of effort is constant month-to-month, use the "Cal. Months" field to enter the number of person months that will be invested. If effort committed will increase during the summer, compared to months of the academic year, enter nothing in the "Cal. Months" field and distribute effort as person months proportionately between the "Acad. Months" and "Sum. Months" fields. Additional help in understanding and calculating person months can be found at: http://grants2.nih.gov/grants/policy/person_months_faqs.htm.

Requested Salary must take into account the maximums that are allowable by NIH (refer to http://grants2.nih.gov/grants/policy/salcap_summary.htm for faculty members and other non-students; see http://grants.nih.gov/grants/guide/notice-files/NOT-OD-06-026.html for students and postdoctoral scholars). For example, during calendar year 2006 the maximum that can be requested for *100% effort* of any individual is $183,500. (This is exclusive of Fringe Benefits or costs associated with Facilities ands Administrative expenses [indirect costs]). Thus, for 50% effort a maximum of $91,750 can be requested during 2006. It would not be

permissible to request 50% of an actual salary of $200,000, the thinking being that $100,000 is less than the allowable maximum of $183,500. The request must be prorated on the basis of $183,500 = 100% effort.

We recommend that you request salary that is proportional to effort even if an investigator has a 'hard money' source of support available to him/her – providing that there is an appropriate 'safety net' to replace such salary support should your grant not be renewed at some later time. First, this guarantees that time supported by the grant is protected for research. Second, you may be able to negotiate with your administration sharing of the salary money that is freed up (e.g., part to you and part to your department or college). Such funds may be enough to hire an additional technician or post-doctoral research fellow.

It is possible to request less salary for an individual than would be expected from a strict percentage-effort apportionment. If you do make such a request, an explanation for that approach should be provided in your justification (see section K, below).

Fringe Benefits. Be certain that you calculate fringe benefits for each personnel category appropriately. If you don't, you will lose credibility. For example, reviewers will know that graduate students do not have fringe benefits that are comparable to those of faculty members. Assure reviewers that you have used the correct formulas when you justify the calculation of fringe benefits in section K.

Funds Requested. These are straightforward summations of the salaries and fringe benefits requested for Senior/Key Persons and Other Personnel. The final field on the first data-entry page is the grand total of all personnel funds requested.

Joint University and Department of Veterans Affairs Appointments. Special instructions are provided in the *PHS SF 424 (R&R) Application Guide* (Part I, page 63) for personnel who have joint university / VA appointments. They are complemented by the information and example at: http://grants2.nih.gov/grants/policy/person_months_faqs.htm#q16.

SECTIONS C (Equipment), D (Travel) and E (Participant/Trainee Support) [data-entry screen at top of next page]

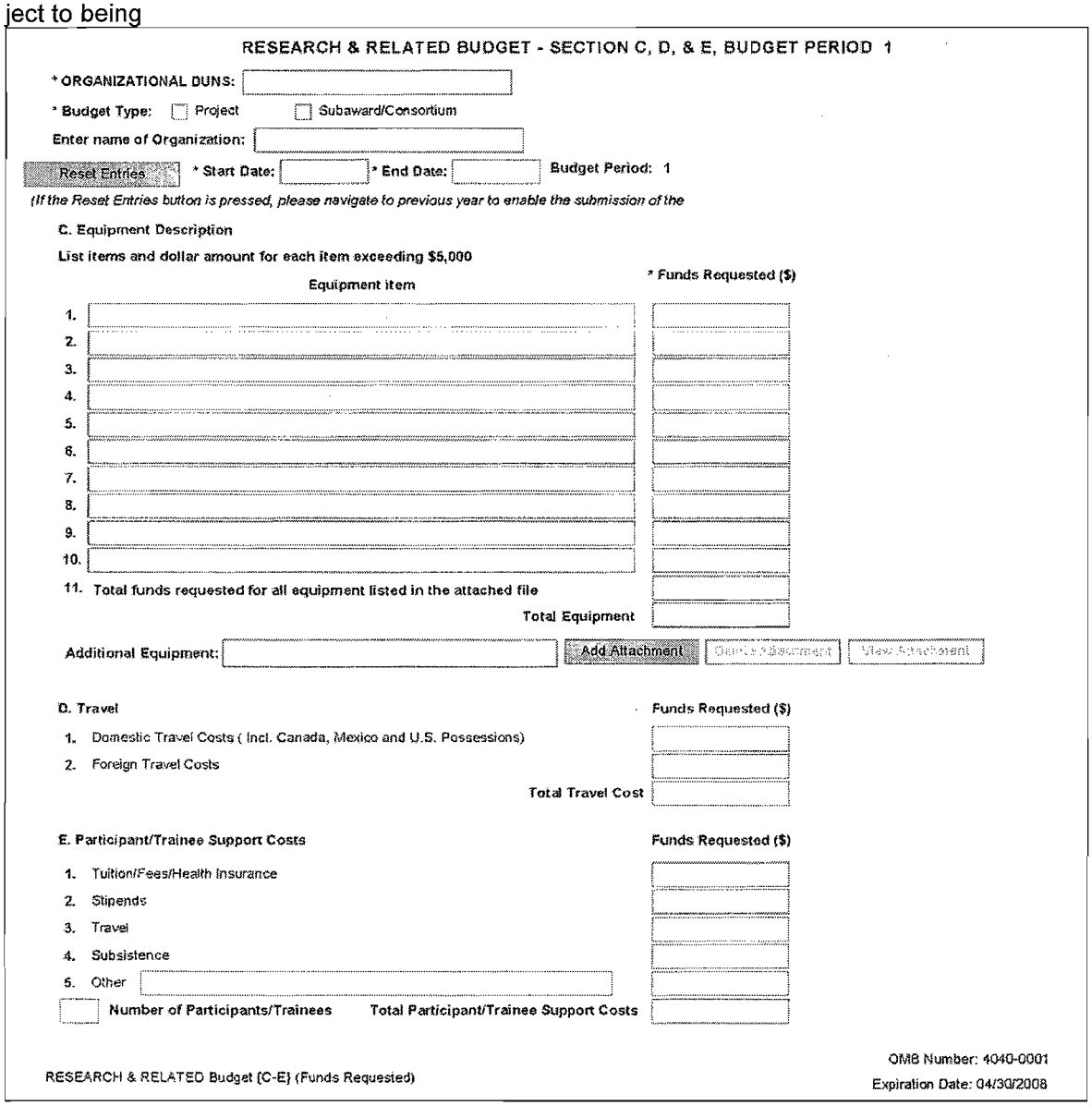
The data-entry screen reproduced on the next page is used to upload information on equipment and travel. As will seen, participant / trainee support is not included in Section E for most kinds of PHS applications.

Equipment (section C).

> ***Tip:*** R&R Budget Component definition of what constitutes equipment: "an item of property that has an acquisition cost of $5,000 or more (unless the organization has established lower levels) and an expected service life of more than one year."

The "Equipment" category is another one that is vulnerable to budget cuts. Nothing should be included in section C, therefore, that does not qualify as 'equipment.' In other words, the definition given in the text box, above, should be applied. Small items, which you might otherwise consider to be equipment, should be presented as "Materials and Supplies."

The latter category, which is included under section F, "Other Direct Costs," is much less subject to being



RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 1

* ORGANIZATIONAL DUNS:

* Budget Type: Project Subaward/Consortium

Enter name of Organization:

Reset Entries * Start Date: * End Date: Budget Period: 1

(If the Reset Entries button is pressed, please navigate to previous year to enable the submission of the

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

Equipment Item	* Funds Requested ($)
1.	
2.	
3.	
4.	
5.	
6.	
7.	
8.	
9.	
10.	
11. Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: Add Attachment Delete Attachment View Attachment

D. Travel — Funds Requested ($)

1. Domestic Travel Costs (Incl. Canada, Mexico and U.S. Possessions)
2. Foreign Travel Costs

Total Travel Cost

E. Participant/Trainee Support Costs — Funds Requested ($)

1. Tuition/Fees/Health Insurance
2. Stipends
3. Travel
4. Subsistence
5. Other

Number of Participants/Trainees Total Participant/Trainee Support Costs

RESEARCH & RELATED Budget (C-E) (Funds Requested)

OMB Number: 4040-0001
Expiration Date: 04/30/2008

cut. If you find that buying a set of items exceeds the amount that will allow it to be included under Materials and Supplies, don't buy the set. Instead, purchase each item in the set independently.

In estimating the cost of each item, make certain that the costs of shipping and any service or maintenance agreements are added. Such costs are included here, not under "Other Direct Costs" in section F.

Equipment requested should be complementary to what has already been provided by your institution. In other words, if you are just getting started, you should not expect

NIH to provide all of the equipment needed to initiate your research program. That is your institution's responsibility. Whether you have been provided a basic equipment package will be used as one means of assessing institutional commitment – or lack thereof – to you and your research program.

Just as there are 'general purpose' categories of personnel (e.g., secretarial and clerical positions), there are categories of equipment that are considered 'general purpose' and, therefore, the responsibility of the institution. Items such as a personal laptop computer, even if used in the project, will usually be cut unless you can prove in your justification that they will be dedicated to some aspect of the research.

Section C has ten fields in which you can list the kinds and costs of equipment that you are requesting. If you are asking more than ten items, you should use a similar format to list them in a separate PDF document, which can then be uploaded into the data-entry screen using the "Add Attachment" button at the end of the section. The total cost of items above ten is then entered in the field at the right of line 11, after which the grand total for equipment should be entered into the "Total Equipment" field.

Travel (section D).

This is the only section for which reviewers will often have a predetermined figure in mind. Unfortunately, this amount is usually significantly less than the real cost of the proposed travel. Therefore, unless you either have an alternative source of travel funds or are willing to re-budget from another category, you need to provide the kind of objective justification that will encourage the reviewers to grant your full request for travel funds (see section K, below). Foreign travel is particularly in need of compelling justification.

Participant/Trainee Support Costs (section E).

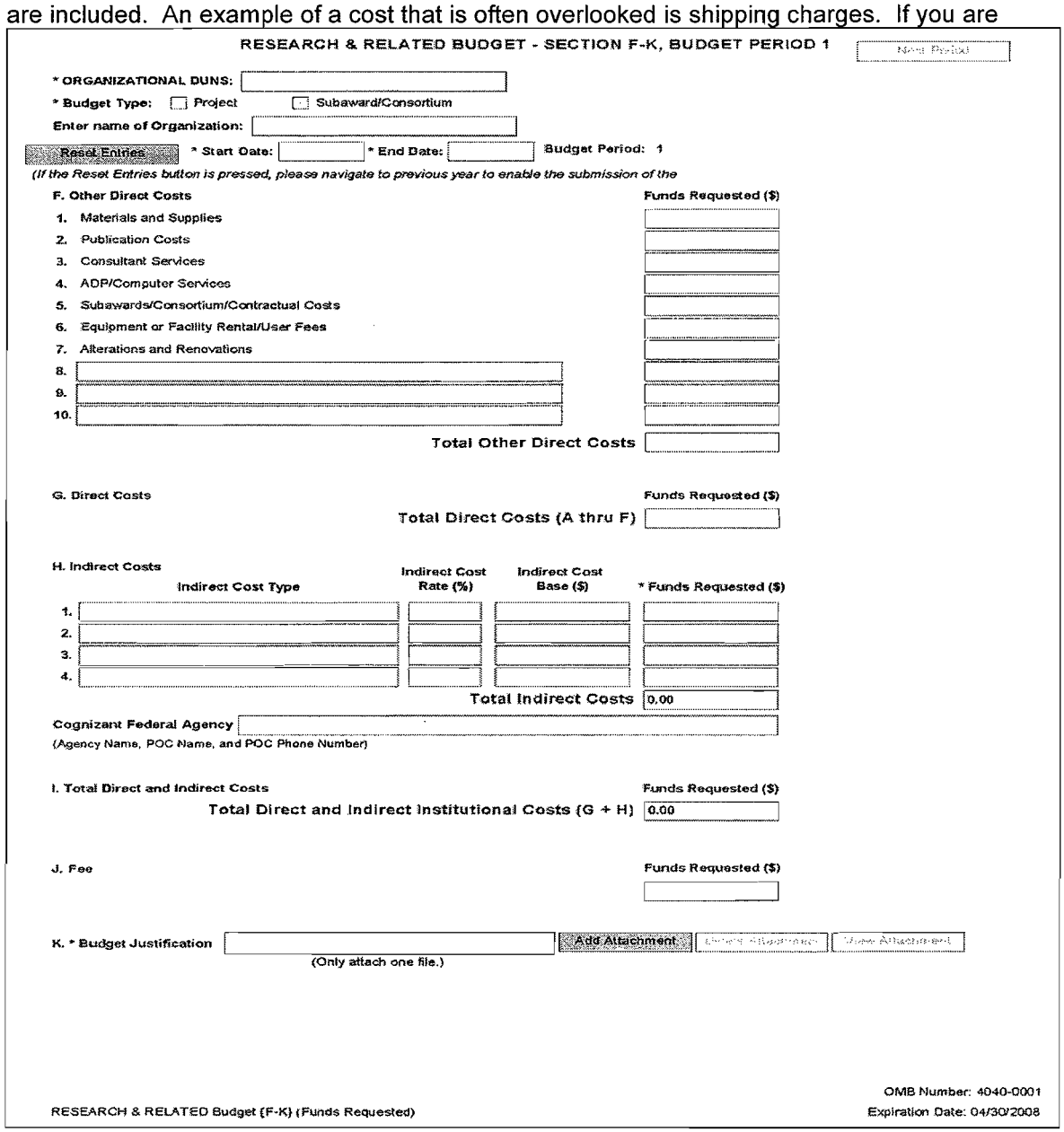
This section should be left blank in almost all cases. If you are responding to a Funding Opportunity Announcement that requires that this section be completed then, of course, do so. Even though line 1 would appear to be where things like tuition remission for graduate students should be included, those costs should not be entered here. They will be included under the "Other" category of the next section (F), "Other Direct Costs."

SECTIONS F (Other Direct Costs), G (Direct Costs), H (Indirect Costs), I (Total Direct and Indirect Costs), J (Fee), and K (Budget Justification) [data-entry screen at top of next page]

Other Direct Costs (section F).

All that is required on each of lines 1 through 7 of section F is the total for that supply category. Lines F.8 through F.10 allow you to create additional categories, which also require only the total funds requested. Thus, as with "Equipment," thorough justification (in section K) of how these amounts were reached is essential if cuts are to be avoided. We recommend that you enter a '0' in the field at the right of any line that is not associated with a budget request.

Materials and Supplies. Each supply category must have at least $1,000 in it to justify making it a separate itemization in your Budget Justification. Make certain that *all* costs are included. An example of a cost that is often overlooked is shipping charges. If you are



RESEARCH & RELATED BUDGET - SECTION F-K, BUDGET PERIOD 1

* ORGANIZATIONAL DUNS:

* Budget Type: Project Subaward/Consortium

Enter name of Organization:

Reset Entries * Start Date: * End Date: Budget Period: 1

(If the Reset Entries button is pressed, please navigate to previous year to enable the submission of the

F. Other Direct Costs — Funds Requested ($)

1. Materials and Supplies
2. Publication Costs
3. Consultant Services
4. ADP/Computer Services
5. Subawards/Consortium/Contractual Costs
6. Equipment or Facility Rental/User Fees
7. Alterations and Renovations
8.
9.
10.

Total Other Direct Costs

G. Direct Costs — Funds Requested ($)

Total Direct Costs (A thru F)

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	* Funds Requested ($)
1.			
2.			
3.			
4.			
Total Indirect Costs			0.00

Cognizant Federal Agency
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs — Funds Requested ($)

Total Direct and Indirect Institutional Costs (G + H) 0.00

J. Fee — Funds Requested ($)

K. * Budget Justification Add Attachment
(Only attach one file.)

OMB Number: 4040-0001
RESEARCH & RELATED Budget (F-K) (Funds Requested) Expiration Date: 04/30/2008

using animals in your project, this is where the cost of their purchase is included. The cost of their maintenance should be included later, on one of lines 8-10.

Publication Costs. The costs associated with publication, which can be a *significant* expense, need to be included here, complemented by detailed justification in section K. Make sure that you include a substantial, but reasonable, amount in this category, because dissemination of results through publication will be expected by reviewers. Requesting little of no

funds here can have the unintended consequence of convincing reviewers that you don't intend to publish.

Consultant Services. The total of Consultants' fees, travel, per diem allowances, and any other costs must be included here — not under Personnel (sections A & B) or Travel (section D). Costs associated with paid Consultants are often consequential, especially when travel and per diem expenses are included. It is very important, therefore, that you use the strategies described under section K to justify their inclusion in the project. Unpaid consultants must be included in the justification, as well, listing their names, organizational affiliations and roles in the project. Therefore, if only unpaid consultants are included, enter '0' in the field at the right of line F.3 and then provide justification for each in section K (see below).

ADP/Computer Services. If you will be paying for computer support, e.g., to search databases or retrieve scientific / technical information, such costs should be totaled here.

Subawards/Consortium/Contractual Costs. If you enter anything in this field, the "Subaward / Consortium" box adjacent to "Budget Type" at the top of each data-entry screen must be checked. The direct costs of all subawards, consortial relationships and contracted (fee-for-service) work should be totaled and entered here, with appropriate breakout and justification under section K. With respect to subawards and consortial arrangements, if they are substantive, i.e., are required to accomplish a significant amount of the work that is proposed, you will need to complete a separate budget for each using the R&R Subaward Budget Attachment(s) Form (see below). Remember that the facilities and administrative (indirect) costs of research sub-awarded to investigators at other institutions will become part of your direct costs (see section H). Also remember that reviewers will often worry that investigators at other, particularly distant, institutions will not really be involved in the research, i.e., that they are 'window dressing.' Therefore, you must present compelling and credible reasons in your justification for including such investigators as part of your research team.

Equipment or Facility Rental / User Fees. In some cases, it is more cost effective / efficient to rent equipment or temporarily occupy space than to purchase it / occupy it permanently. The total costs related to such strategies should be entered here, accompanied by appropriate justification in section K. Enter "0" here if you will not have such costs associated with your project.

Alterations and Renovations. It is unusual for the costs of alterations / renovations to be allowable under a research grant. Most of the time, such costs are considered to be the institution's responsibility. If the costs of alterations / renovations are not prohibited by the Funding Opportunity Announcement to which you are responding, we recommend that you not include these costs in your budget without the prior approval of your Program Officer.

Lines 8 through 10 – Other Direct Costs. As the name implies, direct costs that are not covered under the previous seven subsections should be included here. Three blank lines are provided. If three lines are not enough, use lines 8 and 9 for named categories, e.g., 'Inpatient-Care Costs' and 'Outpatient-Care Costs.' On line 10 enter the category title, 'Sum of All Other Direct Costs' and to the right of that enter the sum of all those costs. You must then provide a breakout of what is included in that sum in section K, Budget Justification.

Tuition Remission. This is where tuition remission for graduate students is included. Create a category with that title and enter it here.

Animal-Care Costs. As already mentioned, the costs of animal care should be included as a category here. Make certain that you query the head of your animal care office to ensure that there are no increases in maintenance fees projected for future years. If there are projected increases, obtain a letter from the appropriate institutional official documenting that fact, and include the projected increases in your budgets for future years.

Patient-Care Costs. If you will have both inpatient and outpatient costs, they must be entered as separate categories on lines 8 and 9 of Section F. The expense of patient accrual should also be included here. Cost account and justify patient travel in the same way that you do your own (see Travel, section K).

Direct Costs (section G), Indirect Costs (section H), and Total Direct and Indirect Costs (section I).

The total for direct costs that is entered in section G is reached by summing the totals for sections A through F.

In section H you need to enter all indirect (facilities and administrative) costs that are associated with research at your institution. The indirect costs associated with researchers at other institutions who will perform a substantive portion of the project should not be entered here; they will be entered when you prepare the "*R&R Subaward Budget Attachment(s) Form*" for each such institution.

Section H has four separate lines under it, which allows you to offer different types of indirect costs, if necessary. For example, there would be a difference between on-site and off-site indirect costs. Or there could be a difference between the negotiated rate for Salary and Wages, compared to Modified Total Direct Costs. If you are confused by these differences – and most applicants are – we recommend that you seek the help of personnel in your Contracts and Grants / Sponsored Programs office to ensure that this part of the application is completed correctly.

The field for section I, Total Direct and Indirect Costs, is calculated by adding the totals for sections G and H.

Fee (section J).

Fees are not allowed in the budgets of most research grants, as opposed to the SBIR/STTR grant mechanisms, which do allow a fee. If you are preparing a research grant, leave this field blank unless a fee is specifically authorized under the Funding Opportunity Announcement to which you are responding.

Budget Justification (section K).

Justification is the key to convincing reviewers that your budget request is appropriate and reasonable. With respect to the amount of support requested, unless there is either a formal cap that limits the amount of funding that can be requested or you are aware from discussions with your Program Officer that there is an unofficial but operational cap (e.g., "Realistically, we just can't support a budget that exceeds $300,000 per year."), let the research dictate the budget. In other words, request what you need — NOT what you or someone else has arbitrarily decided is the maximum that reviewers will approve. Don't make the mistake of low-

balling your budget in the hope that it will help you get funded, because the one thing that you most assuredly don't want is an approved budget that leaves you unable to do all of what you have proposed. Sections A through F have allowed you to enter amounts for each budget category. Here, in section K, you must justify the need for, and the appropriateness of, what you have requested. Unfortunately, many applicants provide insufficient justification, which is why most budgets get cut. Thus, in our opinion, cuts in the budget are usually the fault of the applicant, not the reviewers. There is no limit on the number of pages allowed in section K. You should take full advantage of that fact, because there is rarely such a thing as too much justification.

Note that section K must contain the justification for all years for which support is requested. To make the section more reviewer-friendly we recommend that you separate it into two subsections, 'Justification of Direct Costs for First Year' and 'Justification of Direct Costs for Subsequent Years.'

Justification of Direct Costs for First Year. Each section / subsection of the budget in which specific direct-cost requests are made (sections A through F) should be justified. It is very reviewer friendly to identify each line item in your justification by its letter and numeral, as well as its title. For example, F.2 Publication Costs, which would be followed by justification for the related request.

Personnel (sections A & B). Each person listed in section A, whether paid or not, must be justified with respect to both expertise and effort. List his/her name, the role that s/he will have (e.g., Co-Investigator), the person months s/he will commit to the project, and what responsibilities s/he will have. There must be a clear reason for including each person. Sufficient and credible detail is needed for each request. No one should be included as 'window dressing,' i.e., because of their prominence, especially if that person's expertise overlaps someone else's on the team who is less well known. No one should be included out of respect, e.g., a former mentor who the applicant would like to acknowledge. Such relationships can be described in the Biographical Sketch if it is helpful to do so.

EXAMPLES

Sheldon, Connie J., Co-Investigator, 2 academic + 1 summer person months. Dr. Sheldon has been included in the investigative team to head the molecular biological approaches associated with the proposed research (see her Biographical Sketch), especially the activities that are associated with Specific Aim #2. She will work closely with the PI to design and execute experiments in this area, interpret resultant data and contribute to publication / dissemination of results. In this capacity she will supervise a full-time molecular biology technician (Sandoval – see Other Personnel) and one graduate student (James – see Other Personnel).

Jennings, Alfred F., Collaborator, no measurable effort. Dr. Jennings has agreed to provide us with access to a specimen collection that is critical to completion of Specific Aim 3. His letter of support accompanying this application confirms his willingness to provide us with access to this material.

Section B of the R&R Budget Component, "Other Personnel," grouped such individuals and listed them numerically by "Project Role." Detail that was missing in section B must be provided here. Exactly the same approach that was described in the pre-

ceding paragraph should be applied here for each individual. With respect to justifying a request for personnel who might otherwise be considered 'general purpose and, therefore, not allowable, additional guidance regarding how to justify their inclusion can be found at the following URL: http://www.whitehouse.gov/omb/circulars/a021/a21_2004.html. Remember to use titles for their positions that will not raise a 'red flag,' which 'secretary' or 'clerk' is almost guaranteed to do.

Members of the "Other Personnel" set will not have biographical sketches accompanying the application. If someone has particularly attractive credentials that you want to highlight, e.g., a technician with an extraordinary and difficult-to-find skill or a post-doctoral scholar with background and training that are especially relevant to the project that is being proposed, use the justifications of such individuals to highlight those features. Do not do this for members of the research team who have a Biographical Sketch in the proposal.

EXAMPLE

Post-Doctoral Associate #1: Mallaby, Curtis R., 12 person months. Dr. Mallaby will be working closely with the PI to conduct and interpret the results of all interviews that are designed to identify sources of health-care disparities. These are expected to total 250-300 interviews per year, some at other institutions that have agreed to participate (see accompanying letters of commitment). He is superbly qualified for this role, having done his post-graduate training with one of the leading figures in the field of health disparities research, Dr. Seymour Cantrell. One of Dr. Mallaby's publications with Cantrell (Journal of Health Disparities Research, 2005: **74**, 296-312) is considered a landmark in the field. Dr. Mallaby has had both formal training and practical experience in conducting the kinds of investigative interviews that are proposed in this application. In addition, he is culturally sensitive to the subjects with whom he will be dealing, being a member of the same minority group that many of them are.

Graduate and undergraduate students must be justified on the basis of the research that they will do, not on the basis of giving them training – unless you are using the R15 grant mechanism. In the latter kind of application exposing students, especially undergraduates, to biomedical research in ways that will introduce them to new career directions is an important review criterion. Thus, for most research grants, if you have a graduate student who
will be involved 50% in class work and 50% in research, you should only request support for the 50% that is devoted to research and you should make clear in your justification that only that part of the graduate student's effort will be supported. Where the non-research support will come from should also be described.

EXAMPLE

Graduate Student #2: James, Carol Lee, 8 person months. Ms. James' dissertation research focuses on the hypothesis that is the centerpiece of Specific Aim 2. She has reached the stage where 75% of her time is spent in active research, which is the level of support requested in Budget Period 1. The remainder of her support during the first year will come from departmental funds. She already has two first-author peer-reviewed publications (see Dr. Sheldon's Biographical Sketch). She will work directly with Dr. Sheldon in the design and execution of molecular biological experiments, including those requiring gel-shift and nuclear run-on assays, as well as cloning of relevant genes.

If you request less support for an individual than would be expected on the basis of his/her effort and base salary, you should justify that discrepancy. In such cases, provide a description of the other source of support and its duration (e.g., Dr. Gonzales will be supported throughout the first two years by his own individual post-doctoral research fellowship from the National Cancer Institute [F32CA012345]). Providing objective detail, like grant numbers, increases credibility. You should also justify differences in effort (if any) during academic and summer months. Why is the increase necessary and appropriate during the summer months? The last thing that you want to leave with reviewers is the impression that you are simply providing a source of summer income for the individual with no justifiable basis for doing so.

If a member of the research team has a higher base salary than the maximum that is allowed by NIH, make certain that you indicate in your justification of his/her requested salary and fringe benefits that they are based on the NIH maximum, not his/her actual salary.

The final part of your personnel justification should be detail regarding how fringe benefits are calculated. If there are differences between personnel categories (e.g., faculty members and graduate students) make certain you indicate that the appropriate formula has been used for each category.

Equipment (section C). As noted earlier, the equipment section is one of the most vulnerable in your budget. Success in having your equipment request approved is often attributable to anticipating reviewers' concerns and then prospectively providing justification that will overcome such apprehensions. Some of the commonest concerns that reviewers have about equipment requests follow. Knowing them will help you understand how to better justify your request.

(1) False Claim of Dedicated Need for Expensive Equipment. To overcome this suspicion, you must make clear either that equivalent equipment is not available to you, either in core laboratories or by borrowing from other investigators, or that your use has become so great that it is no longer feasible to share the equipment with others. If the latter argument is the basis for your request, i.e., that you have been monopolizing the equipment, there is an objective means of demonstrating your dedicated need. Create a table that summarizes your use versus others'. Obtain your data from the usage log book for the equipment you have been using. Use the table in the justification to show objectively that you have been monopolizing the equipment, which compromises it as either a core or shared item.

(2) The Amount Requested is Not Correct. To shore up your request, provide a valid bid as part of your justification, especially for an expensive item. Describe the bidding process and how it resulted in the lowest possible cost. Don't use catalog price as a 'bid,' because it will damage your credibility: reviewers know almost all institutions receive substantial discounts. If you have to use the catalog price, reduce it by an amount that is commensurate with the discount that your institution usually receives from the relevant vendor. For this latter approach, get a validating letter from either a purchasing agent or vendor, if possible.

(3) Purchase and Maintenance are not Prorated. If a piece of equipment has a life expectancy of 10 years, why should a three-year grant pay the full cost of purchase? If you are lucky enough to have an alternative source of support for acquisition of equipment (e.g., another grant, start-up funds, endowment), proposing to cost share the purchase and maintenance of a piece of equipment is a very powerful and persuasive means of increasing your budgetary credibility. In the example given, you would request 30% of the pur-

chase price. If you use this approach, you must assure the reviewers that you have the 70% from other sources (e.g., the number of an existing grant that will share the cost of purchase or a letter of commitment from some other source). If your institution will provide a letter of support for the remainder, you have outstanding, objective evidence of institutional commitment, a fact that you should highlight. Service contracts and other costs of equipment maintenance/repair should also be included here. Prorate them among all projects that benefit from the use of the equipment. Make clear in your justification that you are doing so.

(4) The Requested Equipment is More Sophisticated than Needed. When applicants request unneeded 'bells and whistles,' they are often caught out. Your reviewers will be peers who will know what is needed and what is not. If they suspect you of making an excessive request, one of two things will usually happen. Either the reviewers will become sufficiently annoyed to recommend cutting the entire piece of equipment from your budget or, at the least, will cut you back to the lesser model that is justified. Even if the second scenario is the outcome, you lose, because your credibility will be damaged and other parts of your budget request will become suspect. To allay such concerns you need to include in your justification why the characteristics of the requested model are necessary to accomplish the proposed research.

EXAMPLE

Centrifuge (Hettich Rotanta [Advanced Model]), Refrigerated, Large Capacity, with Angle Rotor: $9,877 + $563 shipping + $386 annual service contract; $5,413 is requested. This centrifuge is required to conduct experiments described under each of the three aims, all of which require a bulk-processing step. Estimated use over the course of the project will be 3-4 hrs daily. This level of use would monopolize the only comparable centrifuge, which is used extensively by investigators in two other departments and is located in another, unconnected building. The price for the requested centrifuge has been established on the basis of competitive bids, which accompany this proposal and include the University's 30% discount. Half of the cost is requested because the instrument will be used, in part, for other projects in the PI's laboratory. The other half of the cost will come from the PI's endowment funds (see accompanying letter of commitment from the Endowment Association).

(5) Existing Equipment Isn't Really Worn Out. Reviewers' concerns about requests for replacement equipment are often exacerbated by the perfunctory justifications provided by applicants ("Replacement of worn-out centrifuge: $????"). Use the same strategies to create your justification here that are listed above (e.g., prorate with other projects), but with an added wrinkle. Get a letter from the company that made the equipment certifying why it is worn out (e.g., lack of replacement parts, inability to provide a service contract, no longer providing repair service, etc.). Vendors will often provide such a letter, especially if you plan to purchase the replacement equipment from them.

Travel (section D).

Reviewers' concerns about travel can usually be overcome with strong, detailed justification. Your justification needs to include two different but equally critical kinds of information.

(1) Who Will Travel and Why? Your first obligation is to make certain that the reviewers know who will travel and why such travel will *tangibly* benefit the pro-

ject. "Travel for PI and one postdoc to one national meeting each." is clearly not sufficient. Rather, detailed justification is absolutely essential, because there is no "God-given" right to travel under the auspices of an NIH research grant. Justifying that travel will tangibly contribute to the project is usually easy, because most of the time you will be proposing to attend meetings where you and your co-investigators will have the opportunity to present data, discuss your field with investigators who are at other institutions, keep up with latest developments, etc. Your justification should clearly and persuasively state these (or similar) points. Remember that training of students, *per se*, is NOT appropriate justification for travel in a research grant application.

(2) Cost Account Your Proposed Travel. Most societies have their annual meetings scheduled years in advance. Call the society that will sponsor the meeting you have decided to attend. Determine where the next meetings will be held. Ask what the convention hotel will be and what room rate has been negotiated. Ask what the registration fee and any incidental costs associated with the meeting will be. Also ask whether or not the organizers have arranged for transportation to and from the airport and, if so, what those costs will be. If they cannot provide that information for you, make a reasonable estimate, based either on calls to cab companies in the convention cities or on your own past experience. From a travel Web site or your travel agent, determine what a full-fare coach ticket to each of the convention

EXAMPLE

Travel to the annual meeting of the American Nephrology Society ($3,068) is requested for the PI and one Co-I; the two co-investigators will alternately attend future meetings. This meeting is the principal scientific venue related to the subject of this proposal. Results of the proposed research will be presented there, constructive feedback will be obtained from colleagues and new ideas and collaborations will be developed. The cost of attending has been cost accounted on the basis of actual quotes: coach-fare ticket = $540; convention hotel rate $90/night X 4nights = $360; transportation to & from airport = $86; university per diem = $87/day X 4 days = $348; meeting registration = $200. Total per individual = $1534 X 2 individuals = $3,068

cities will cost. You know what your institution allows per day for meals. Increase the travel estimates for future years by the appropriate percentage that is allowed for inflation. And so on. By taking this approach, you can come up with an *unassailable* estimate of what the cost of attending each meeting will be. Therefore, *providing that you have made a strong enough case for who should travel and why*, you should be awarded most, if not all, of the funds required to attend the meeting.

Participant/Trainee Support Costs (section E). This section is rarely included in PHS applications. Therefore, no justification is required in almost all cases.

Other Direct Costs (section F).

As noted earlier, each of the line items that is included in your budget must be accompanied by substantive justification. Application of the following strategies will decrease the likelihood that any of your requests in this section will be cut.

(1) F.1 Materials and Supplies. The most common mistake made in this subsection, in our opinion, is use of 'made-up' numbers, i.e., ones that have no basis in fact. This problem is compounded when applicants telegraph that the numbers aren't real

by using only round numbers. As an alternative and much more persuasive approach, we suggest that you make your request much more credible (and accurate — which will benefit you) by cost accounting. Assuming that the majority of items will be the same as those that you have purchased previously (both with respect to kind and quantity), consult your file of purchase orders and, for each supply category, determine *exactly* what you spent during the past year. Increase such figures 3-4% to adjust for inflation. *If you use this approach to generate your request for supplies, make clear in your justification that you have done so.* It also shows a level of commitment to accuracy that is not often seen by reviewers. If your proposed research will differ significantly from that of previous years, which would preclude your use of previous purchase orders, develop your new supply budget by a careful needs analysis. Group your supplies into logical categories, each of which must be ≥$1,000. List them and justify each.

EXAMPLE

F.1 Materials and Supplies: $16,863 total. The amount requested in each of the following categories has been derived by cost accounting using actual expenditures over the past year (from purchase orders) increased by 3% for inflation. Iododeoxyuridine: $4,608 (4 mCi; sp. act. ~2,000 Ci/mmol in buffered aqueous solution). This radiochemical is required for radiolabeling RNA, as proposed in specific aim 3. Plasticware: etc.

(2) F.2 Publication Costs. First, make a realistic estimate of the number of papers that you and your colleagues expect to publish per year (based on past rates of publication, if you are an established investigator) and identify the journals in which you intend to publish. Second, estimate what the cost of publishing in those journals will be, including submission and/or review fees, page charges, reprint charges, the cost of color illustrations, and any other publication costs that are applicable. It is critically important that you do a detailed analysis of these costs, because the cost of publishing continues to escalate and, like travel, can be a cause of having to re-budget from other categories if you underestimate what will be needed.

EXAMPLE

F.2 Publication Costs: $5,680 Our rate of publication has been 5 papers/year, each averaging 10 pages with one color and four half-tone figures. The *Journal of Biophysical Chemistry* is preferred. On average, one 10-page publication in that Journal is estimated to cost $1,136 (submission fee $60; half-tone figure charge $25/figureX4 = $100; color figure (1) charge = $300; page charges $50X10 = $500; etc.) X 5 = $5,680.

(3) F.3 Consultant Services. Consultants have important but limited roles in a proposed research project. Each should have an established reputation and unassailable expertise in an area for which there is limited need. The need will be limited to the extent that it makes little sense to create such expertise *de novo* in your own group. Thus, consultants should usually be justified on the basis that it will be more time- and cost-effective to have an already established individual meet the limited need, rather than train a member of your own group. A consultant's Biographical Sketch should be constructed to highlight the reputation and expertise that have caused you to engage him/her. Consultants who are classified as Other Significant Contributors, i.e., who have no measurable effort invested in the project, must

provide a letter of commitment that confirms their willingness to provide the consultation. In addition to organizational affiliation and role in the project you need to include in your justification of each consultant the consultation fee, if any; duration of the consultation; the cost of travel; per diem allowance; lodging; and any other justifiable costs. The per diem costs for food and lodging should be those allowed by your institution, a point that should be made in the justification. It is relatively rare for an investigator from your own institution to be approved as a paid consultant; such individuals are expected to provide their knowledge and expertise without compensation as evidence of institutional commitment. In addition to such a narrative description for each consultant, for the sake of reviewer friendliness, we recommend that you provide a summary table as part of this justification.

EXAMPLE

F.3 Consultant Services:

SUMMARY OF COSTS FOR CONSULTANT SERVICES

	Sandoval	Oliver
Affiliation	Univ. of ???	[Applicant's Institution]
Duration of consult	9 days	3 days
Consultation fee	$8,550	-0-
Travel	524	-0-
Lodging	882	-0-
Per diem	585	-0-
Parking	108	-0-
Other costs	-0-	-0-
Total cost	$10,649	-0-

Consultant #1 ($10,649), Maximillion Sandoval, PhD, Regents Professor, University of ???. Dr. Sandoval is an international expert on the extremely demanding process of isolating nanosomes from fruit-fly mitochondria. We have a very limited but important need to isolate such organelles in order to accomplish a key experiment under Specific Aim #1 (see section D.4.3 of the Research Plan). Professor Sandoval has agreed to assist us in accomplishing this part of the work. He estimates that his involvement will be needed for 9 days. We will compensate him with a per diem honorarium of $950 (consultation fee = $950X9 = $8,850). He will drive the 560 miles one-way from his institution to ours and expects to be busy enough that he will make only limited use of his automobile while here (hotel to laboratory = 23 mi round trip). Mileage reimbursement will be $0.395/mile. Travel = ($0.395[560X2] + [23X9]) = $524. Parking at the university is $12/day X 9 = $108. Per diem and lodging allowances allowed by the university are $65 and $98, respectively ($65X9 = $585 and $98X9 = $882). No other expenses are anticipated.

Consultant #2, ($0.00), Ernestine Oliver, M.D., Professor, [Applicant's Institution]. Dr. Oliver has agreed to ...

(4) F.4 ADP/Computer Services. Justify these by relating them closely to the research that is proposed and why it is necessary to have others do this for you. Computer services can include, among other things, computer-based retrieval of scientific, technical and educational data. Objective detail should be provided that will allow reviewers to

understand how the total figure was derived. If applicable, be sure to include the computer service rates that have been established at your institution.

(5) F.5 Subawards / Consortium / Contractual Costs. The total amount entered on line F5 should include subawards / consortial arrangements, as well as any services that you contract for. For any subawards / consortial arrangements that are substantive, you will need to provide a separate budget AND budget justification using the R&R Subaward Budget Attachment(s) Form (see below). There, your colleagues at the separate institution(s) will justify each component of their budget(s). Here, you justify the need for each subaward or contractual arrangement. The best approach is usually to make the case that such expertise is not available at your own institution. To overcome the suspicion that the relationships with investigators at other institutions will not be integrated into the research effort, it is important to include a 'management plan,' either in the Research Plan or here, in the justification for the subaward / consortial arrangement. The advantage of putting such a plan in the Budget Justification is that it does not count against the page limit for your Research Plan. An unassailable way to substantiate that the relationship is both real and practicable is essential. The most compelling is evidence in your justification that you have been working productively with the investigators from whom you are geographically separated. The best evidence of this kind that you can offer is co-authored peer-reviewed publications. If you don't have any, and there is sufficient time to write an abstract or review together, we recommend that you do so. Another important means of establishing that the relationship is real would be to include evidence that you have been meeting through teleconferences. If you include the latter approach, be sure to include the costs in your budget and describe the teleconferencing equipment, either in the Facilities and Other Resources or Equipment section.

Any services you contract to use should be justified on the basis of why it is more efficient / cost-effective / dependable to use this approach rather than do those things yourself.

(6) F.6 Equipment or Facility Rental / User Fees. Occasionally there are times when it is justified to rent rather than to purchase. Such justification usually pertains when the need for equipment or space is temporary. If you include rental / user fees in your budget, make the case here that this is the most cost-effective approach. Also provide evidence that you have sought bids to ensure that you have obtained the best deal.

(7) F.7 Alterations and Renovations. If you include alterations / renovations, you will need to provide especially compelling justification, because most reviewers and granting agencies will expect such costs to be borne by your institution, especially if the utility of the altered / renovated space will extend beyond the duration of funding that you are requesting. To justify alterations / renovations, provide evidence that you have bid every aspect of the project to accomplish it at the lowest possible cost. Break out the total cost in categories, each one of which is justified with objective detail. Such categories might include such things as demolition, framing, finish carpentry, cabinets, plumbing, electrical, heating / air conditioning, painting, etc. If appropriate, be certain to provide the cost per square foot. The latter is a very important figure, because reviewers and program staff will have a good idea of what is reasonable in this regard.

(8) F.8-10 Other Direct Costs. These are the categories that you create yourself. These, of course, must be justified to the same extent that you did the pre-set lines. If you have more than three of your own lines the total cost on line F.10 will be the sum of costs for items 10 through the total number that you have. In this circumstance you need to

provide the breakout for the line F.10 total here, item by item. If you include patient-care costs, remember that you need to provide separate line-item costs AND justifications for inpatient and outpatient care. In creating your justification for patient care you should be sure to address what is included in the "Special Instructions for Patient Care Costs," which are provided at the end of section F (page I-70) of the *PHS SF 424 (R&R) Application Guide*, Version 2. The number of subjects that will be needed should be estimated statistically, e.g., on the basis of power analysis. The justification for patient care costs should include the statistical calculations used to derive the number. Make certain that you document that your institution can supply the numbers needed. If recruitment will be problematic relying only on your own institution, include a believable and manageable contingency plan, such as recruitment from other institutions (backed by letters of support), that can be implemented if it becomes necessary to do so.

Justification of Direct Costs for Subsequent Years. This second section of the Budget Justification has several purposes. First, it is used to justify the total number of years requested. Second, describe here how recurring direct costs have been adjusted upward for inflation. And, third, use this subsection to justify any significant increase / decrease in requests that are made in years after the first.

Duration of the Project. The years requested must be justified by the content of your Research Plan. A common mistake made by applicants is to request the maximum time allowed by NIH (5 years) without adequately justifying that there is a need for that length of time. To help confirm that there is a real basis for the number of years that you have chosen, reproduce the timetable here that appears at the end of your *Research Design and Methods* section (see chapter 10). Make sure that there is sufficient detail in the timetable to allow reviewers to see, at a glance, what will be done and when it will be done. Write a narrative description that accompanies the timetable.

Inflationary Adjustments. Currently, the annual increase for inflation to use is 3-4% compounded across the years requested. Choose and justify such increases objectively using current estimates of the rate of inflation. Some institutions have a specific figure that they require applicants to use. Check with your Sponsored Programs / Research Office to determine if there is such a figure at your institution. If your institution has such a figure, don't use that fact as the justification; use the objective criteria that went into deriving the figure.

Significant Increases / Decreases. A frequent error is to forget that decreases, as well as increases, in the out years must be justified. If there are neither extraordinary increases (more than the cost of inflation) nor decreases in the years after the first one, don't include this subsection in your justification. If there are such increases / decreases (e.g., created by the purchase of equipment in a given year or the addition or deletion of personnel), describe the basis for the increase / decrease and justify why that change is necessary and appropriate.

CUMULATIVE BUDGET

The Cumulative Budget form page looks daunting, but it isn't, because it auto-populates as you fill in the other sections of your budget. You can't make entries in this form, even if you would want to do so.

After completing the budget for each of the periods for which funds are requested, carefully review the totals that are generated automatically on the Cumulative Budget form. If any total

looks off, review the related entries in the individual budget periods and change anything that is incorrect. Making such changes will correct the related totals on the Cumulative Budget form.

R & R SUBAWARD BUDGET ATTACHMENT(S) FORM

If a subaward / consortial agreement will be included to accomplish a substantive amount of the proposed research, then the *R&R Subaward Budget Attachment(s) Form*, below, must be completed:

R&R SUBAWARD BUDGET ATTACHMENT(S) FORM

Instructions: On this form, you will attach the R&R Subaward Budget files for your grant application. Complete the subawardee budget(s) in accordance with the R&R budget instructions. Please remember that any files you attach must be a Pure Edge document.

Click here to extract the R&R Subaward Budget Attachment

Important: Please attach your subawardee budget file(s) with the file name of the subawardee organization. Each file name must be unique.

1) Please attach Attachment 1		Add Attachment	Delete Attachment	View Attachment
2) Please attach Attachment 2		Add Attachment	Delete Attachment	View Attachment
3) Please attach Attachment 3		Add Attachment	Delete Attachment	View Attachment
4) Please attach Attachment 4		Add Attachment	Delete Attachment	View Attachment
5) Please attach Attachment 5		Add Attachment	Delete Attachment	View Attachment
6) Please attach Attachment 6		Add Attachment	Delete Attachment	View Attachment
7) Please attach Attachment 7		Add Attachment	Delete Attachment	View Attachment
8) Please attach Attachment 8		Add Attachment	Delete Attachment	View Attachment
9) Please attach Attachment 9		Add Attachment	Delete Attachment	View Attachment
10) Please attach Attachment 10		Add Attachment	Delete Attachment	View Attachment

OMB Number: 4040-0001
Expiration Date: 04/30/2008

The investigators at the institution with which you have a substantive subaward / consortial relationship must complete their own budget form, including justification of the requests, which they then e-mail attach to them as a Pure-Edge document. Click on the bar in the upper middle of the form to extract the document. Follow the step-by-step special instructions given in section 4.8 of the *PHS SF 424 (R&R) Application Guide* (Part I, page 74-75, Version 2) to complete this part of your proposal.

If the other institution's indirect-cost rate is less than yours, make certain that you prominently highlight that fact in your justification and underscore that the approach for that part of the re-

search will actually be less expensive, in terms of total costs, than if all activities were performed at your own institution.

DEVELOPMENTAL STEPS FOR CHAPTER FIFTEEN:

1. Determine whether your department, Research Office, or Sponsored Programs Office provides assistance with the development of a budget.
2. Determine when you must submit your Budget, Budget Justification, and Face Page to your institution's Sponsored Programs Office.
3. Confirm that you need to prepare a non-modular, breakout budget.
4. Establish the type of breakout budget you need to prepare, "Project" or "Subaward / Consortium and check the appropriate field at the top left of the first budget form page (sections A & B).
5. List the Senior / Key Persons and Other Personnel who will be participants in the project, with each group in alphabetical order. Create your personnel budget for the first year.
6. Determine what the definition of non-expendable 'equipment' is at your institution and whether it differs from NIH's (≥$5,000 and a useful life of greater than 1 year). Your institution's definition supersedes NIH's.
7. Create your equipment budget, being sure to include shipping and maintenance costs in each item's cost.
8. Establish who will travel to what event and why. Create your travel budget by accounting for all expected costs for each person who will travel.
9. Determine the amount that will be requested on each pre-named line of section F, Other Direct Costs.
10. If substantive subawards or consortial arrangements will be included in the project e-mail a Subaward Budget Attachment Form to the investigators who will be involved. Include their costs in the total for line F.5 of Other Direct Costs.
11. Create a category for any Other Direct Costs that cannot be accommodated by one of the pre-named lines in section F. Enter the related amounts you are requesting.
12. Total your direct costs (sections A through F) and enter that number under section G.
13. If your annual budget will exceed $500,000 in annual direct costs, you must contact the NIH program you are targeting and obtain their approval before submitting your proposal.
14. Enter indirect (facilities and administrative) costs in section H, taking into account different approaches to calculating them, if applicable.
15. Inflate first year figures 3-4% (or by whatever the current estimate is for the rate of inflation) compounded across all years to create budgets for the out years. Extraordinary increases or decreases (greater or less than the rate of inflation) in later years should be flagged and must be justified in section K.
16. Copy and import the Timetable from your Research Design and Methods section into the justification of the number of years being requested.
17. Create your Budget Justification (section K for the first year) for all years, line by line, remembering that there is no page limit and that there is no such thing as too much objective justification.

CHAPTER 16

PROJECT PERFORMANCE SITE LOCATIONS, FACILITIES & OTHER RESOURCES SECTION, and EQUIPMENT SECTION

GENERAL CONSIDERATIONS

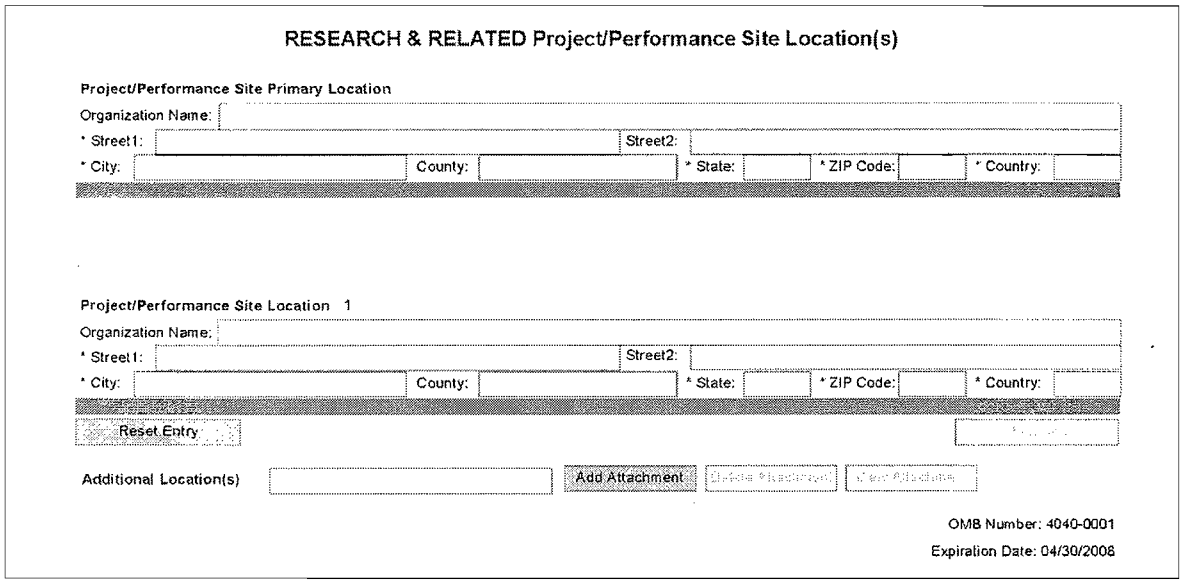
The project performance site(s) is(are) included by completing the *Project/Performance Site Location(s)* component. The number of sites informs how the *Facilities & Other Resources* and *Equipment* sections will be completed. The latter are attached to the application as PDF files using the "Add Attachment" buttons that are associated with lines 9 and 10, respectively, of the SF424 *Other Project Information* component.

These sections, together with the *Biographical Sketch* and *Preliminary Studies* sections, are designed to help reviewers assess the feasibility of the proposed research (in your hands, at your institution). They are usually some of the least thought about sections, to the extent that they are often given little more than superficial attention. In fact, these are *very* important sections, especially for New Investigators. Regardless of the level at which an investigator is established, they contribute significantly to reviewers' appreciation for the applicant's research environment — one of the five mandatory review criteria that will be used to evaluate the application. New Investigators have a lot to gain from this section if it is done well, and a lot to lose if it is done badly. Why? Because they have the opportunity here to demonstrate two things of importance: 1) the extent to which their institution is committed to them, and 2) how well equipped they are to conduct the proposed research.

Do not use 'boiler plate' supplied by either your institution or departmental office to create these sections. Similarly, do not copy these sections from a colleague's proposal. Either approach will likely introduce extraneous information that has little or no meaning to the work that is proposed. Worse, these approaches can even result in listing of the very same equipment that you are requesting in your budget. In addition, if you create these sections in this way, critically important resources may be overlooked. Finally, such 'shortcut' approaches will make it abundantly clear to reviewers that you have given little, if any, thought to these important parts of your application.

PROJECT PERFORMANCE SITE LOCATION(S) COMPONENT

The component into which you enter information about the performance site(s) is reproduced at the top of the next page. Note that there is an initial subsection that is for the primary location. That is all that is completed if there is but a single performance site. If there is more than one, up to 8, the lower part of the component is completed. The part of the component that is titled


RESEARCH & RELATED Project/Performance Site Location(s)

Project/Performance Site Primary Location

Organization Name:

* Street1: Street2:

* City: County: * State: * ZIP Code: * Country:

Project/Performance Site Location 1

Organization Name:

* Street1: Street2:

* City: County: * State: * ZIP Code: * Country:

Reset Entry

Additional Location(s) Add Attachment

OMB Number: 4040-0001

Expiration Date: 04/30/2008

"Project/Performance Site Location 1" should not be a repetition of the Primary Location. It should be the location of the *second* performance site. The instructions go on to read: "For additional performance site locations, click "Next Site" to display the fields for Project/Performance Site Locations 3 through 8." This validates that Project / Performance Site Location 1 is actually the location of the second Project / Performance Site. Should there be a requirement for more than eight project/performance site locations, they should be described in a separate file using the same format as is shown in the illustration, above. This process has been simplified by the fact that NIH has provided a Word-base format page for site locations greater than 8. It can be found at: http://grants.nih.gov/grants/funding/424/SF424R-R_AdditionalLocations.doc. Simply delete the instructions, fill out as many of the Word tables as are required and then delete what isn't needed. If enough additional tables are not supplied, simply highlight, copy and paste until you have the number of tables needed. When all Project/Performance Site locations have been listed, convert the file to a PDF document and upload it using the "Add Attachment" button.

FACILITIES & OTHER RESOURCES SECTION

> PHS SF424 R&R Instructions: "This information is used to assess the capability of the organizational resources available to perform the effort proposed. Identify the facilities to be used (Laboratory, Animal, Computer, Office, Clinical and Other. If appropriate, indicate their capacities, pertinent capabilities, relative proximity and extent of availability to the project. Describe only those resources that are directly applicable to the proposed work. Provide any information describing the Other Resources available to the project (e.g., machine shop, electronic shop) and the extent to which they would be available to the project."

In describing your access to facilities and other resources, be specific and objective. Present only relevant items, and do so in such a way that it will be clear why each is important and sufficient to accomplish the work that is to be undertaken. Avoid subjective assessments and cli-

chés, such as 'adequate' office space, and 'cutting-edge' or 'state-of-the-art' equipment, respectively. Such assertions provide no objective detail that reviewers need to evaluate for themselves what is available to the project. If you have a 10 ft X 12 ft office that is adjacent to your laboratory and is equipped with telephone, fax and a copy machine, that is what the reviewers want to know. When you describe your computer system and peripherals, the details of the hardware, the software and your levels of access to relevant databases and the Internet should be included. Be sure to include *relevant* resources of your co-investigators, collaborators and consultants, especially if they are at other Project/Performance Sites. As noted earlier, the number of Project/Performance Sites informs how this section should be organized. If you plan to conduct some of the proposed work at a location that is separate from the primary site, the *relevant* facilities and resources at the other location(s) should be detailed separately in a subsection that is clearly labeled with the name of the other performance site. For example, the first part of the document might be labeled: **FACILITIES & OTHER RESOURCES – NAME OF PRIMARY LOCATION**. The relevant facilities and resources of the second site might be titled something like: **FACILITIES & OTHER RESOURCES – NAME OF SECOND LOCATION**.

We recommend that you use bolded, italicized subheadings for each of the facilities/resources categories, i.e., like those included below. If one or more of the subsections is not applicable to your application, include the heading followed by "Not Applicable." Otherwise, reviewers could form the opinion that you overlooked the missing subsection(s).

Laboratory: Describe its size, configuration and relevant contents. Be specific.

Animal: If you will be using experimental animals, provide detailed information on the quality of your source, the relative availability of the species/strain chosen (if it is an uncommon one), and the quality of the facilities/veterinary care that will be associated with maintenance of the animals. Remember that your institution must have an approved Animal Welfare Assurance on file with the Office of Laboratory Animal Welfare (http://grants.nih.gov/grants/olaw/olaw.htm). If your institution's animal care facilities have been accredited by the AAALAC (Association for Assessment and Accreditation of Laboratory Animal Care, International), you should indicate that fact. This field should contain information that is complementary to and not repetitious of what is included in the Vertebrate Animals attachment to the Research Plan Component (section 5.5.11 of Part I of the PHS SF424 [R&R] Application Guide).

Clinical: If your proposal is one that will require patients or patient-derived materials, there is no such thing as too much detail: One of the principal causes for the failure of clinical applications is insufficient documentation of access to the quantity and quality of clinical material that will be needed to complete the study. Description of relevant physical facilities should be included, as well. Last but not least, if there are other complementary clinical programs and/or investigators in your environment, describe them and the relevance that they have to the proposed project.

Computer: Provide detailed information about hardware and software that are in your laboratory and office. Also include information about your local area network. The administrator of your LAN is a very important resource. Therefore, s/he should be described here, especially if computers and your LAN are particularly relevant to the proposed research. Finally, if you are a member of a wider network, which includes colleagues at other institutions, describe that resource here – providing, of course, that it will contribute to your project in a meaningful way.

Office: Provide relevant details about your office and its proximity to the other parts of your operation. If office space for co-investigators, technical personnel and/or students is relevant, be sure to describe those facilities.

Other Resources: Although the instructions for this section would appear to restrict your discussion to physical facilities and other resources (see text box, above), we recommend that you also include 'Intellectual Resources.' For example, if there are other investigators in your research environment who are funded to do research that is complementary to your own, list them here. Doing so gives reviewers an objective means of assessing the quality of your intellectual environment – i.e., who you have the opportunity to interact with. List them by name, their granting agencies and grant titles. These should be investigators other than those who are included in your application as co-investigators, collaborators or consultants. Indicate how they will contribute to your ability to do what you propose, whether it is through critical discussions of research results, the opportunity to share reagents/equipment, or some other reason. If you have regular interactions with colleagues at other institutions via teleconferencing, e-mail, and/or telephone, particularly if these are substantive relationships in which data are exchanged and evaluated, include them as intellectual resources. Provide factual, not subjective, information about these relationships, so that reviewers will be able to assess your intellectual environment objectively. This is also where your administrative support should be described. Core Facilities and their relation to your project should be included here, along with descriptions of your proximity to them. Major equipment in these facilities should not be described here. Instead, such components should be included under the "Equipment" section, which will be considered below. Access to, and the operation of, relevant core facilities, e.g., a statistical core, a high-throughput screening facility, or an editing/publishing support group, should be described in sufficient detail to give reviewers precise understanding of how these resources will facilitate the work that your are proposing. Make certain that you include all relevant core and shared facilities. For example, don't forget things like your institution's library and relevant specialized Centers (e.g., a Cancer Center, a Center for the Study of the Family, or a GCRC [General Clinical Research Center]).

EQUIPMENT SECTION

> PHS SF424 R&R INSTRUCTIONS: "List major items of equipment already available for this project and, if appropriate, identify location and pertinent capabilities."

"Major Equipment" includes not only that which is assigned to you, but also that which is shared and in institutional cores. In the "Other" field of the *Facilities & Other Resources* section you should describe institutional core facilities that will support the research you are proposing. Here, you detail the major equipment that is assigned for your dedicated use, as well as that which is present in those cores. For example, if you will be using a flow cytometry core facility, under "Other" you would describe its characteristics, relevance to your project and the kind of access and proximity that you have to it. Here, under "Major Equipment," you would describe the equipment in it: what kind(s) of flow cytometer(s) and what characteristics they have that are pertinent to your research. Include all major equipment that is applicable to your needs. Do not include equipment that is irrelevant to your project – no matter how contemporary and 'sexy' it may be.

DEVELOPMENTAL STEPS FOR CHAPTER SIXTEEN:

1. List the Project/Performance Sites for your project.
2. Inventory and characterize the physical resources at the primary location that are assigned to you – that are 'yours' – using the subheadings for the fields included under the subsections under the *Facilities & Other Resources* as your guide.
3. Inventory and characterize the physical resources at the primary location to which you either have shared access or that are available to you through institutional core facilities.
4. Make a separate inventory of major equipment to which you have access at the primary location, either on a dedicated or shared basis.
5. If the research proposed requires human subjects, thoroughly document the demographics of the population and characterize your access. If clinical facilities will be needed, detail their characteristics.
6. If sub-human vertebrate animals will be used, investigate and characterize the facilities in which they will be housed and cared for.
7. Inventory and characterize the intellectual resources that are either located in your research environment or that are available to you at other institutions through your wide-area network.
8. Create the *Facilities & Other Resources* and *Equipment* sections as separate PDF files. Upload these files into your application by clicking the relevant "Add Attachment" button, after which you browse to where you have saved the file and then click "Open."

Examples of the Facilities & Other Resources and Equipment sections follow this page.

EXAMPLE OF *FACILITIES & OTHER RESOURCES* SECTION

FACILITIES AND OTHER RESOURCES – PRINCIPAL INVESTIGATOR

Laboratory: The PI is assigned a 1200 sq ft laboratory that is located in departmental space, adjacent to his office. It is subdivided into a general purpose area (800 sq ft), a positive-pressure cell-culture room (200 sq ft), a medium preparation area (100 sq ft) and a walk-in cold room (100 sq ft).

Animal: Mice (C57BL6) will be housed in the institution's AAALAC-accredited animal care facility, which is in a dedicated building adjacent to the one that houses the PI's laboratory (see above). Cages will be located on laminar-flow racks in a 100 sq ft room dedicated to this project.

Clinical: Not applicable.

Computer: The PI has two computers: (1) Dell PC located in the PI's office (Windows XP Professional); and (2) a Compaq laptop model Evo N1000c (Pentium 4; 170GHz; 256 MB of RAM; Windows XP Professional). Each technician and student is equipped with a similar laptop.

Office: The PI's 144 sq ft office is adjacent to his laboratory. It is equipped with desk, credenza, desk and task chairs, two 4-drawer filing cabinets and hardwired high-speed access. There is also access to the Internet through the University's wireless network. The students' / technician's shared office space, which contains 356 sq ft, has similar access and is equipped with four individual desks, four task chairs and four 2-drawer filing cabinets.

Other: Flow Cytometry Core Facility located on same floor as the PI's laboratory; full access by appointment on a fee-for-service basis.

Intellectual Resources: The following are funded investigators in the PI's research environment who are doing research that is complementary to that proposed here:

James, Michael; NIH/NCI R01CA05163; Mechanism of Interference with Cell-Cycle Regularity

Guerra, Anita; NIH/NIA R01AG06159; Cell Cycle as a Contributor to Delayed Wound Healing

Xu, Jennifer; American Cancer Society; 056921-AFW; Inhibited Cycling of Thyroid Cancer Cells by Dihydroamanitin: Mechanism of Effect

EXAMPLE OF *EQUIPMENT* SECTION

EQUIPMENT – PRINCIPAL INVESTIGATOR

(Adapted from http://fbi.gov/hq/lab/fsc/backissu/april2003/lacey.htm)

The following equipment is available, collectively constituting an audio-video forensic laboratory that has the full range of capabilities needed to complete the proposed project:

Assigned to the PI:

1. Standard professional audiocassette decks (3; Sony model 810) with heavy-duty transports, a three-head design and Dolby-noise-reduction systems B, C and S.
2. Video recorders / playback units (4; Frontier model 8C) with formats ranging from analog U-Matic to the latest digital configurations, including VHS, VHS-C, SVHS, 8mm, Hi8, time-lapse, 6mm digital, and 8mm digital.
3. Etc.

Core: The equipment in the core Audio Enhancement Laboratory, which has been described in the *Facilities and Other Resources* section, includes:

1. Digital-adaptive enhancement processor (Acoustic Engineering, model E) that allows implementation of the full range of filter algorithms, as well as compression and limiting functions.
2. Spectrum analyzer (Harmon model 1600) with fast-Fourier transform device (>16-bit resolution and frequency-display ranges adjustable from 0-100 Hz up to 0-20 kHz) and single-channel capability. It has at least 800 lines of resolution on any frequency range and zoom capability.
3. Etc.

Shared With Other Investigators: The following pieces of equipment are in the laboratories of other investigators who have agreed to provide access on a 'demand' basis (see letters of support from Oliphant and Kaplan) for the purpose of making and authenticating computer-based voice identifications. Use of the equipment will be granted 2-24 hours after a request is made, maximum, with most access made available immediately.

1. Analog sound spectrograph (DC Live / Forensics , model B), which is in the laboratory of Dr. Maynard Oliphant. It has up to 32,000 band graphic EQ; flashback review; real-time coefficient display; time domain adaptive filter and frequency; time stamp; DeClipper; and signal-triggered VOX recording.
2. High-speed IBM computer system (located in the laboratory of Dr. James Kaplan) with a fast processor, a large (32 inch) monitor, an input for digital video, and hard-drive storage sufficient (24 terabytes) to handle the video applications of this project.

CHAPTER 17

HUMAN SUBJECTS, VERTEBRATE ANIMALS, SELECT AGENT RESEARCH, CONSORTIUM / CONTRACTUAL ARRANGEMENTS, RESOURCE SHARING PLAN(S), ENVIRONMENTAL IMPACT and INTERNATIONAL COLLABORATIONS

GENERAL CONSIDERATIONS

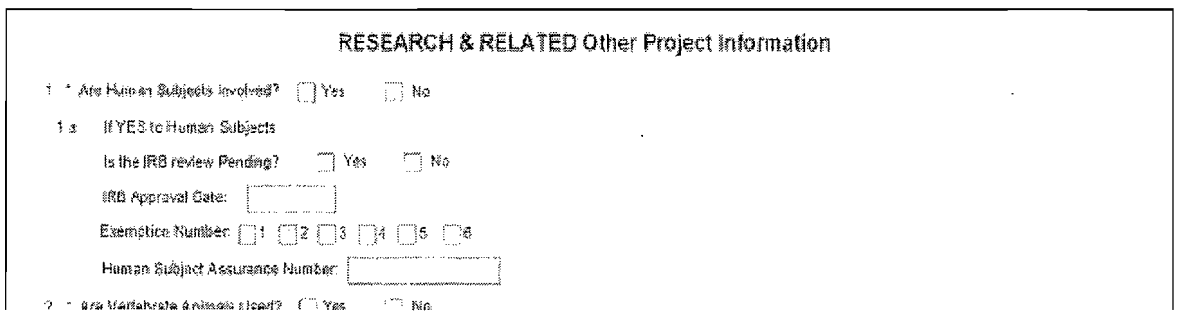
The parts of the application covered by this chapter may or may not be relevant to your proposal. If none of the parts named in the title is applicable to your needs, skip to the next chapter. If one or more of the parts is, the key to success in completing that(those) part(s) is careful reading of the detailed instructions that are contained in the *PHS SF424 (R&R) Application Guide*, which will not be repeated here. What is provided here will be assistance in finding those instructions and a few tips that are relevant to being fully responsive.

HUMAN SUBJECTS SECTIONS

Considerations relevant to use of human subjects are included in two different places in the application, the *Other Project Information* and the *PHS 398 Research Plan* components (sections 4.4 and 5.5 of the *PHS SF 424 [R&R] Application Guide*, respectively).

Other Project Information Component – Section 1, Are Human Subjects Involved?

The information needed to complete this component is relatively simple to provide, consisting of one-or-more boxes to check and two fields that may need to be filled in.


RESEARCH & RELATED Other Project Information

1 * Are Human Subjects Involved? ☐ Yes ☐ No

1 a If YES to Human Subjects

Is the IRB review Pending? ☐ Yes ☐ No

IRB Approval Date:

Exemption Number: ☐1 ☐2 ☐3 ☐4 ☐5 ☐6

Human Subject Assurance Number:

2 * Are Vertebrate Animals Used? ☐ Yes ☐ No

If no human subjects will be involved at any project/performance site, then you simply check "No" on line 1 and you are finished here. If human subjects will be involved at any project / performance site, you must check "Yes" on that line and respond to the remaining queries. Respond to the query regarding Institutional Review Board (IRB) approval. If approval has been obtained, check the "No" box and then fill in the IRB approval number in the field provided. If IRB approval has not been obtained, check the "Yes" box, even if you have not yet submitted your request for approval at the time that your proposal is submitted. If you check "Yes," leave the field for the IRB approval number blank. Although you have the latter option, we strongly recommend that, if feasible, you obtain approval before preparing your proposal. Doing so is a form of 'insurance' against the unlikely possibility that IRB approval cannot be obtained for the project at a later time. With respect to the Exemption Number, if the human subjects in your study are exempt, check off the appropriate category after choosing the appropriate one from among the descriptions of the exemptions under *Exempt Human Subjects Research*, *Question 2*, which begins on page II-8 of Part II of the *PHS SF424 (R&R) Application Guide*. If your institution has no Human Subject Assurance Number on file with the Office for Human Research Protections, enter "None" in the field provided. If you have such a number, enter only the 18 numerals, i.e., do not include the "FWA" prefix.

If you checked "Yes" for involvement of human subjects, go to the second part of what must be completed, the *PHS 398 Research Plan* component that pertains to Human Subjects.

PHS 398 Research Plan – Human Subjects Sections

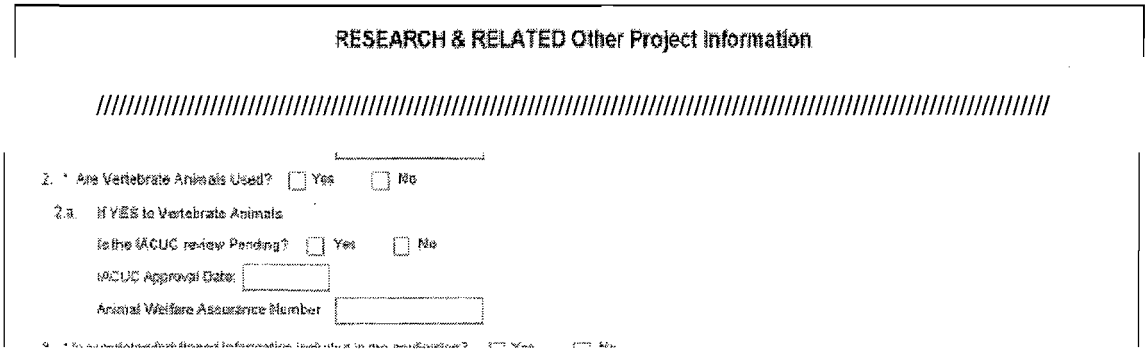
As is evident from the *Research Plan* component, there are up to four subsections that may need to be completed here if you checked "Yes" in section 1 of the *Other Project Information* component. They include: (1) Protection of Human Subjects; (2) Inclusion of Women and Minorities; (3) Targeted / Planned Enrollment; and (4) Inclusion of Children. The secret to knowing which one(s) to complete is to read Part II, *Supplemental Instructions for Preparing the Human Subjects Section of the Research Plan* of the *PHS SF424 (R&R) Application Guide* and/or the specific Funding Opportunity Announcement (FOA) to which you are responding. Part II of the *Guide* has been set up to present six scenarios that cover any kind of research that involves human subjects. After carefully reading the six and answering the five questions that are designed to indicate which scenario is applicable to your needs, complete the Human Subject sections that are relevant to your project. Follow the uploading instructions that are contained in the Part I instructions (section 5.5.8-11 of the *Guide*) for each of the Human Subjects Sections that is relevant to the project you are presenting.

VERTEBRATE ANIMALS

There are also two parts of the application that must be completed if you are using vertebrate animals (also sections 4.4 and 5.5 of the *PHS SF 424 Application Guide*).

Other Project Information Component – Section 2, Are Vertebrate Animals Used?

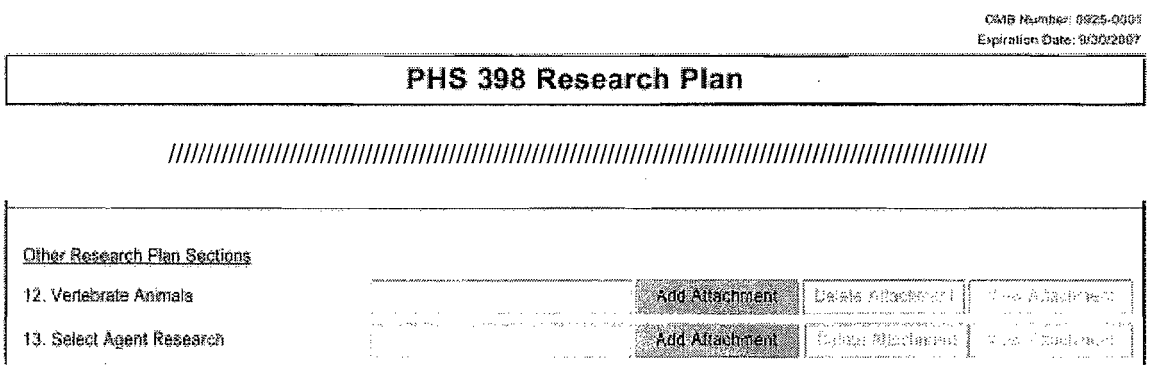
As with the Human Subjects, if you check "No" on line 2 section of the *Other Project Information* component (see relevant part of the form at the top of the next page) you will have completed this part of the application and will not need to do anything further in the *PHS 398 Research Plan* component. If you check "Yes" regarding the use of Vertebrate animals, you must complete all of the related information that follows.



After checking "Yes" to the question regarding use of vertebrate animals, you need to address approval of your research plan by your Institutional Animal Care and Use Committee (IACUC). If you have approval, enter the date that it was given. If approval is pending, leave the field blank. If you do not have approval, check "Yes" next to the question regarding whether approval is pending. You should check "Yes" even if the process to obtain approval has not been initiated. Again here, we strongly encourage you to get IACUC approval of your project before you get very far into writing your Research Plan. It's good insurance against potential rejection later. Enter your institution's Animal Welfare Assurance Number in the field provided (those with numbers are identified at: http://grants.nih.gov/grants/olaw/assurance/300index.htm). Note that it must be your institution, not that of a collaborating institution. If your institution has no Assurance number, write "None" in the field.

PHS 398 Research Plan Component – Section 12, Vertebrate Animals

This part of the application, which has no page limit, is relatively easy to complete, but adequate detail must be included to make it fully credible. It is especially easy to complete if you have read the excellent NIH tutorial titled, "How to Write an Application Involving Research Animals, which can be found at: http://www.niaid.nih.gov/ncn/clinical/researchanimals/tutorial/index.htm. The key is to be fully responsive to each of the five subsections that must be addressed. Then, upload the PDF file using the "Add Attachment" button at the right of line 12 of the form (shown below). *Because there is no page limit, this is a place where details pertinent to experimental animals can be included that might otherwise cause page-limit problems in the Research Plan.* If you use this approach, in the Research Plan you must refer reviewers to the Vertebrate Animals section for details.

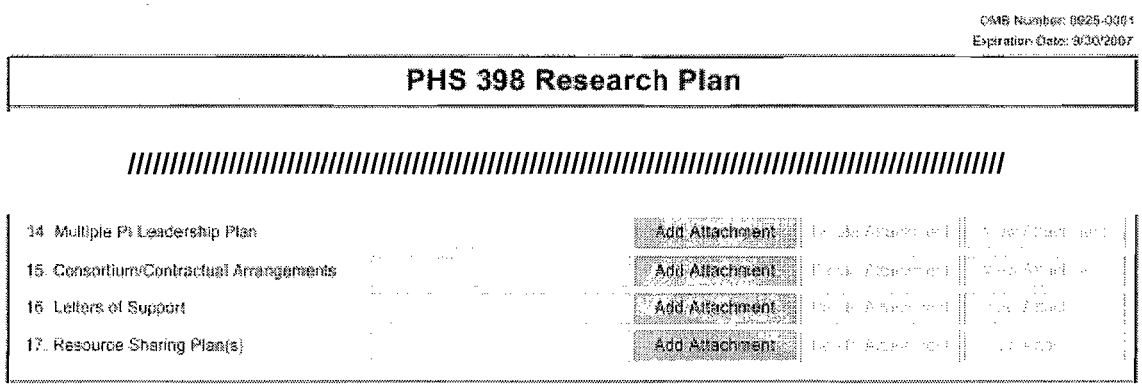


SELECT AGENT RESEARCH

If your research involves biohazardous agents, either at your institution or at a collaborating one, you must address the three points that are set out in the instructions for the *Research Plan* component. They can be found right after the instructions for Vertebrate Animals and the comment that pertains to how to handle citations of the literature. Definition of what constitutes a hazardous agent is given through a CDC URL (http://www.cdc.gov/od/sap/docs/salist.pdf), together with another URL for less virulent strains of the same agents that are exempt. If you need to complete this section, create a PDF file and upload it using the "Add Attachment button at the right of line 13 of the *PHS 398 Research Plan* component, which is shown on the preceding page.

MULTIPLE PI LEADERSHIP PLAN

NIH is phasing in the ability to designate multiple Principal Investigators, which, in our opinion, will have a very positive impact on how credit for grants will be distributed among the participating investigators. If the Funding Opportunity Announcement to which you are responding stipulates that you can include multiple PIs, and you choose to do so you, you must include a Multiple PI Leadership Plan with your proposal. It is essential that this plan be sufficiently detailed and well-conceived that it will be received by reviewers as credible. The instructions that accompany the *PHS 398 Research Plan* component are clear (section 5.5.14 of the *PHS SF 424 [R&R] Application Guide*); all you have to be is responsive to them. Then, upload your PDF file into the application using the "Add Attachment" button at the right of line 14, as shown below.



CONSORTIUM / CONTRACTUAL ARRANGEMENTS

Consortial / contractual arrangements are covered under subsection 15 of section 2 of the *PHS 398 Research Plan* component (see above). NIH policy regarding consortia can be found at: http://grants2.nih.gov/grants/policy/nihgps_2003/NIHGPS_Part12.htm#_Toc54600251), which is part of the NIH Grants Policy Statement (12/03). The following is a direct quote from that document: "The signature of the AOO on the application signifies that the applicant organization and all proposed consortium participants understand and agree with the statement in the text box at the top of the next page:

"The appropriate programmatic and administrative personnel of each organization involved in this grant application are aware of the NIH consortium agreement policy and are prepared to establish the necessary inter-organizational agreement(s) consistent with that policy."

Many Principal Investigators make the mistake of setting up relationships with investigators at other institutions without administrators at those institution(s) knowing about it. This is not to mean that they are *consciously* doing something behind the backs of administrators at the other institutions. They simply get on with the research without understanding that there are rules and regulations that govern such collaborations, and that these are an especially important if one or more investigators at the other institution(s) will be investing time in the proposed project, once it is funded. Under such circumstances, the institution that is home to the collaborating investigators usually has the right to receive F&A reimbursement at their negotiated rate. Rarely are such institutions willing to waive that right. Thus, the appropriate administrative officials at collaborating institutions must always be made aware that their investigator(s) is(are) involved. This approach will avoid nasty surprises and conflict later, and will keep your application in compliance with NIH policy, as stated above.

If you have the need to set up a consortial relationship, once the details have been worked out among the investigators and the various administrations that will be involved, you must describe the programmatic, fiscal and administrative details of it in this part of the application. *If a substantial part of the proposed work will be done elsewhere, you must justify here why your institution and not the other one should be the grantee.*

RESOURCE SHARING PLAN(S)

Resource sharing is covered by subsection 17 of section 2 of the *PHS 398 Research Plan* component (see preceding page). There are two parts: (1) Data Sharing Plan, and (2) Sharing Model Organisms, neither of which count against the page limit of your Research Plan.

Data-Sharing Plan

You only have to worry about a data-sharing plan if one or more of your requested years has / have direct costs of $500K or more associated with it / them – or the funding opportunity announcement (FOA) to which you are responding requires it, regardless of the size of the budget. If you must create a data-sharing plan, it can be very brief – one paragraph – but it must be credible, i.e., not come across as an afterthought. NIH encourages you to consult your Program Officer or FOA contact person before creating this subsection.

Plan to Share Model Organisms

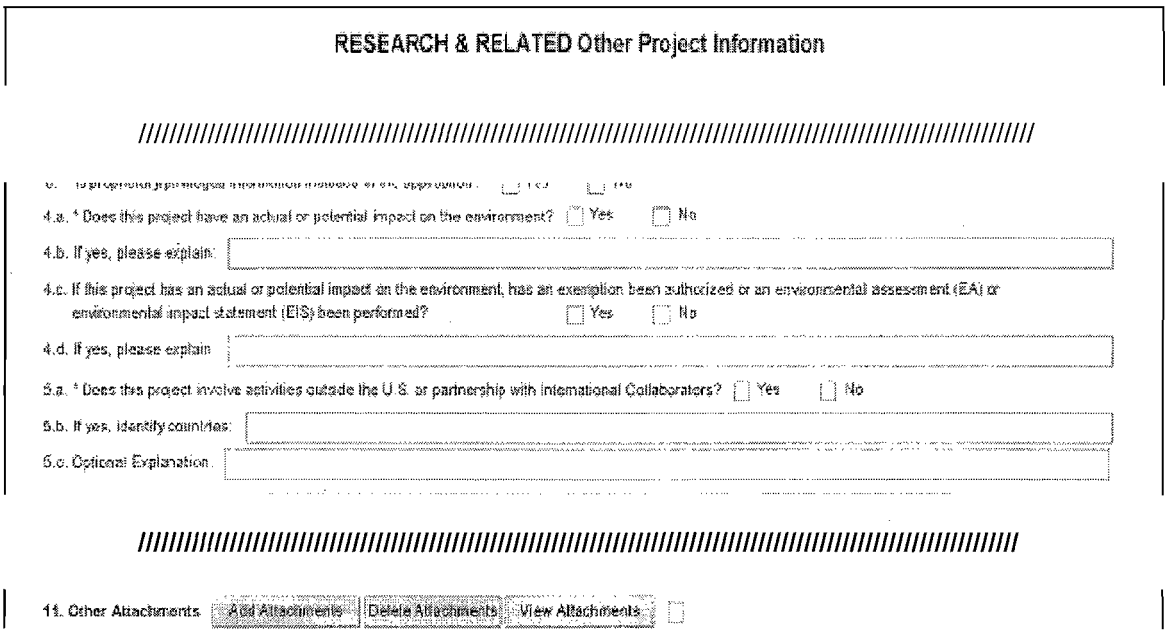
Any application that is likely to result in the development of a model organism must address how it will be shared and distributed. The NIH policy pertaining to sharing model organisms is given on pages III-4 and III-5 of Section III of the *PHS SF424 (R&R) Application Guide.*

If you need to create either of these plans, simply follow the clear instructions that can be found

in section 5.5.17 of the *Guide* and upload this document using the "Add Attachment" button on line 17.

ENVIRONMENTAL IMPACT

This part of your proposal (see figure, below) needs to be completed only when the Funding Opportunity Announcement to which you are responding stipulates that the National Environmental Policy Act applies. In most cases, therefore, you will check Section 4a on the *Other Project Information* component "No." If there is such a stipulation in your FOA, check "Yes" for 4a and follow the instructions that are given in section 4.4.4 of the *PHS SF 424 [R&R] Application Guide* to complete 4b through 4d.



INTERNATIONAL COLLABORATIONS

The instructions that accompany the *Other Project Information* component (section 4.4.5 of the *PHS SF 424 [R&R] Application Guide*) are clear and should be followed to reflect either activities that will be conducted outside the United States or collaborations with investigators in other countries. Note that, if you checked "Yes" for 5a, despite its title, for PHS agencies line 5c, "Optional Explanation," is not optional. Special resources or characteristics of the research (e.g., human subjects, animals, disease, equipment and techniques) must be described along with your opinion as to whether similar research is already being conducted in the United States. If there is, you justify why more research of the same kind is needed. Create your explanation as a separate PDF file. Do not enter it in the field for 5c. Rather, upload it into the application using the "Add Attachment" button on line 11, "Other Attachments," of the *Other Project Information* component (see above). The attachment should be titled "Foreign Justification" and the file must be given the same name when it is saved and uploaded.

DEVELOPMENTAL STEPS FOR CHAPTER SEVENTEEN:

1. Answer the question on the *Other Project Information* component regarding involvement of human subjects. If "No," skip to bullet 5, below.
2. If "Yes," human subjects will be involved, obtain IRB approval for the project.
3. If "Yes," complete the relevant ones of the five considerations that are associated with the "Human Subjects Protection" section of the *PHS 398 Research Plan* component.
4. Answer the question on the *Other Project Information* component regarding involvement of vertebrate animals. If "No," skip to bullet 8, below.
5. If "Yes," vertebrate animals will be used, obtain IACUC approval of your project.
6. If "Yes," check to determine whether or not your institution has an Animal Welfare Assurance Number.
7. If "Yes," review the NIH tutorial, "How to Write an Application Involving Research Animals." Use what you learn to write the responses to the five considerations that must be addressed under section 12, Vertebrate Animals, of the *PHS Research Plan* component.
8. Determine whether hazardous agents will be used in your project, either at your institution or in those parts of the project that will be performed at other institutions. If you are unsure of what constitutes a hazardous agent, refer to http://www.cdc.gov/od/sap/docs/salist.pdf. If hazardous agents will be used, complete subsection 13 of section 2 of the *PHS 398 Research Plan* component.
9. If allowed by the Funding Opportunity Announcement to which you are responding, decide whether or not your project will have multiple PIs. If there will be more than one, develop the required Multiple PI Leadership Plan and upload through subsection 14 of section 2 of the *PHS 398 Research Plan* component.
10. If investigators at other institutions will be investing time on your project, determine whether you will be required to set up an official consortial relationship with the collaborating institution. If yes, follow the instructions related to subsection 15 of section 2 of the *PHS 398 Research Plan* component.
11. If applicable, create plans to share and distribute data and model organisms, which should be uploaded using subsection 17 of section 2 of the *PHS 398 Research Plan* component.
12. Check the Funding Opportunity Announcement to which you are responding and determine whether or not the National Environmental Policy Act applies. If it does, check "Yes" on line 4a of the *Other Project Information* component and then complete parts 4b-4d, which follow.
13. If applicable, create an attachment covering research activities associated with your project that will be conducted outside of the United States and/or collaborators in other countries. Appreciate that this document must be uploaded using the "Other Attachments" section of the *Other Project Information* component, not the 5c line, "Optional Explanation."

CHAPTER 18

SF 424 COVER COMPONENT, PHS 398 COVER PAGE SUPPLEMENT and APPENDIX MATERIAL

SF 424 COVER COMPONENT

This part of the application, the first page of which is reproduced below, can easily be completed successfully after reading and following the instructions that are included in the *PHS SF 424 (R&R) Application Guide* (section 4.2).

APPLICATION FOR FEDERAL ASSISTANCE
SF 424 (R&R)

2. DATE SUBMITTED	Applicant Identifier
3. DATE RECEIVED BY STATE	State Application Identifier
4. Federal Identifier	

1. * TYPE OF SUBMISSION
Pre-Application Application
Changed/Corrected Application

5. APPLICANT INFORMATION * Organizational DUNS:
* Legal Name:
Department: Division:
* Street1: Street2:
* City: County: * State:
Province: * Country: * ZIP / Postal Code:

Person to be contacted on matters involving this application
Prefix: * First Name: Middle Name: * Last Name: Suffix:
* Phone Number: Fax Number: Email:

6. * EMPLOYER IDENTIFICATION (EIN) or (TIN):	7. * TYPE OF APPLICANT:
8. * TYPE OF APPLICATION: New Resubmission Renewal Continuation Revision	Other (Specify): Small Business Organization Type Women Owned Socially and Economically Disadvantaged
If Revision, mark appropriate box(es). A. Increase Award B. Decrease Award C. Increase Duration D. Decrease Duration E. Other (specify)	9. * NAME OF FEDERAL AGENCY:
* Is this application being submitted to other agencies? Yes No What other Agencies?	10. CATALOG OF FEDERAL DOMESTIC ASSISTANCE NUMBER: TITLE:

11. * DESCRIPTIVE TITLE OF APPLICANT'S PROJECT:

12. * AREAS AFFECTED BY PROJECT (cities, counties, states, etc.)

13. PROPOSED PROJECT: * Start Date * Ending Date	14. CONGRESSIONAL DISTRICTS OF: a. * Applicant b. * Project

15. PROJECT DIRECTOR/PRINCIPAL INVESTIGATOR CONTACT INFORMATION
Prefix: * First Name: Middle Name: * Last Name: Suffix:
Position/Title: * Organization Name:
Department: Division:
* Street1: Street2:
* City: County: * State:
Province: * Country: * ZIP / Postal Code:
* Phone Number: Fax Number: * Email:

There are some parts that are particularly in need of careful reading of the instructions, because they are modified in specific ways for PHS proposals. They are designated in the instructions by the logo of the Department of Health & Human Services. There are also parts of the component that can be confusing. For example, "Applicant Information" (field 5) is not about you. Information about the Applicant Organization is what is sought here – which would be evident after close reading of the instructions. Those who don't do this often fill in this part of the component incorrectly.

Before creating the title for your application (field 11), please read the suggested approach to doing so that is described in chapter 19. This is an exceptionally important part of your proposal. Therefore, you should put extensive thought and effort into creating the kind of title that will leave a positive initial impression on your reviewers.

Field 12, "Areas Affected by Project (Cities, Counties, States, Etc.), is another one that is often completed incorrectly by applicants, who assume that its title is so clear that there is no need to read the instructions. This field is completed in NIH and other PHS applications by entering 'N/A' (not applicable).

In field 15, do not use the "Suffix" subsection to enter your degrees. These will be provided later, when you complete the *PHS Cover Page Supplement* (see below). It is permissible to enter a suffix such as 'Jr.' here.

The second page of the *SF 424 (R&R) Cover Component* is shown below. Again here, there

SF 424 (R&R) APPLICATION FOR FEDERAL ASSISTANCE **Page 2**

16. ESTIMATED PROJECT FUNDING	17. * IS APPLICATION SUBJECT TO REVIEW BY STATE EXECUTIVE ORDER 12372 PROCESS?
a. * Total Estimated Project Funding	a. YES THIS PREAPPLICATION/APPLICATION WAS MADE AVAILABLE TO THE STATE EXECUTIVE ORDER 12372 PROCESS FOR REVIEW ON:
b. * Total Federal & Non-Federal Funds	DATE:
c. * Estimated Program Income	b. NO PROGRAM IS NOT COVERED BY E.O. 12372; OR
	PROGRAM HAS NOT BEEN SELECTED BY STATE FOR REVIEW

18. By signing this application, I certify (1) to the statements contained in the list of certifications* and (2) that the statements herein are true, complete and accurate to the best of my knowledge. I also provide the required assurances * and agree to comply with any resulting terms if I accept an award. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. (U.S. Code, Title 18, Section 1001)

* I agree

* The list of certifications and assurances, or an Internet site where you may obtain this list, is contained in the announcement or agency specific instructions.

19. Authorized Representative

image of S F 424 cover component, page 2

Prefix: * First Name: Middle Name: * Last Name: Suffix:

* Position/Title: * Organization:

Department: Division:

* Street1: Street2:

* City: County: * State:

Province: * Country: * ZIP / Postal Code:

* Phone Number: Fax Number: * Email:

* Signature of Authorized Representative — Completed on submission to Grants.gov

* Date Signed — Completed on submission to Grants.gov

20. Pre-application — Add Attachment

21. Attach an additional list of Project Congressional Districts if needed. — Add Attachment

OMB Number: 4040-0001

Expiration Date: 06/30/2008

are parts of it that are not intuitive. Field 17 is one of them. For NIH and other PHS agencies, the circle labeled "Program is not covered by E. O. 12372" should be checked to the right of "b. No." Another is "Pre-application (field 20), which should be left blank unless you are responding to a Funding Opportunity Announcement that requires it.

PHS 398 COVER PAGE SUPPLEMENT

In NIH applications the SF 424 (R&R) Cover Component just discussed is complemented by the *PHS 398 Cover Page Supplement*. It consists of two parts, the first of which is shown below.

PHS 398 Cover Page Supplement

OMB Number: 0925-0001
Expiration Date: 9/30/2007

1. Project Director / Principal Investigator (PD/PI)

Prefix: * First Name:
Middle Name:
* Last Name:
Suffix:

* New Investigator? No Yes

Degrees:

2. Human Subjects

Clinical Trial? No Yes

* Agency-Defined Phase III Clinical Trial? No Yes

3. Applicant Organization Contact

Person to be contacted on matters involving this application
Prefix: * First Name:
Middle Name:
* Last Name:
Suffix:

* Phone Number: Fax Number:
Email:

Person to be contacted on matters involving this application
Prefix: * First Name:
Middle Name:
* Last Name:
Suffix:

* Phone Number: Fax Number:
Email:

* Title:

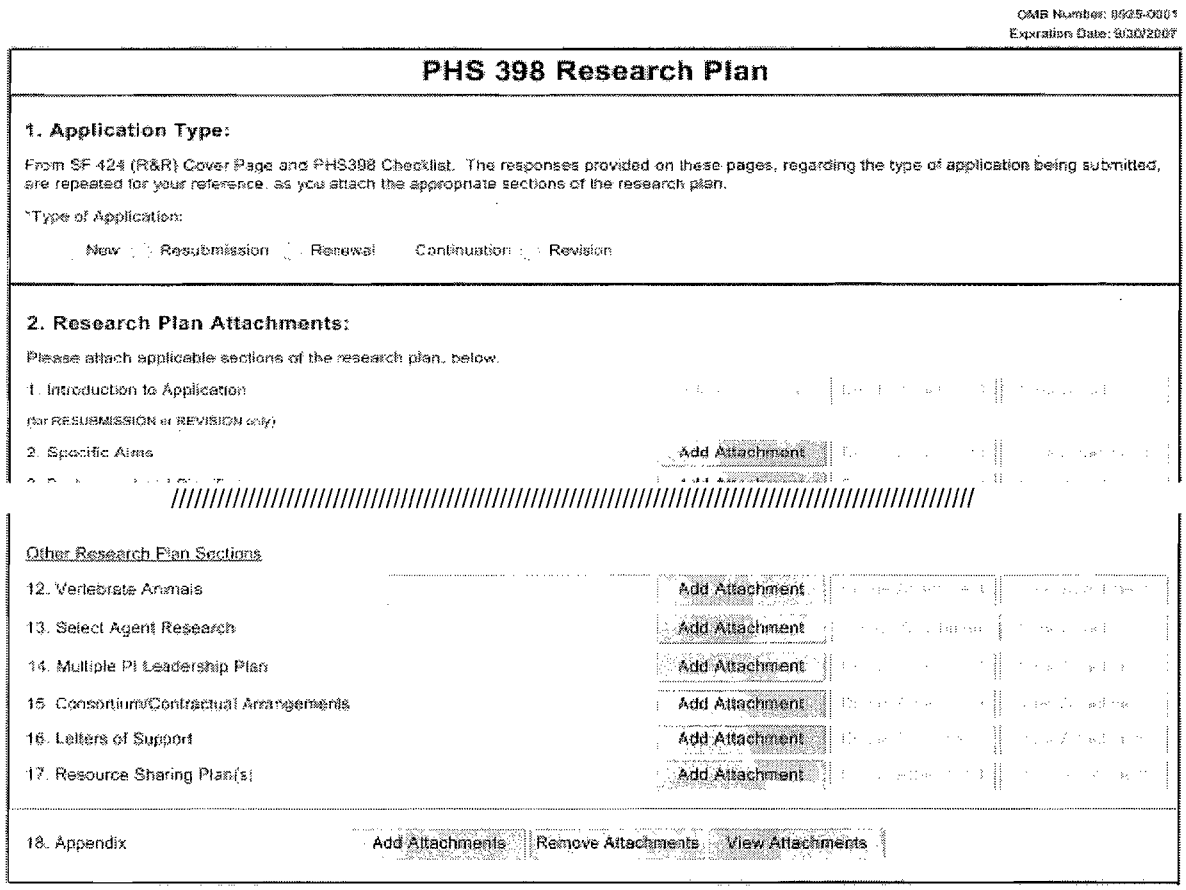
* Street1:
Street2:
* City:
County:
* State:
Province:
* Country: * Zip / Postal Code:

Be sure that you understand the definition of a NIH New Investigator if you check "Yes" under section 1. It is very different than that for other agencies. To refresh your memory, you cannot have been the Principal Investigator for an R01 or equivalent grant (e.g., the Project Leader on a Program Project grant). Thus, if you have been the PI for a R03, R15 or R21 you are still eligible as a New Investigator. *If there are multiple PIs on your proposal, each must meet the definition of a New Investigator for this field to be checked "Yes."*

The second part of the *PHS 398 Cover Page Supplement* pertains exclusively to use of human embryonic stem cells. Completing this part, which is not shown here, is very straightforward: either you are using them or you aren't. If you aren't, check "No." If you are, check "Yes" and provide the registration number of the line that you propose to use. If you don't yet know which line will be used, there is a box that can be checked to indicate that.

APPENDIX MATERIAL

If you are going to submit appendices, up to 10 PDF files are allowed. Use the "Add Attachments" button at the right of line 18 of the *PHS SF424 Research Plan Component* (see below) to upload them, not the "Other Attachments" part of the *PHS SF424 Other Project Information Component*. The latter section is not used in the development of NIH and other PHS agency proposals.


OMB Number: 0925-0001
Expiration Date: 9/30/2007

PHS 398 Research Plan

1. Application Type:

From SF 424 (R&R) Cover Page and PHS398 Checklist. The responses provided on these pages, regarding the type of application being submitted, are repeated for your reference, as you attach the appropriate sections of the research plan.

*Type of Application:

New | Resubmission | Renewal | Continuation | Revision

2. Research Plan Attachments:

Please attach applicable sections of the research plan, below.

1. Introduction to Application (for RESUBMISSION or REVISION only) — Add Attachment
2. Specific Aims — Add Attachment

Other Research Plan Sections

12. Vertebrate Animals — Add Attachment
13. Select Agent Research — Add Attachment
14. Multiple PI Leadership Plan — Add Attachment
15. Consortium/Contractual Arrangements — Add Attachment
16. Letters of Support — Add Attachment
17. Resource Sharing Plan(s) — Add Attachment

18. Appendix — Add Attachments | Remove Attachments | View Attachments

Your first job is to decide whether or not you want to include appendices. Consider that appendix material can have a negative psychological impact on your assigned reviewers (usually only they will receive copies of this part of your application) because the additional material likely means more work for them. To overcome this problem, if you decide to include appendices, it should be readily evident (e.g., from the title of each) that they contain information that is genuinely important to the review of your application. Appendices should never contain material that the reviewer must read in order to understand what is being proposed; everything needed by the reviewer should be contained within the body of the grant application. Thus, you would never include something like a 'Methods' appendix. If NIH staff members decide that you are trying to circumvent the page limitation for the Research Plan by forcing reviewers to read the appendix material, they have the option to return your application without review. The instructions pertinent to this point are very clear:

> *PHS SF 424 (R&R) Application Guide* Instructions: "Do not use the Appendix to circumvent the page limitations of the Research Plan. An application that does not observe these limitations will be withdrawn from review."

Appendix material, if used, should facilitate the job of your assigned reviewers. In other words, it should be restricted to supporting documentation that you make available as a courtesy, should your reviewers choose to use it. A reviewer-friendly approach that is encouraged by NIH is to include a summary of the appendices that have been included – a 'table of contents' for the appendix section if you will, which should be the first PDF file that is uploaded.

Several kinds of appendix material are allowed:

Publications

> *PHS SF 424 (R&R) Application Guide* Instructions: Submit up to 10 publications or manuscripts **accepted** for publication. *Do not include abstracts, unpublished theses, or manuscripts* ***submitted*** *for publication.* [NIH emphases]

For publications that are in press, do not submit the entire manuscript if it is possible to provide either a link to an on-line journal that is publicly available, or the NIH PubMed Central submission identification number.

Unpublished, but accepted, manuscripts that are not publicly available are good examples of the kind of thing that *should* be included as appendix material, because the reviewers would otherwise have no access to such information. Submit the entire manuscript as a PDF file. It is especially important to include such manuscripts if they are a source of details of a study that you have summarized in the *Preliminary Studies* section.

If you are a New Investigator, because so much emphasis is placed on assessment of your background and training, we recommend that you include your dissertation abstract as one of the 10 publications that you are allowed.

Instruments

> *PHS SF 424 (R&R) Application Guide* Instructions: Surveys, questionnaires, data collection instruments, clinical protocols, and informed consent documents [may be submitted as appendix material]

It is sometimes necessary for reviewers to physically inspect instruments that will be used in the research project. Such 'blank forms' take up too much space in the body of the Research Plan, so their inclusion as appendix material has been approved.

Illustrations

> *PHS SF 424 (R&R) Application Guide* Instructions: Photographs or color images of gels, micrographs, etc., provided that the image (may be reduced in size) is also included within the 25-page limit of Items 2-5 of the Research Plan [Component]. No images may be included in the Appendix that are not also represented within the Research Plan.

Note that, if you include photographs or color images as appendix material, you must include that same material in the Research Plan. If you include illustrations only in the appendix, i.e., don't include a copy in the body of the Research Plan, it is almost certain that you will be judged as trying to circumvent the page limitation, in which case NIH will return your proposal without review. You might use an appended illustration do so to provide reviewers with higher resolution than is possible in the body of the proposal; to provide unequivocal evidence that a faint part of an illustration is real; or provide a larger, more reviewer-friendly version of something that is reduced in size in the body of the Research Plan.

DEVELOPMENTAL STEPS FOR CHAPTER EIGHTEEN:

1. Complete the *SF 424 Cover Page* component and *PHS 398 Cover Page Supplement* after carefully reading the instructions that guide their preparation (sections 4.2 and 5.3, respectively).
2. Decide what appendix material will be submitted, if any.
3. Evaluate your choice to include each appendix using this litmus test: Is this being included as a courtesy to the reviewers – to make their jobs easier? If the answer is 'Yes,' retain that part of the appendix.
4. Assure that you understand the nuances that govern which unpublished manuscripts can be included as appendices and which cannot.

OVERVIEW: PART FOUR

MAXIMIZING YOUR APPLICATION'S COMPETITIVENESS

Small things can make a big difference in how well your proposal is received by reviewers.

This part of the *Workbook* addresses components and steps in the developmental process that are relatively minor in terms of the space / time that is related to them. However, they are critically important to maximizing the competitiveness of your proposal. These are the last things to be done, but they shouldn't be done in haste or at the last minute, because they are essential to the success of your application. Thus, you need to plan to have time enough at the end of the developmental process to complete these final steps.

Chapter nineteen offers strategies for the development of a compelling and informative title, which is what conveys the first impression of your application.

Chapter twenty addresses how to safely include proprietary or privileged information in your proposal, as well as how to prepare the all-important *Project Summary/Abstract* and *Project Narrative* sections.

Chapter twenty-one will guide you through preparation of the cover letter that should accompany your application, as well as how to obtain letters of support that will maximally support your proposal.

Chapter twenty-two describes the final – and most important – step in developing a competitive application: pre-submission review of your final draft by knowledgeable colleagues.

CHAPTER 19

HOW TO CREATE A COMPELLING, INFORMATIVE TITLE FOR YOUR PROPOSAL

PHS SF424 (R&R) Application Guide Instructions: "NIH and other PHS agencies limit title character length to 81 characters, including the spaces between words and punctuation. Titles in excess of 81 characters will be truncated. A "new" application must have a different title from any other PHS project with the same program director / principal investigator. A "resubmission" or "renewal" application must normally have the same title as the previous grant or application. If the specific aims of the project have significantly changed, choose a new title. A "revision" application must have the same title as the currently funded grant."

GENERAL CONSIDERATIONS

The title is critically important, because it will likely be the first thing related to the content of your proposal that a reviewer will see. It, therefore, gives the first impression that s/he will have of your application — and we all know that you get only one chance to make a good first impression. The title is also important, because it will be one of the things that will be used by staff at the Center for Scientific Review to assign your application to a Scientific Review Group. Thus, it behooves you to make your title as interesting and informative as you can.

TIP: Your title should emphasize the payoff – the product of the research.

An especially important point is to emphasize with your title what the research will produce, not the process that will yield that product. You should never offer a generic, process-oriented title like, 'Investigations of *Bacillus megaterium*.' Rather, your title should immediately convey to the agency and its reviewers what the mission-relevant payoff from the research will be. Thus, the objective of your application and the description of your expected contribution from the significance subsection of *Background and Significance* will be particularly useful in the development of your title.

TIPS ON CREATING YOUR TITLE

If you are going to capture the attention of your reviewers, the title must be maximally informative and should convey as much about the novelty of your idea as is possible. Titles with this

kind of impact aren't often created with the small amount of time and thought that are usually invested.

As a strategy, we recommend that you create your title by using a modification of an approach that is often used by marketers to develop advertising slogans. They often begin the selection process with as many as 100 'catchy' slogans that they have created. Then, they narrow the number down to the most appealing one using focus groups. They invest this kind of effort in identifying the best slogan because millions of dollars will likely be riding on that slogan's subsequent capacity to capture the interest and attention of the marketer's target audience. *Your stakes as a proposal writer are no less great.* Therefore, it is smart business, in our opinion, to apply the same strategy to the development of the 'slogan' – the title – that will catch the interest and attention of your target audience, the reviewers of your proposal.

Steps in Creating a Set of Titles

1. As noted in the text box, above, the title of an NIH application is restricted with respect to its length – 81 characters and spaces, including punctuation.

2. To begin, review your application and list all words/phrases that convey important information, significant impact, and/or the novelty of your project. Many of these will be things that you have highlighted in the text with italics. Pay particular attention to the application's objective and the description of your expected contribution in the significance paragraph of the *Background and Significance* section. The adjacent statement of significance may be of use, as well.

3. Of these words and phrases, consider whether any of them have widely understood, standard abbreviations / acronyms that can be substituted, e.g., DNA for deoxyribonucleic acid or CNS for central nervous system. List such abbreviations and acronyms. *Under no circumstances should you use non-standard abbreviations or acronyms in your title that you have made up and defined in the text of your application.*

4. Once you have listed all words and standard abbreviations / acronyms that might have a role in conveying information about your application, begin arranging them (or variations of them) in combinations and permutations that do not exceed the 81 letters and spaces (including punctuation) that are allowed. For example, were your application about writing successful grant applications to the NIH, and you had listed such key words as success/successful, grants, grant writing, grantsmanship, NIH, creativity, and competitive, you might formulate titles like:

   Creative Formats for Writing Competitive Grant Applications to the NIH (71 characters and spaces)

   NIH Proposal Writing Made Simple: Creative Formats for Successful Applications (78)

   Creative Ways To Develop Your Competitive NIH Proposal-Writing Skills (68)

   Keys to Success for Writing Creative, Competitive NIH Grant Proposals (69)

   Competitive NIH Grantsmanship Skills Made Simple & Successful (62)
   ["&" is an example of a fully understood, standard abbreviation]

5. Create as many titles as you can in an hour. Then, reduce the number to what you think are your 'Top 10.' Print them.

Steps in Identifying the Best Title

1. Show your list of titles to colleagues, both those who are closely related to your field and those who are good scientists but not members of your field. Ask each of them to select the one (or at most two) title(s) from the list that s/he thinks is maximally informative and evocative of interest. It has been our experience that most of your colleagues will select the same one or two, which should tell you that there is something especially appealing about those particular titles.

2. Because titles have to be understood and used by lay persons, also take your list of titles to several such individuals -- a spouse or a neighbor, for example. Ask them to choose. You probably will find that they select the same title(s) that your colleagues chose.

3. Use the information that you have gathered in this manner to narrow the possibilities to no more than three titles. Further refine them until one begins to stand out clearly over the others because of its informative, novel, stimulating character. You will know it when you see it, because it will convey succinctly and compellingly what the payoff of the proposed research program will be. That's your title!

Now, enter the title that you have chosen in field 11 of your application's *SF 424 (R&R) Cover Component*.

DEVELOPMENTAL STEPS FOR CHAPTER NINETEEN

1. Appreciate that your title should emphasize the payoff from the proposed research.
2. Appreciate that the length of your title is limited to no more than 81 characters and spaces, including punctuation.
3. Make a list of words and standard abbreviations that are candidates for use in your title.
4. Create a set of approximately ten titles, using combinations and permutations of the words and abbreviations you have selected.
5. Ask colleagues and lay persons to select the title from the list that is most informative and evocative of interest.
6. Refine the final candidate(s) until it is possible to settle on one of them as your title.
7. Enter the title you have selected in field 11 of your application's *SF 424 (R&R) Cover Component*.

CHAPTER 20

PROJECT SUMMARY/ABSTRACT, PROJECT NARRATIVE and PROPRIETARY / PRIVELEGED INFORMATION

PROJECT SUMMARY/ABSTRACT and PROJECT NARRATIVE

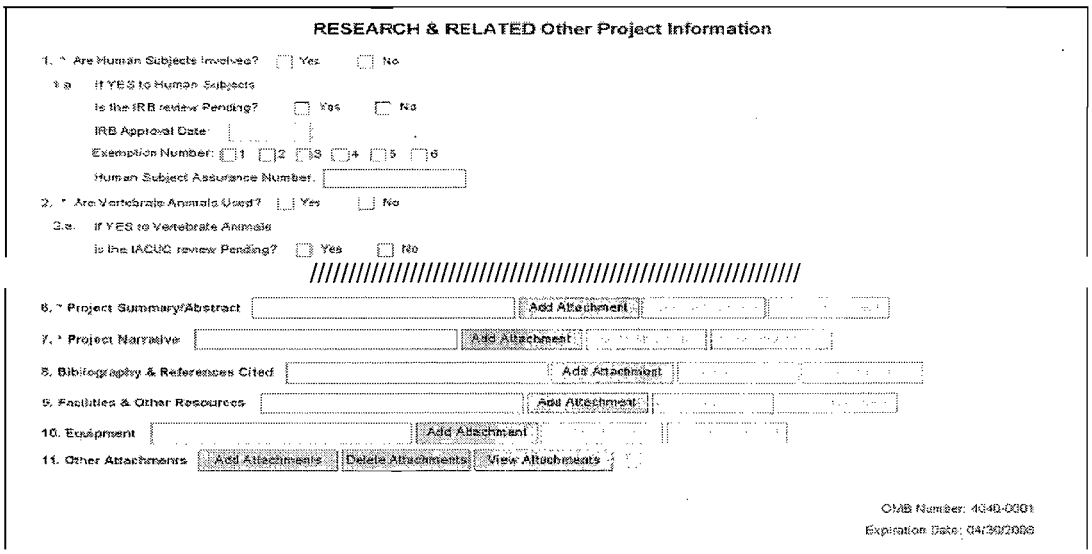
The *Project Summary/Abstract* and *Project Narrative* collectively constitute your application's Project Summary. They will be read by every reviewer, most especially by those who will be seeing your application for the first time at the review-panel meeting. In our opinion, therefore, these two parts are the most important ones in terms of developing advocacy for funding of your proposal among its reviewers. In addition, the *Project Summary/Abstract* and *Project Narrative* will be read by others who will make important decisions regarding your proposal. These will include, but will not necessarily be limited to, those who will assign your application for review – both in terms of the review panel that will receive it and the persons who will be appointed as your reviewers; those who need to convey what NIH is funding; and administrators who will catalog the application with respect to its content. As will be detailed later in this chapter, sensitive information must not be included in the *Project Summary/Abstract* and/or *Project Narrative* because these two sections will be published in the CRISP database as your Project Summary. NIH's instructions to the applicant, which are quoted in the text box, below, make this point clearly and unequivocally.

> *PHS SF 424 (R&R) Application Guide* Instructions (section 4.4.6):
> "This Summary must not include any proprietary/confidential information."

You also have to consider what is included in the *Project Summary/Abstract* and *Project Narrative* from that standpoint that your closest competitor will have the opportunity to read your Project Summary when it is published in the CRISP database. Thus, you walk a fine line when you write these parts of the application between including enough to get your reviewers excited and including things that will tell your competitors too much.

Tips on Creating the Project Summary/Abstract

The *Project Summary/Abstract* is created by adding an attachment of 30 lines or less. Exceeding 30 lines will, in all likelihood, generate an 'error' message during the initial validation of your proposal. The *Project Summary/Abstract*, which must be in the form of a PDF file, is attached through the SF 424 *Other Project Information* Component, line 6 (see top of next page).


RESEARCH & RELATED Other Project Information

1. * Are Human Subjects Involved? Yes No

1.a If YES to Human Subjects

Is the IRB review Pending? Yes No

IRB Approval Date:

Exemption Number: 1 2 3 4 5 6

Human Subject Assurance Number:

2. * Are Vertebrate Animals Used? Yes No

2.a. If YES to Vertebrate Animals

Is the IACUC review Pending? Yes No

6. * Project Summary/Abstract Add Attachment

7. * Project Narrative Add Attachment

8. Bibliography & References Cited Add Attachment

9. Facilities & Other Resources Add Attachment

10. Equipment Add Attachment

11. Other Attachments Add Attachments Delete Attachments View Attachments

OMB Number: 4040-0001

Expiration Date: 04/30/2008

In addition to being informative of what is in the proposal, the *Project Summary/Abstract* must communicate this material with contagious enthusiasm. It is one of the key means by which you create advocacy for the funding of your proposal, especially among the majority of reviewers who have probably not seen your proposal before it comes up for evaluation at the meeting of the review panel. While your proposal is being considered, they will almost certainly read this part of your application, as well as the *Specific Aims* section, as they strive to reach the point where they can make an informed vote.

The instructions that guide preparation of the *Project Summary/Abstract* are contained in section 4.4.6 of the *PHS SF 424 (R&R) Application Guide*. They are, in part:

> The *Project Summary/Abstract* is "meant to serve as a succinct and accurate description of the proposed work when separated from the application. State the application's broad, long-term objectives and specific aims, making reference to the health relatedness of the project (i.e., relevance to the **mission of the agency** [NIH emphasis]). Describe concisely the research design and methods for achieving the stated goals. This section should be informative to other persons working in the same or related fields and insofar as possible understandable to a scientifically or technically literate reader. Avoid describing past accomplishments and the use of the first person."

This part of your application can be a very difficult section of the application to write well. A great deal of information must be coherently distilled into 30 lines or less. Assure that only meaningful, essential information is included. There just isn't room to include descriptions of past accomplishments, which is why such information is explicitly prohibited by the instructions. For the same reason, background information should not be included. You have to assume that the reader, especially the members of your review panel, will be sufficiently conversant with the area that background is not needed in this part of the application. You will be safe in making this assumption because the instructions specifically state that: "This section should be informa-

tive to other persons working in the same or related fields ..." Don't worry if there appears to be duplication here of other parts of your application. Such duplication can't be – shouldn't be - avoided because the *Project Summary/Abstract* must be a stand-alone document that does not need the rest of the proposal to be understood.

Here are the steps that we recommend you take to develop your critically important *Project Summary/Abstract*:

1. The *Project Summary/Abstract* should not be written until you have completed sections A through D of your Research Plan, i.e., the *Specific Aims, Background and Significance, Preliminary Studies*, and *Research Design and Methods* sections. In other words, it should be written last – but not at the last minute.
2. Do not write this section in the first person.
3. Create the first draft of your *Project Summary/Abstract* as a separate file. Use 11-point Arial or one of the other allowed typefaces (Helvetica, Georgia or Palatino Linotype). Use left and right margin settings of 0.5 inch here, rather than the 1 inch that we recommend for the Research Plan. You need every millimeter of space that you are allowed to assure that you include everything that is relevant to your application.
4. Do not worry if you initially write more than the 30 lines that are allowed; there will be an editing phase after the first draft has been written.
5. Open the *Project Summary/Abstract* with a sentence that succinctly describes the gap in the knowledge base or unmet need that will drive the application.
6. Copy and paste into the file the sentences in the *Specific Aims* section that contain words that you highlighted in italics. They are designed to set up a compelling progression of logic when they are juxtaposed, one after the other.
7. Add your specific aims and the primary methods/approaches that will be used to accomplish them.
8. Conclude the *Project Summary/Abstract* with a combination of the 'contribution' sentence and the 'statement of significance' sentence from the first, significance paragraph of the *Background and Significance* section.
9. Edit the file to be no more than 30 lines, with 0.5-inch margins and lines spaced no closer than 6 per vertical inch.
10. Highlight key words in the edited *Project Summary/Abstract* using either italics or, if you are using Arial or Helvetica, underlined italics.

Tips on Creating the Project Narrative

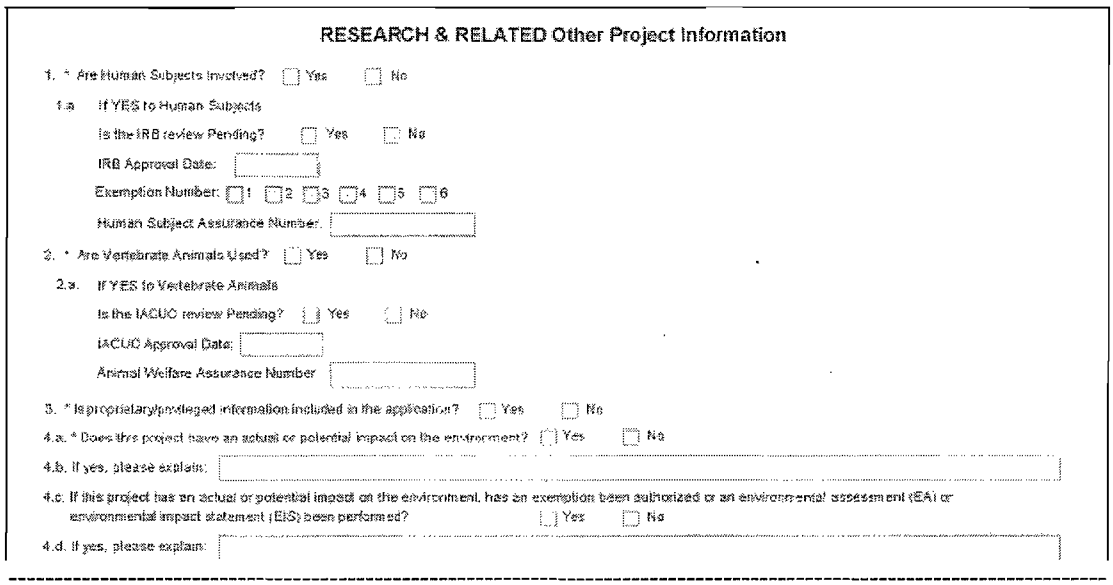
Line 7 of the SF 424 *Other Project Information* component (see above) allows you to attach a separate PDF file of no more than 2 or 3 sentences, which are meant to complement the *Project Summary/Abstract*. They will be ultimately be combined with your *Project Summary/Abstract* as an integral part of the Project Summary that is published in CRISP. Despite what its name implies, the *Project Narrative* is meant to reflect the relevance that the proposed work has to public health. Ideally, it should also reflect how the proposed research relates to one or more of the components that constitute NIH's mission.

To write these sentences, we recommend that you synthesize them from what you have written in the last, 'positive impact' part of the *Specific Aims* section and the third, 'benefits' part of the first, significance subsection of *Background and Significance*.

PROPRIETARY / PRIVELEGED INFORMATION

Information that is either proprietary, patentable, a trade secret, or privileged / confidential commercial or financial information can be included in your grant application – but you should think twice before doing so. Such information should never be included in the Project Summary/Abstract because when it is funded, that part of your proposal will be published in the CRISP database. In other words, it will enter the public domain. In addition, you have to remember that any funded federal grant can potentially be obtained at a later time in its entirety through the Freedom of Information Act. Therefore, putting the sensitive information in the body of your proposal doesn't necessarily protect it.

If you must include sensitive information in your application to give reviewers a full appreciation of it, you must make clear to NIH that your proposal contains such information. You do so by checking "Yes" on line 3 of the *Other Project Information* component, the relevant part of which is reproduced below.



RESEARCH & RELATED Other Project Information

1. * Are Human Subjects Involved? ☐ Yes ☐ No

1.a If YES to Human Subjects

Is the IRB review Pending? ☐ Yes ☐ No

IRB Approval Date:

Exemption Number: ☐1 ☐2 ☐3 ☐4 ☐5 ☐6

Human Subject Assurance Number:

2. * Are Vertebrate Animals Used? ☐ Yes ☐ No

2.a. If YES to Vertebrate Animals

Is the IACUC review Pending? ☐ Yes ☐ No

IACUC Approval Date:

Animal Welfare Assurance Number

3. * Is proprietary/privileged information included in the application? ☐ Yes ☐ No

4.a. * Does this project have an actual or potential impact on the environment? ☐ Yes ☐ No

4.b. If yes, please explain:

4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? ☐ Yes ☐ No

4.d. If yes, please explain:

To further inform NIH as to precisely which parts of your application are sensitive, you need to mark them clearly. We recommend that you do so using a vertical line in the left margin. The sensitive information should also be preceded by a legend that is similar to the one that NIH suggests in the *PSH SF 424 (R&R) Application Guide* (section 4.4.3): "The following information, which is marked with a vertical line in the left margin, is proprietary/privileged information that (PI's name) requests not be released to persons outside the government, except for purposes of review and evaluation." There are two parts of the NIH-suggested legend that should give you pause. One is the word "requests." As noted above, any funded PHS grant is potentially obtainable through the Freedom of Information Act. Thus, 'requesting' that the information be protected and the reality of whether it 'will be' protected are two different things. The second concerning part is the final phrase, "except for purposes of review and evaluation." That means that the information can and probably will be released to persons outside the government who are involved in the review process, i.e., reviewers. Therefore, before including such information, we recommend that you first discuss including sensitive information in your application with the

person at your institution who is responsible for protecting intellectual property. If s/he is not concerned, you probably shouldn't be, either. If s/he is, we recommend that the two of you directly contact the Scientific Review Administrator of the review panel that you are planning to target. If s/he cannot answer your questions satisfactorily, keep asking higher levels of authority until you are satisfied that the NIH-recommended approach will (or won't) truly safeguard what you want to include.

DEVELOPMENTAL STEPS FOR CHAPTER TWENTY:

PROJECT SUMMARY/ABSTRACT & PROJECT NARRATIVE

1. Do not write the *Project Summary/Abstract* and *Project Narrative* until after the Research Plan has been completed.
2. Write the *Project Summary/Abstract* – 30 lines or less – using the 9 steps offered above.
3. Review NIH's mission, which is reproduced on page 2 of this *Workbook*.
4. Write the *Project Narrative* – 2 or 3 sentences – emphasizing the importance that the proposed research has to public health, as well as its relevance to NIH's mission.
5. Show the final drafts of your *Project Summary/Abstract* and *Project Narrative* to several colleagues. Ask whether or not: the flow of logic in them is clear; the gap or need to be addressed is well delineated; the importance of the proposed work and its impact on the field and public health are evident; and whether or not they engender enthusiasm.
6. Use the feedback you obtain to revise these components, if necessary.
7. Convert the (revised) *Project Summary/Abstract* and *Project Narrative* into PDF files.
8. Upload the *Project Summary/Abstract* and *Project Narrative* PDF files into your application using the "Add Attachment" buttons at the right of lines 6 and 7, respectively.

PROPRIETARY/PRIVILEGED INFORMATION

9. Assure that nothing sensitive is included in your *Project Summary/Abstract* and/or *Project Narrative*.
10. Decide whether or not it is necessary to include proprietary / privileged / confidential information in the body of your application.
11. If so, mark such information using a vertical line in the margin and precede it with a legend similar to the one suggested in this chapter.
12. Consult the official at your institution who is in charge of protecting intellectual property regarding what you are considering meets with his/her approval.
13. If necessary, together with your institution's intellectual-property administrator, contact an official at NIH, starting with the Scientific Review Administrator of the review panel you are targeting. Determine officially the extent to which what you have included will / will not be protected.

EXAMPLE OF A WELL-WRITTEN PROJECT SUMMARY/ABSTRACT

There is a fundamental gap in understanding how variation in the expression of conserved appendage-patterning genes leads to the enormous range of morphological variation that is observed among animals, including human beings. The *long-term goal* is to better understand the genetic variation and architecture of the complex phenotypes that attend limb development, both within and between species. The *objective of this particular application* is to identify how hind-limb development and variation are genetically controlled in hemimetabolous insects – an excellent model, because their hind legs often exhibit dramatic species-specific morphological diversification. Such a difference is not characteristic of holometabolous species, such as the familiar *Drosophila* and *Tribolium* models. Most conspicuous is differential enlargement of the hemipteran's hind (T3) legs, compared to the two pairs of forelegs. The *central hypothesis* is that diversification of hind-limb development results from temporal and spatial changes in the expression of specific regulatory genes. The *rationale* for the proposed research is that understanding evolutionarily conserved fundamental mechanisms of limb differentiation has the potential to translate into better understanding of the pathogenesis of hind limb developmental defects. Thus, the proposed research is *relevant to that part of NIH's mission* that pertains to developing fundamental knowledge that will potentially help to reduce the burdens of human disability. Guided by strong preliminary data, this hypothesis will be tested by pursuing two *specific aims*: 1) Determine the function and relative importance of *Ubx* in developing T3 legs; and 2) Identify the role of *dpp* and *ds* gene expression in regulating T3 leg development. Under the first aim, an already proven RNA interference (RNAi) approach will be used to inhibit expression of *Ubx*, after which T3-specific changes in structure and gene expression will be analyzed across a wide range of hemipteran insects. Antibodies and RNA-hybridization probes that are already on hand will be used. Under the second aim, homologs of the genes *dpp* and *ds* will be cloned and patterns of expression analyzed and related to T3 leg development using *in situ* hybridization. The approach is *innovative*, because it utilizes naturally occurring variation in the structure of insect legs to better understand the complexity of limb development. The *proposed research is significant*, because it is expected to advance and expand understanding of how natural variation in patterns of gene expression produces evolutionarily conserved complexity in the phenotype of hind limb development.

EXAMPLE OF A WELL-WRITTEN PROJECT NARRATIVE

The proposed studies are of an important and under-investigated area of limb biology that has potential applicability to understanding the pathogenesis of developmental abnormalities, as well as risk prediction for such abnormalities. The proposed research has relevance to public health, because the fundamental mechanisms to be investigated are evolutionarily conserved. Thus, the findings are ultimately expected to be applicable to the health of human beings.

CHAPTER 21

COVER LETTER COMPONENT and LETTERS OF SUPPORT

PHS 398 COVER LETTER COMPONENT

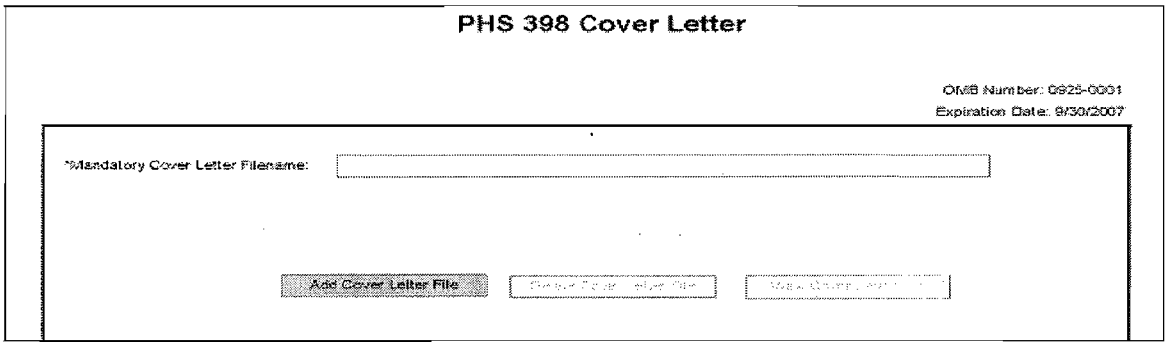
As the title of this section implies, this is one of the PHS 398 components that are specific to NIH grant applications.

> ***PHS SF 424 (R&R) Application Guide, Section 5.2:*** "Applicants are encouraged to include a cover letter with the application. The cover letter is only for internal agency use and will not be shared with peer reviewers."

As implied in the instructions above, this is an optional component. We join with NIH, however, in urging you to submit one. We do so because a good cover letter can accomplish a great deal with respect to assignment and review of your proposal. The "internal agency" referred to in the text box, above, is the Division of Receipt and Referral at the Center for Scientific Review – to which your cover letter should be addressed. The salutation should either be "Dear Sir/Madam," "To Whom It My Concern" or "Referral Officer."

The letter should be brief and to the point. It should concentrate on issues that are related to assignment and review, i.e., it should not contain such things as an overview of what is proposed in the grant application. CSR staff will get that information by reading your Project Summary/Abstract, Project Narrative and, perhaps, other parts of your proposal. The letter should be written so that it can be interpreted and understood by a highly qualified layperson, which is the kind of person who will likely read and act upon your cover letter. To maximize your letter's clarity, we recommend that you make each point an independent paragraph.

The document should be created as a separate file that is converted to PDF and uploaded using the "Add Cover Letter File" button, which is reproduced at the top of the next page. Give the file a clear and descriptive title when you save it onto your hard drive. When you upload the file its title will automatically appear in the "Mandatory Cover Letter Filename" field.



We recommend that you consider including one or more of the following sections in your letter:

Title of the Proposal. See chapter 19 for tips on how to create a strong title for your proposal.

Name of the Funding Opportunity Announcement. This is the title of either the Program Announcement (PA) or Request for Applications (RFA) to which you are responding. Include its exact name.

Request for Assignment to a Specific Scientific Review Group. Using the approaches described in chapter 4, you should have identified the most appropriate Scientific Review Group for your application. You should make a request for that SRG in your cover letter, and provide justification as to why, in your opinion, it is the most appropriate choice. Usually, your justification will be based on the kinds of expertise on the panel. If two or more SRGs would be applicable to the review of your proposal, you should indicate that fact. As part of your justification, you should rank order them, if possible, from most to least appropriate. If the most qualified SRG is missing a kind of expertise that is necessary for you to receive a fair review, you should point that out in your letter and request that an *ad hoc* (temporary) reviewer with that expertise be added for the purpose of reviewing your proposal.

Who Should Not Review Your Proposal. You should also make clear who should not review your application, if that is appropriate. For example, while making your analysis of SRGs, if you were to discover that your closest competitor is a member of the most appropriate panel, you should point that out in your cover letter; it would not be fair for a variety of reasons for such a person to be involved in the review of your application. If there are those outside the panel who should not review your proposal, they should also be named, because they might otherwise be selected to provide an outside review. The name of any person you include must be accompanied by credible justification as to why that individual should not be involved in the review of your proposal. Avoid subjective reasons, such as "She doesn't appreciate the importance of the area." Also avoid making allegations that reflect negatively on the person you are trying to exclude, e.g., "He would likely steal my idea." The least controversial approach is to name those you want to exclude as close competitors.

You should also name anyone who has been involved in the development of your proposal, e.g., the members of your pre-submission review committee. For this reason you should avoid asking anyone to serve on your pre-submission review committee who you think would potentially be a sympathetic official reviewer.

Request Assignment to an Awarding Component. You can also suggest which of NIH's awarding components (Institute, Center or Office – see chapter 1) should consider your proposal for funding after it has been reviewed and rated. If you have a topic that is pertinent to the mission of more than one awarding component, you can request in your cover letter that your proposal be given a multiple assignment. If you have such a cross-cutting subject, you should definitely take advantage of that fact because it potentially gives you multiple chances at funding. Indicate in your cover letter which awarding component should be primary. Provide justification for why. Rank order the remaining ones (as many as are applicable), including justification for each. You should consider both subject applicability to the awarding components and the relative levels of enthusiasm of their Program Officers (see chapter 3) in making your prioritization. As an example, let's say that your topic is a cardiovascular disease that is seen exclusively in elderly persons. The relevant Program Officer at the National Heart, Lung and Blood Institute is very enthusiastic about the topic and has indicated how funding your idea would help the Institute accomplish its near and long-term goals. By contrast, the PO at the National Institute on Aging was supportive but not strongly so. Under such circumstances you would justify NHLBI as primary and NIA as secondary, based on relative programmatic relevance. After its review your proposal would go first to NHLBI for consideration of funding. If program staff there elected to do, so that would be the end of the story – a happy ending. If, on the other hand, they elected not to fund your proposal it would automatically go to NIA for a second chance at funding.

Approval Documents. If you had to get permission from NIH to make your application (e.g., the budget exceeds $500,000 per year or it is for a Cooperative Agreement [U13]), you should state this fact in your cover letter that you have obtained such approval and that the pertinent document of approval is attached as an appendix item. Simply append the necessary documentation before creating and uploading the PDF file for the cover letter.

Two additional buttons are found on the Cover Letter Component, "Delete Cover Letter File" and "View Cover Letter File." Their titles are self-explanatory. These allow you to retract / change what has been uploaded, should you decide to do so.

LETTERS OF SUPPORT

Letters of support are uploaded into your application using line 16 of section 2, Research Plan Attachments, of the *PHS 398 Research Plan Component*, which is shown at the top of the next page.

These are essential parts of your application, especially if they pertain to the commitment of individuals who have no measurable effort invested in the project. Without such letters reviewers can – and often do – conclude that the individuals named in the proposal are not committed in the ways that you describe.

A second way to judge when a letter of support is needed, is to think like a reviewer. Any relationship about which you would be concerned as a reviewer is one for which you should have a letter of support. For example, if another institution has agreed to use and help disseminate the findings of the research you are proposing, a letter to that effect from someone who has the authority at that institution to obligate it should accompany your proposal.

OMB Number: 8925-0001
Expiration Date: 6/30/2007

PHS 398 Research Plan

1. Application Type:

From SF 424 (R&R) Cover Page and PHS398 Checklist. The responses provided on these pages, regarding the type of application being submitted, are repeated for your reference, as you attach the appropriate sections of the research plan.

*Type of Application:

New Resubmission Renewal Continuation Revision

2. Research Plan Attachments:

Please attach applicable sections of the research plan, below

1. Introduction to Application (for RESUBMISSION or REVISION only)			
2. Specific Aims	Add Attachment		

Other Research Plan Sections

12. Vertebrate Animals	Add Attachment		
13. Select Agent Research	Add Attachment		
14. Multiple PI Leadership Plan	Add Attachment		
15. Consortium/Contractual Arrangements	Add Attachment		
16. Letters of Support	Add Attachment		
17. Resource Sharing Plan(s)	Add Attachment		

18. Appendix Add Attachments Remove Attachments View Attachments

You should draft the letters of support yourself. There are three reasons why you should do so. First, no one knows better than you why a given letter of support is needed, i.e., what it has to address. Second, you can't afford to get a poorly written letter of support from someone. How do you go back to that person to get a better one? Finally, those for whom you write a suggested letter of support will almost always be grateful for the time you will have saved them.

We recommend the following approach. After clearing it with the person in question, draft an 'example' of what is needed. Deliver it along with a disk and a clear expression that s/he can scrap it and start over, modify it or use it as written. In most cases the choice will be to embellish what you have provided, making the letter even stronger. At the least, you will get back exactly what you provided, which will specifically and precisely underpin what you want supported.

Each letter must appear as though it was written by the person who has signed it. Therefore, when writing more than one letter of support, make certain that you vary the style, choice of words, punctuation, and even formatting of each, thereby giving the impression that they were written by different persons. If the 'writer' of a letter decides to embellish / modify what you have suggested, the likelihood is that such additions will help to overcome the problem of 'sameness.'

Scan the letters that you receive and combine them into a single PDF file before uploading them using the "Add Attachment" button at the right of line 16.

DEVELOPMENTAL STEPS FOR CHAPTER TWENTY-ONE:

Creating a Cover Letter

1. Use the title created earlier as the 'opening' of your cover letter.
2. If you are responding to an NIH Funding Opportunity Announcement, include its exact title.
3. Designate the Scientific Review Group(s) that should review your application and provide justification for the choice(s).
4. Determine whether the full complement of expertise needed to give your proposal a fair review is included among members of the selected SRG(s). If additional expertise is needed on the most appropriate panel, request and justify its addition on an *ad hoc* basis.
5. List persons who should not review your proposal and provide objective justification relevant to why each should be excluded.
6. Decide on the basis of subject applicability and Program-Officer enthusiasm whether you should ask for assignment to more than one awarding component. If so, select one as primary and rank order the others, from most to least applicable, with justification provided for the inclusion of each.
7. Append any documents required to reflect NIH agreement to submission of your application.

Creating Letters of Support

9. Think like a reviewer and ensure that any aspect of your application that could be the subject of reviewer concern is supported precisely and specifically by a letter of support.
10. Draft an 'example' for each letter of support, being careful to ensure that each gives the impression that it was written by a different person.
11. Ensure that each letter writer understands that s/he has the option to ignore your example, embellish it or use it as written.
12. After receiving them, scan the letters and combine them into a single PDF document, which should then be uploaded into your application using the "Add Attachment" button on line 16 of section 2 of the *PHS 398 Research Plan Component*.

Example of a Good Cover Letter:

Division of Receipt and Referral
Center for Scientific Review
National Institutes of Health

To Whom It May Concern:

Enclosed, please find our grant application, "Objective Means of Identifying Manipulative Advertising Aimed at Children."

We are responding to Program Announcement PA-06-999, "Negative Health Influences on Children."

We request that our proposal be assigned to two of the several sponsors of the Program Announcement, namely the National Institute for Child Health and Development (primary assignment) and the National Institute of Mental Health. The application is particularly relevant to NICHD's programmatic focus on manipulation of children, which we determined by speaking with that Institute's relevant Program Officer, Dr. Oliver Cantor. The subject is also pertinent to NIMH's focus on means of influencing cognitive development, according to Dr. Elizabeth Smart, NIMH's Program Officer on the cited Program Announcement.

The disciplines needed to evaluate all parts of our proposal include child psychology, developmental neurology and marketing. These disciplines are best reflected, in our opinion, among members of the Pediatric Psychology and Neurobiology (PPN) Study Section. We request, therefore, that our application be assigned to this panel for its review.

Although PPN appears to us to be most qualified to review our application, there is no one on the panel with marketing expertise. We request, therefore, that an *ad hoc* reviewer with such qualifications, preferably with direct experience in television advertising that is directed at children, be appointed for the purpose of assisting with the review of our proposal.

If our application is assigned to the PPN Study Section we additionally ask that one of its members, Dr. Samuel Jenkins, be excluded from the review of our application. Dr. Jenkins is our closest competitor and it would not be fair – either to us or to him – to have him participate in the review of our proposal.

Finally, appended to this cover letter is NIH's approval of an annual budget in excess of $500,000.

Sincerely,

James D. Hawkins, Ph.D.
Associate Professor

Example of a Good Letter of Support:

Professor James A. Tiegood
Department of Anatomy and Cell Biology
University of Somewhere
2300 Pendergast Street
City, State 12345

Dear Jim,

This letter confirms my willingness to provide you with sufficient XYZ reagent for the project, "Identification and Functional Characterization of Mitochondrial Nanosomes," the proposal for which will be submitted to the National Institutes of Health. There will be no cost associated with my supplying the preparation.

As you know, this reagent was created in our laboratory, which is currently the only source for it. It is specific for mitochondrial nanosomes, as we have documented in *The Journal of Cell Science*, 74, 2006: 2598-2614.

I confirm that you worked in our laboratory for two weeks last year, developing a good appreciation for how to employ this reagent optimally. In the unlikely event that you experience difficulty using it for the purposes described in your proposal, I will be available to help you expeditiously overcome the related problems.

I look forward to our continued collaborations.

Sincerely,

Alton Hemingway, Ph.D.
Tantaro Distinguished Professor of Cell Biology

CHAPTER 22

PRE-SUBMISSION REVIEW OF YOUR APPLICATION

GENERAL CONSIDERATIONS

If English isn't your first language, unless you have extraordinary facility with languages and don't need it, obtain help pre-submission in eliminating minor mistakes in English usage that you have probably made. You want reviewers to concentrate exclusively on the content of your proposal and not be distracted by mistakes in the way that it is written. To eliminate such mistakes, you can turn to a colleague who is a native English speaker. However, we caution you to select such a person carefully because there are those who have difficulty writing English even though native-born. A second approach is to determine whether your institution's English department has a graduate student or junior faculty member who wants to make a little extra income by providing editorial assistance. As a third possibility, some institutions have one or more English editors on staff. Check with your Research Office to see if this is the case at yours. As a final consideration, there are commercial organizations that are comfortable handling scientific and medical-research documents. They offer revising, editing and proofreading services that will help you to overcome problems that are related to grammar, vocabulary and style. Three that are recommended by the *Journal of Biological Chemistry* can be accessed at: (1) www.biosciencewriters.com; (2) www.bostonbioedit.com; and (3) www.prof-editing.com. English editorial assistance, if needed, should be obtained before you send your proposal to members of your pre-submission review committee.

If we could offer you only one thing that would make the difference between success and failure, it would be pre-submission review of your application by knowledgeable colleagues. Your colleagues have the capacity to pick up the same scientific and technical errors in your proposal that would otherwise be caught by the official reviewers. Why allow review-panel members to detect mistakes that could be removed prior to submission?

If pre-submission review is so important, why don't most applicants take advantage of what it has to offer? In most cases, it is because they haven't planned to have sufficient time before the deadline to do so. *Ideally, you should allow members of your pre-submission review committee two weeks to evaluate your draft, after which you should give yourself at least one week to respond to their criticisms.* Even if you are following a compressed schedule because of a close deadline, don't make the mistake of eliminating this important part the developmental process. You may have to shorten the time that your committee members and you have to work with, but don't delete this step.

CHOOSING THE MEMBERS OF YOUR PRE-SUBMISSION REVIEW COMMITTEE

There should be at least three reviewers on your pre-submission review committee. We recommend that two of them be very close to your own area of expertise, because they will be the

ones who will be most capable of picking up scientific and technical errors that you may have made. They will be the ones who can best assess whether or not the research proposed is significant. These reviewers do not necessarily have to be from your own institution. Take advantage of your network and utilize colleagues at other institutions if they are the ones who are most qualified to help you. The third member of the committee should be a strong general scientist, but not someone who is intimately familiar with what you are proposing. Remember that most review panels are quite heterogeneous with respect to their members' range of expertise (see chapter 4). The 'generalist' on your committee should represent the kind of expertise that you expect on the panel as the farthest removed from the subject you will be presenting. This is important, because if you have written a grant application that can only be understood and appreciated by an expert, you have written a poor proposal. Your 'generalist' will often notice things that are overlooked by reviewers who are intimately familiar with your subject (e.g., jargon, unclear abbreviations / acronyms, the necessity to read between the lines to interpret what is being presented, etc). Any good academician should be able to read the grant application of any other academician and, regardless of the field, become excited about what is proposed. The scientific and technical nuances may be missed, but the idea driving the proposal and its significance should be clear. Anyone reading your proposal should be able to appreciate that, when your idea is acted upon, it will make a vertical difference in the field.

In addition to their scientific expertise, the reviewers on your pre-submission review committee must have several other characteristics. First, they must be colleagues who you can trust. You will be giving them some of your best thinking, and you want to be as certain as possible that they won't 'take the idea and run.' Second, they have to be the kinds of individuals who are willing to give you sharp, even trenchant, criticism if it is justified. If you have an 'ugly baby,' you want to know about it – and it is *very* difficult to tell someone that s/he has an 'ugly baby.' So, when you give them your draft to review, you must emphasize that you are soliciting *meaningful, sharp* constructive criticism. You need to underscore that your feelings won't be hurt, even if they are sharply critical. It is much better to hear it from them than from the official review panel. Third and last, they need to be colleagues who will take / make the time to thoroughly review your draft. When you give them the application, you need to emphasize that performing a complete review will not be a serious drain on their time because it is your best shot, i.e., a final, complete draft – what you would submit if they weren't willing to review it pre-submission. Also make clear that you expect to provide the same service for them at some future time, should they ask for it. Collectively, such assurances will hopefully convince them to provide more than just a cursory read-through. Some institutions offer committee members compensation for their input, which helps motivate them to take the necessary time. Check with your upper administration (e.g., department, college, Research Office) to determine if your institution is in this category.

OBTAINING PRE-SUBMISSION REVIEW

While the primary responsibility of members of your pre-submission review committee is to review your final draft, if you select them early on in the developmental process, you would be well served to have them review your idea, as a starting point, and then your template or master plan (*Specific Aims* section and significance subsection from the *Background and Significance* section) for the application. With respect to the latter review, we have found it to be very worthwhile, because if there is something fundamentally wrong with what is being proposed discovering that fact early on in the developmental process is invaluable.

There are many different ways in which to approach the review of your final draft. For example, you might take the approach of distributing it to the members of your pre-submission review committee with the request that each member evaluate it independently before they meet as a group. They would then give you both their individual critiques and a collective opinion, much as an NIH review panel would. While this works for some, it is very formal and requires a lot of work on the parts of the reviewers. Alternatively, you might seek a brief written review from each member (a summary of the most important problems), together with handwritten annotations on your draft. After analyzing the reviewers' comments obtain verbal clarification during a telephone conversation or face-to-face meeting of anything that is unclear or with which you may disagree. In our experience, the latter approach is the one that works best.

FINAL REVISION AND SUBMISSION

After receiving the comments and suggestions of your pre-submission committee members, you should make the revisions that you think are indicated before submitting it the Center for Scientific Review at NIH. It will be considered 'on-time' if it is accepted by Grants.gov no later than 5 pm (your local time) on the deadline day. Your Authorized Organizational Representative (AOR) will be sent an e-mail message from Grants.gov indicating that you proposal has been received. Once validation by NIH has been completed, you and the AOR will be sent an e-mail message confirming that fact. If there are problems with the validation step, NIH provides a one-week opportunity to correct them.

Once Grants.gov accepts your submitted proposal, you have two business days in which to view the assembled application. If everything is as it should be, no further action is necessary; the application will automatically proceed through the review process. If anything wrong is found in the way that the application has been assembled (e.g., a component did not transmit or has become corrupted), you should immediately contact your Authorized Organizational Representative and discuss how to use the "Reject" option and submit a Changed / Corrected application (see section 2.11 of the *PHS SF 424 (R&R) Application Guide* for details).

At this point, you're done. Accordingly, there is only one last thing left for us to do, and that is to give you our congratulations. Although we realize that this has not been an easy process, we assure you that the investment you have made will pay dividends: Most applicants don't go to the trouble that you have gone to which is why most applicants go unfunded. We wish you and your application well. Congratulations, again, on having completed the process!!!!

DEVELOPMENTAL STEPS FOR CHAPTER TWENTY-TWO:

1. If English is not your native language, consider obtaining editorial assistance to remove errors in grammar, choice of wording and style. Do so before submitting your draft to your pre-submission review committee.
2. Choose the members of your pre-submission review panel early in the developmental process – at least two experts and one generalist.
3. Obtain their independent, informal feedback on the significance of the idea you plan to develop into a grant application.
4. Submit the two-page template or master plan (*Specific Aims* section and significance paragraph of the *Background and Significance* section) members of your committee. Revise, if necessary, to eliminate any flaws that exist at this early stage.

5. Obtain critical evaluation of your final draft by the members of your pre-submission review committee. Emphasize that you want serious criticism and set up the way that you will receive their feedback. Ideally, give them two weeks in which to perform their reviews.
6. Revise your final draft based on their feedback.
7. Submit your application through Grants.gov by following the instructions that are contained in section 2.10 of the *PHS SF 424 (R&R) Application Guide*.
8. Repay your pre-submission reviewers at some later time by acting as a pre-submission reviewer of applications that they are developing.