1st Edition

SBIR Grant Application Mentor

An Educational How-to Manual



A Note from the Publisher

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Thank you for ordering NIH SBIR Grant Application Mentor: An Educational How-to Manual from the Principal Investigators Association Library. This resource is designed to help you better understand — and make the most of — your SBIR grant application to the National Institutes of Health (NIH).

John W. Ludlow, Ph.D, is the author of this manual, and we gratefully acknowledge his input. Dr. Ludlow began his academic faculty career at the University of Rochester (NY) in 1991, with appointments in the department of biochemistry at the medical school and the university's cancer research center. During this time he maintained an independently funded research laboratory training graduate students and post doctoral fellows in the area of tumor suppressor gene expression, protein structure, and function. Funding for his laboratory came from a variety of sources, including the NIH, the American Cancer Society, and private foundations.

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Best Regards,

Leslie Norins, MD, PhD Retired Founder Principal Investigators Association 9990 Coconut Road Suite 316 Bonita Springs, FL 34135 Info@principalinvestigators.org



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This report is endorsed as a valuable tool for continuing professional development by Principal Investigators Association.

Retired Founder: Leslie C. Norins, MD, PhD

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Color Key:

Throughout this report, we have used highlighted text to indicate the following:

- _____ original text by authors of this report (no color)
- (pink) directly quoted NIH information
 - paraphrased NIH information
 - directly quoted information from successful NIH grant applications

(blue)

(yellow)

Introduction

The Small Business Innovation Research (SBIR) program is a highly competitive program encouraging small businesses to explore their technological potential by supporting research alone as well as research and product or technology development. In so doing, this program provides the incentive to profit from any outcomes which are successfully commercialized. Coordinated by the Small Business Administration (SBA) of the federal government, this program has set-aside funds (2.8% of an agency's extramural budget in FY2014), and increase on 0.1% over the FY2013 budget, for qualified domestic small business concerns to engage in these activities. The agency which the SBA is referring to is the National Institutes of Health (NIH). SBIR Programs are fully integrated within NIH research agenda to improve human health through prevention, detection, diagnosis and treatment of disease or disability, speed the discovery process, reduce the cost of medical care, improve research tools with an eye towards reducing research costs, and increase the health knowledge base.

The SBIR Program is structured in three phases. The Phase I goal is to determine technical merit, feasibility, and commercialization potential of the proposed project while at the same time verifying the performance quality of the awardee organization. This verification is crucial before the small business can receive Phase II funding. Phase II support is directly related to the achievements made during Phase I, in addition to the commercial potential and the scientific and technical merit of the new work proposed during Phase II. Assuming that all goes according to the plan followed during Phase I and II, Phase III is when the small business uses non-SBIR funds to realize the commercialization objectives resulting from the Phase I and II activities. This manual will guide you through the SBIR program application process, with the goal of positioning your proposal in the best place possible for funding consideration. While the SBIR program has a total of three phases, Phase I will be covered in detail with reference to Phase II, since these are the two phases that directly involve applying to government agencies for funding. *Keep in mind that Phase I awardees are the only ones eligible to apply for a Phase II. So, while being awarded a Phase II is not automatic, the competition for these monies is far less than it is for a Phase I, which often translates into higher funding rates for this phase.

*NIH Implements an SBIR Direct-to-Phase-II Funding Option. On February 5, 2014, the NIH published a new Funding Opportunity Announcement ("FOA"), **PAR-14-088**. See <u>http://grants.nih.gov/grants/guide/pa-files/PAR-14-088.html</u>.

Direct from NIH:

Under Section 5106 of the Reauthiorization Act, NIH may 'issue a Phase II award to a small business concern that did not receive a Phase I award for that research/research & development'. This is a so-called 'Direct-to-Phase II'SBIR award. This authority would permit small businesses to submit Direct-to-Phase-II SBIR applications, if the small business had performed the Phase I stage-type of research through other funding sources. The legislative rationale for permitting the Direct-to-Phase II award is to allow a SBC that has already built a technology prototype and tested its feasibility (i.e. completed Phase-I-type R&D) to move directly into a Phase-II-type R&D that tests the functional viability of the prototype according to scientific methods and potential for commercial development The Direct-to-Phase-II SBIR mechanism eliminates the need for the SBCs to propose additional small feasibility studies, if the technology is ready for the Phase II stage of development. The Direct-to-Phase II authority is not available to the STTR program and not available for the CDC, FDA, and ACF SBIR progams.

Learn more here: http://grants.nih.gov/grants/guide/pa-files/PAR-14-088.html

Note from Author: This educational manual will assist you with the grant application process for the NIH SBIR Phase I, NIH SBIR Phase II and the NIH Direct to Phase II.

Chapter 1: Beginning the Grant Application Process

While true for any worthwhile task under consideration, having a solid plan of approach for writing an SBIR grant goes a long way towards managing the process and optimizing the likelihood for a successful outcome. Breaking the process down into distinct steps and having well defined starting and stopping points will help ensure process completion while reducing the chance of becoming overwhelmed. First and foremost, come up with a solid description of the idea for the research project. Development of this description is seldom easy, nor is it usually straightforward. A refined description of the idea becomes the foundation for further development into a focused and strong project. Mapping out the strategy for your writing should include:

- Making certain that the SBIR program is the appropriate funding mechanism for your idea.
- Leveraging your passion and scientific strengths for the project while making sure that the project addresses the mission and priorities of the agency
- Enlisting the help of colleagues who have depth and breadth of experience in competing for SBIR grants and who understand your project goals so they can provide critical feedback

Putting together a schedule for your writing will help to keep you on track so that you can monitor your progress and to make sure that important dates and submission deadlines are not missed. Developing this schedule with your colleagues who have agreed to help will go a long way towards ensuring that the proposal receives the critical attention it deserves.

There are fundamental concepts which every SBIR application must include to be considered for review; project title and how the hypothesis or feasibility study is conveyed can impact the chances of the grant being awarded. The remaining sections of this manual will further detail the steps in this process.

Before Writing Your Application

Ideally, a small business would first identify an unmet public health need and then spend time and effort developing a product or service technology that would address this unmet need. As a small business, you will need a clear vision of the product you will make, or the service you will provide with your technology, well in advance of writing a grant application. Product development and service pathways both require market research and strategic planning; it is probably a poor idea to let SBIR Funding Opportunity Announcements (FOA) dictate what you make or what problem you try to solve by developing new technology. For your product or technology, you will need to fully understand its market advantages and the milestones which must be met to achieve commercialization, as well as the time and costs to reach each milestone. Finally, you must also develop your exit strategy along the development pathway.

SBIR Program Participating Agencies

Listed below are the current Federal agencies that participate in the SBIR program:

- Department of Agriculture
- Department of Commerce National Institute of Standards and Technology
- Department of Commerce National Oceanic and Atmospheric
 <u>Administration</u>
- Department of Defense
- Department of Education
- Department of Energy
- Department of Health and Human Services
- Department of Homeland Security
- Department of Transportation
- <u>Environmental Protection Agency</u>
- National Aeronautics and Space Administration
- <u>National Science Foundation</u>

This manual will use the Department of Health and Human Services (DHHS) agency to illustrate the steps of the application process. While all of these agencies solicit proposals for research and research and development projects on topics relevant to their goals and mission statements, each individual agency controls how it administers its own program. The one common feature for all of these agencies is that every award is made on a competitive basis after proposal review. So, while the focus of this manual will be on SBIR grant applications submitted to the DHHS, the information contained herein can also be applied to applications submitted to other agencies.

Qualifying for an SBIR Grant

There are many excellent proposals that are never considered simply because they failed to meet the requirements set by the NIH and its Institutes, Centers and Offices. Make certain that your proposal address the mission statement of the NIH, which states:

"NIH's mission is to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce the burdens of illness and disability."

The goals of the agency are:

- to foster fundamental creative discoveries, innovative research strategies, and
- their applications as a basis for ultimately protecting and improving health;
- to develop, maintain, and renew scientific human and physical resources that will ensure the Nation's capability to prevent disease;
- to 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
- to 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; and
- 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.

What this means:

The agency supports a wide range of biomedical research areas that have the potential to improve human health, contribute towards disease prevention, and improve treatment outcomes. It achieves this goal by:

- Fostering fundamental creative discoveries, innovative research strategies and their applications as a basis for ultimately protecting and improving health
- Facilitating the development, maintenance, and review of scientific human and physical resources that will ensure the nation's capability to prevent disease
- Expanding the knowledge base in medical and associated sciences to enhance the nation's economic well-being and ensure a continued high return on the public investment in research; and
- Exemplifies and promotes the highest level of scientific integrity, public accountability and social responsibility in the conduct of science

The agency conducts and supports research addressing the:

- Causes, diagnosis, prevention and cure of human diseases
- Processes of human growth and development
- Biological effects of environmental contaminants
- Understanding of mental, addictive and physical disorders
- Programs for the collection, dissemination and exchange of information in medicine and health, including development and support of medical libraries and the training of medical librarians and other health information specialists.

After carefully reviewing these criteria, make sure there is a good match with your proposed research and development idea. If you decide that there is not a good match, you may want to consider approaching another organization for support. Be advised, however, that for commercial businesses, the SBIR program is one of the few federal grant programs which support research and development; alternative granting organizations for companies is extremely limited.

If there is a good match with your idea and the NIH mission, then moving on to determine that your idea is consistent with the mission and goals of the SBIR program is next in order.

SBIR Program Mission and Goals

If you can answer 'yes' to these following questions, you are well on your way towards being aligned with the mission and goals of the SBIR Program:

- 1. Are you as an individual, or are you employed by, a small business?
- 2. Are you on the lookout for research and development (R&D) potentials?
- 3. Would receipt of funding to address scientific and technological areas identified by federal agencies assist in the commercial growth of your business?

The mission statement and program goals are as follows:

"The mission of the SBIR program is to support scientific excellence and technological innovation through the investment of Federal research funds in critical American priorities to build a strong national economy."

The program's goals are four-fold:

- Stimulate technological innovation
- Meet Federal research and development needs.
- Foster and encourage participation in innovation and entrepreneurship by socially and economically disadvantaged persons.
- Increase private-sector commercialization of innovations derived from Federal research and development funding.



For commercial businesses, the SBIR program is one of the few federal grant programs which support research and development; alternative granting organizations for companies is extremely limited.

What this means:

The objectives of the SBIR program are to:

- Leverage the resources and expertise residing in small businesses to stimulate technological innovation
- Enlist the efforts of small business to meet Federal research and research and development needs
- Socially and economically disadvantaged small business and women-owned businesses are especially encouraged to apply
- Increase commercialization of more research and research and development efforts while increasing small business participation in Federal research and research and development activities

If there is a good match with your idea and the SBIR program mission, then the next step is to determine your company's SBIR eligibility.

SBIR Program Eligibility

"To receive an SBIR or STTR award, the awardee must qualify as a Small Business Concern (SBC) as defined by SBA regulations at 13 C.F.R. §§ 701-705. The eligibility requirements for the SBIR/STTR programs are unique and do not correspond to those of other small business programs.

A Small Business Concern (SBC) must satisfy the following conditions on the date of award for both Phase I and Phase II funding agreements:

- is organized for profit, with a place of business located in the United States, which operates primarily within the United States or which makes a significant contribution to the United States economy through payment of taxes or use of American products, materials or labor;
- 2. is in the legal form of an individual proprietorship, partnership, limited liability company, corporation, joint venture, association, trust or cooperative, except that if the concern is a joint venture, each entity to the venture must meet the requirements set forth in paragraph (3) below;

- is more than 50 percent directly owned and controlled by one or more individuals (who are citizens or permanent resident aliens of the United States), other small business concerns (each of which is more than 50% directly owned and controlled by individuals who are citizens or permanent resident aliens of the United States), or any combination of these; and
- 4. has, including its affiliates, not more than 500 employees. (For explanation of affiliate see <u>www.sba.gov/size</u>).

What this means:

Only small companies residing in the United States and meeting all of the following are eligible to apply:

- Must be a for-profit business in the United States
- Majority ownership and control must be by US citizens or permanent residents, or
- Majority ownership and control by another for-profit business, which is also majority owned and controlled by US citizens or permanent residents. A new SBA rule, which became effective on January 28, 2013, now expressly permits participation of Venture Capital -backed small businesses in the SBIR program. A small business may be majority-owned by multiple venture capital operating companies, hedge funds, or private equity firms and still be eligible to receive an award.
- Must be a total of 500 employees or less, which includes associates, partners, and any other members working for the company or in companies affiliated with the company.

You will notice that the agency mentions SBIR and STTR (Small Business Technology Transfer) together. The STTR is a similar program, except that the PI's primary employment is not stipulated, so he/she may be from the small business or the collaborating non-profit research institution. These differences will be covered in more detail later in this chapter.



Only small businesses with less than 500 people are eligible to apply.



Winning a grant is an acknowledgement of the research and development efforts pursued by the business, and provide scientific credibility and validation for the company's program.

The Value of SBIR Funding for Small Companies

SBIR funding is an excellent mechanism to provide seed money for high risk/ high return innovative projects to start or further develop an existing business. The small business retains all rights to intellectual property developed with this funding, and an SBIR award provides recognition and visibility for the company. Winning a grant is also an acknowledgement of the research and development efforts pursued by the business, and provides scientific credibility and validation. Used strategically, the grant can also be leveraged to attract additional capital, assess the market and business opportunities, determine competitive advantage, and balance costs, benefits, and risks.

NIH INSTITUTES, CENTERS, AND OFFICES (ICOS)

The NIH is comprised of 27 semiautonomous ICOs, each having their own defined research and research and development focus. The DHHS releases an annual Funding Opportunity Announcement (FOA) inviting eligible United States small business concerns (SBCs) to submit Small Business Innovation Research (SBIR) grant applications. Unsolicited proposals are not accepted for the SBIR programs, a proposal must respond to a solicitation published by one or more of the participating agencies. SBIR solicitations are specific Requests for Proposals released by the federal agencies participating in the program which may result in the award of Phase I SBIR funding agreements. SBIR Pre-Solicitations that are about to be released by the participating federal agencies.

The activity codes for SBIR grants are R43 for the Phase I, and R44 for the Phase II. Of the 27 ICOs, the following accept SBIR grant applications as per the most recent FOA, PA-13-34, which is a re-issue of PHS 2013-02 Omnibus Solicitation of the NIH, CDC, FDA and ACF for Small Business Innovation Research Grant Applications (Parent SBIR [R43/R44]):



Unsolicited proposals are not accepted for the SBIR program, a proposal must respond to a solicitation published by one or more of the participating agencies.

AWARDING COMPONENT AND FOCUS	PROGRAM CONTACT
National Institute on Aging http://www.nia.nih.gov Biomedical, social and behavioral aspects of the aging process, age-related disease and disability prevention.	Dr. Michael-David A.R.R. Kerns Phone: 301-402-7713 Fax: 301-402-2945 Email: Michael-David.Kerns@nih.gov
National Institute on Alcohol Abuse and Alcoholism http://www.niaaa.nih.gov Research to improve the treatment and preven- tion of alcoholism and alcohol-related problems.	Dr. Gary Murray Phone: 301-443-9940 Fax: 301-594-0673 Email: Gary.Murray@nih.gov
National Institute of Allergy and InfectiousDiseaseshttp://www.niaid.nih.govResearch on understanding, treating, and preventing infectious, immunologic, and allergicdiseases.	Dr. Paula Strickland Phone: 301-435-8563 Fax: 301-480-1993 Email: pstrickland@nih.gov

AWARDING COMPONENT AND FOCUS	PROGRAM CONTACT		
National Institute of Arthritis and Musculoskeletal and Skin Diseases http://www.niams.nih.gov/ Research into the causes, treatment, and preven- tion of arthritis and musculoskeletal and skin diseases; basic and clinical scientist training to carry out this research.	Dr. Xibin Wang Phone: 301-451-3884 Fax: 301-480-1284 Email: wangx1@mail.nih.gov		
National Institute of Biomedical Imaging and Bioengineering http://www.nibib.nih.gov/ Fundamental discoveries, design, development, translation and assessment of technological capabilities in biomedical imaging and bioengi- neering, enabled by relevant areas of informa- tion science, physics, chemistry, mathematics, materials science and computer sciences.	Mr. Todd Merchak Phone: 301-496-8592 Fax: 301-480-1614 Email: merchakt@mail.nih.gov		
National Cancer Institute http://www.nci.nih.gov or http://www.cancer.gov http://sbir.cancer.gov Basic and clinical biomedical research and training; supports research regarding cancer prevention and/or manageability, early-stage identification, innovative treatment development.	Mr. Michael Weingarten Dr. Greg Evans Dr. Andrew Kurtz Phone: 240-276-5300 Fax: 240-276-5236 Email: ncisbir@mail.nih.gov		
<i>Eunice Kennedy Shriver</i> National Institute of Child Health and Human Development http://www.nichd.nih.gov Child-centered research regarding fertility, pregnancy, growth, development and medical rehabilitation.	Louis A. Quatrano, Ph.D. Phone: 301-402-4221 Fax: 301-402-0832 Email: Quatranol@mail.nih.gov		
National Institute on Drug Abuse http://www.nida.nih.gov Research across several disciplines to improvedrug abuse and addiction prevention, treatmentand policy.	Elena Koustova, Ph.D., MBA Phone: 301-496-8768 Email: koustovae@nida.nih.gov		
National Institute on Deafness and OtherCommunication Disordershttp://www.nidcd.nih.govBiomedical research and research training onnormal mechanisms, diseases and disorders ofhearing, balance, smell, taste, voice, speech andlanguage.	Dr. Roger L. Miller Phone: 301-402-3458 Fax: 301-402-6251 Email: Roger.Miller@nih.gov		

AWARDING COMPONENT AND FOCUS	PROGRAM CONTACT		
National Institute of Dental and Craniofacial Researchhttp://www.nidcr.nih.govResearch to understand, treat, and prevent infectious and inherited craniofacial-oral-dental diseases and disorders.	Dr. R. Dwayne Lunsford Phone: 301-594-2421 Fax: 301-480-8319 Email: lunsfordr@mail.nih.gov		
National Institute of Diabetes and Digestive and Kidney Diseases http://www.niddk.nih.gov Supports basic and applied research regarding diabetes, endocrinology and metabolic diseases; digestive diseases and nutrition; kidney, urologic and hematologic diseases.	Ms. Christine Densmore Phone: 301-402-8714 Fax: 301-480-8300 Email: densmorec@niddk.nih.gov		
National Institute of Environmental HealthSciences http://www.niehs.nih.gov Define how environmental exposures, geneticsusceptibility and age interact to affect health.	Dr. Daniel T. Shaughnessy Phone: 919-541-2506 Fax: 919-541-4606 Email: shaughn1@niehs.nih.gov		
National Eye Institute http://www.nei.nih.gov Research to prevent and treat eye diseases, vision disorders, sight-saving treatments, visual impairment and blindness reduction.	Dr. Jerome Wujek Phone: 301-451-2020 Fax: 301-496-2297 Email: wujekjer@nei.nih.gov		
National Institute of General Medical Sciences http://www.nigms.nih.gov/ Basic biomedical research not targeted to spe- cific diseases. Includes studies on genes, proteins and cells, cell-cell communication, energy usage, response to pharmaceuticals, research training programs, encouragement of underrepresented minorities to pursue biomedical research careers.	Dr. Scott Somers Phone: 301-594-3827 Fax: 301-480-2802 Email: somerss@nigms.nih.gov		
National Heart, Lung, and Blood Institute http://www.nhlbi.nih.gov Focuses on treating diseases of the heart, blood vessels, lungs and blood; blood resources; and sleep disorders.	Kurt Marek, Ph.D. Phone: 301-443-8778 Fax: 301-480-0422 Email: Kurt.Marek@nih.gov		
<u>http://www.genome.gov</u> Advancing health through genome research.	Phone: 301-496-7531 Fax: 301-480-2770 Email: Bettie graham@nih.gov		

AWARDING COMPONENT AND FOCUS	PROGRAM CONTACT	
National Institute of Mental Health http://www.nimh.nih.gov Understanding, treating and preventing mental illnesses through basic research on the brain and behavior, and through clinical, epidemiological and services research.	Dr. Margaret C. Grabb Phone: 301-443-3563 Fax: 301-443-1731 Email: mgrabb@mail.nih.gov	
National Institute on Minority Health and Health Disparities <u>http://www.nimhd.nih.gov/</u> Understanding the causes of health disparities, developing effective interventions to eliminate these disparities, strengthen research capacity in institutions with significant numbers of racial and ethnic minority group students, research on health disparities within several disease areas including cancer, cardiovascular diseases, stroke, diabetes, nutrition, obesity and maternal and infant health.	Mr. Vincent A. Thomas, Jr., MSW, MPA Phone: 301-402-2516 Fax: 301-480-4049 Email: thomasvi@mail.nih.gov	
National Institute of Neurological Disorders and Stroke http://www.ninds.nih.gov Basic and clinical research on the normal and diseased nervous system, investigator training in basic and clinical neurosciences, and under- standing, diagnosis, treatment and prevention of neurological disorders.	Ms. Stephanie Fertig Phone: 301-496-1779 Fax: 301-402-1501 Email: fertigs@ninds.nih.gov	
National Institute of Nursing Research <u>http://www.ninr.nih.gov/</u> Clinical and basic research to establish a scien- tific basis for individual patient care, including patient management during illness and recovery; risk reduction for disease and disability; promot- ing healthy lifestyles and quality of life for those with chronic illness; and caring for those at the end of life. This research may also include fami- lies within a community context, and may focus on the special needs of at-risk and underserved populations, emphasizing health disparities.	Dr. Paul A. Cotton Phone: 301-402-6423 Fax: 301-480-8260 Email: Paul.Cotton@nih.gov	

AWARDING COMPONENT AND FOCUS	PROGRAM CONTACT		
National Center for Advancing Translational	Lili M. Portilla, MPA		
Sciences	Phone: 301-402-0304		
http://www.ncats.nih.gov	Fax: 301-480-3661		
Using science to create powerful new tools and	Email: Portilll@mail.nih.gov		
technologies that can be adopted widely by			
translational researchers in all sectors.			
National Center for Complementary and	Dr. Craig Hopp		
Alternative Medicine	Phone: 301-496-5825		
http://www.nccam.nih.gov/	Fax: 301-480-1587		
Explores complementary and alternative medi-	Email: hoppdc@mail.nih.gov		
cine (CAM) practices in the context of rigorous			
science and trains CAM researchers.			
National Library of Medicine	Dr. Jane Ye		
http://www.nlm.nih.gov	Phone: 301-594-4882		
Research in biomedical communications, train-	Fax: 301-402-2952		
ing, medical library resources, and biomedical	Email: yej@mail.nih.gov		
informatics and communications research.			
Division of Program Coordination, Planning,	Dr. Miguel Contreras		
and Strategic Initiatives, Office of Research	Phone: 301-594-9410		
Infrastructure Programs	Fax: 301-480-3819		
http://dpcpsi.nih.gov/ORIP/index.aspx	Email: contre1@mail.nih.gov		
Provides grants for comparative medicine and			
for K-12 educational resources.			
Administration for Children and Families	Anne F. Bergan		
http://www.acf.hhs.gov	Phone: 202-260-8515		
Promotes the economic and social well-being of	Fax: 202-205-3598		
families, children, individuals and communities.	Email: abergan@acf.hhs.gov		

How might your particular research or research and development idea fit into an area of interest for one of these ICOs? The first place to look is on the <u>nih.gov</u> website and search for the current Omnibus Solicitation of the NIH, CDC, FDA and ACF for Small Business Innovation Research Grant Applications (Parent SBIR [R43/R44]) document. This document is a wealth of information regarding what the specific ICOs, and their respective divisions, are looking for. To illustrate, the Division of Aging Biology (DAB), under the National Institute on Aging (NIA), sponsors research on the molecular, cellular, genetic, and physiological causes and consequences of aging processes.



TIP:

Look on the <u>nih.gov</u> website and search for the current Omnibus Solicitation of the NIH, CDC, FDA and ACF for Small Business Innovation Research Grant Applications (Parent SBIR [R43/ R44]) to see where your research and development idea may best fit.



Remember that your proposal could fit with more than one ICO, so take advantage of contacting program officers at other institutes for guidance. Of particular interest is molecular probe development for studying cellular senescence and longevity in cultured cells and in animals. These probes include antibodies, unique DNA and RNA sequences, and expression vectors. Another area of specific interest is development and validation of interventions which can enhance longevity or slow the aging process, once again in cultured cells and animal models, but also in humans. If your idea is to commercially develop a reporter assay for cells about to go into senescence, using an RNA intron sequence, this may be the place for your proposal. On the other hand, if you are developing an intervention to combat the aging effects of an environmental toxin, the National Institute of Environmental Health Sciences (NIEHS) may be a better audience for your application.

One of the better tactics for selecting which ICO(s) might be the best fit is to contact program officers at specific institutions and have a discussion with them about your idea. All institutes have a link to contacts on their website. To help narrow down your choices, take a look at the types of SBIR awards that have been made under the various ICO's. This may be accomplished by accessing the NIH RePorter website (http://projectreporter.nih.gov/reporter.cfm) and choosing from the Agency/Institute/Center dropdown menu. To limit the search to SBIR awards, check the SBIR/STTR box found in the Activity Code dropdown menu. Is there one that is somehow like yours - similar topic area, question being addressed, model system, technology? This can help you better target your proposal. Remember that program officers are at least as busy as you are, so to get the most out of this discussion, perhaps you can schedule a phone call well in advance and provide a short written layman's synopsis (1 page or less) for them to review beforehand. That way, the focal point of the discussion can be on funding ideas rather than on fine technical details. Often you can gain some insight into their level of enthusiasm for your project and how it may fit into any initiatives under consideration. Take any offered advice seriously, as the program officer can be your champion during the submission and review process, and all proposals need a champion to be best positioned for funding. Also remember that your proposal could fit with more than one ICO, so take advantage of contacting program officers at other institutes for guidance.

Another approach to see where your idea best fits is to take a look at past SBIR topic solicitations. If you wait until the current solicitation is posted to draft a proposal, and then go ahead and make contact with the sponsor, you will be off to a very late start with regard to submission deadlines. Seek topics that align well with your research capabilities and take note of the sponsoring agency and the program officer for follow up. SBIR grants are often sponsored by the same smaller group within a much larger agency, so there is a very good chance that past program officers will be sponsoring additional research and research and development efforts.

There are study sections dedicated to reviewing SBIR and STTR applications. They can be found at <u>http://public.csr.nih.gov/StudySections/</u> <u>SmallBusinessTechnologyTransfer/Pages/default.aspx</u>. These study sections have more representation from industry than standard study sections, but the majority of the reviewers are still academicians.

How to Identify SBIR Funding Priorities

Just as the funding goals for each NIH institute, center, and office changes over time, so do the goals of the SBA. These changes are in direct response to advances in science and emerging new technologies, and will invariably be reflected in SBIR funding priorities. These changes can provide new grant opportunities for you. You may want to consider subscribing to a weekly e-mail with new NIH Guide postings (http://grants.nih.gov/grants/guide/listserv.htm) so that you are continually up-to-date.

Another efficient way to identify new and existing funding opportunities is to regularly visit the NIH website. There is a 'Grants & Funding' tab, which will take you to a funding search box which has a 'Funding Opportunities & Notices'. This link will allow you to search the NIH Guide for Grants and Contracts for active Request for Applications (RFAs), Request for Proposals (RFPs), Program Announcements (PAs), and Notices. New funding-related announcements and Requests for Information (RFIs), in which the agency requests input from the scientific community regarding a specific question or general topic are also readily available to potential applicants at each institute's website. These pages are updated as new notices are announced, and the NIH encourages you to visit these pages often to view new opportunities. You may also sign up to receive email updates from the institutes SBIR & STTR Program announcing new notices and funding opportunities. The NIH describes these funding mechanisms accordingly:

Request for Application (RFA)

An RFA is a formal statement that solicits grant or cooperative agreement applications in a well-defined scientific area to accomplish specific program objectives. An RFA indicates the estimated amount of funds set aside for the competition, the estimated number of awards to be made, whether cost sharing is required, and the application submission date(s). For cooperative agreements, the RFA will describe the responsibilities and obligations of NIH and awardees as well as joint responsibilities and obligations. Applications submitted in response to an RFA are usually reviewed by a Scientific Review Group (SRG) specially convened by the awarding component that issued the RFA.

Request for Proposals (RFP)

Announces that NIH would like to award a contract to meet a specific need, such as the development of an animal model. RFPs have a single application receipt date and are published in the NIH Guide for Grants and Contracts.

Program Announcement (PA)

A PA is a formal statement about a new or ongoing extramural activity or program. It may serve as a reminder of continuing interest in a research area, describe modification in an activity or program, and/or invite applications for grant support. Most applications in response to PAs may be submitted to a standing submission date and are reviewed with all other applications received at that time using standard peer review processes. NIH may also make funds available through PARs (PAs with special receipt, referral, and/or review considerations) and PASs (PAs with set-aside funds). PAs may be used for any support mechanism other than construction awards. Unless otherwise specified in the PA, new applications (and associated renewal and revision applications) submitted in response to PAs are treated as investigatorinitiated. PAs also are used to annually solicit applications for the SBIR and STTR programs. Those applications must be received by the dates specified in the PA.

Notice (NOT)

A Notice (Guide Notice) is an official NIH announcement relating to a change in policy, procedure, form, or system. Notices are posted on the NIH website and users can be notified via a variety of NIH listservs. You can search for notices and funding opportunities at the NIH Guide.

What this means:

A **Request for Applications (RFA)** is an invitation to submit grant proposals focused on defined, high-priority, and high-opportunity areas of science relevant to the agency mission. Often these requests are designed to address unmet needs that have either pre-existed in a particular field, or have just recently been identified. RFAs often require a letter of intent to be submitted prior to the submission deadline for the full application. The intent by the agency here is to gauge the response, so that they will be prepared for the number of applications needing review. They can also assess their budget to see if it is in alignment with the scientific community's view of the cost to address the subject area. If the RFA requires a pre-proposal submission, the information you provide may be used to determine if your idea is in alignment with the intent of the request. The agency may use this pre-proposal as the first cut, and notify the applicants as to whether they should or should not submit a full proposal. Such requests may add review requirements (often topical) or adjust eligibility criteria, so as to elicit proposals that aim to accomplish the specific goals of the announcement.

Depending on the RFA, there can be single or multiple submission dates, which generally do not fall on the standing SBIR submission dates on the 5th of April,

TIP:

According to the National Institutes of Health, a cooperative agreement includes characteristics of a research grant and a contract job. August, and December of each year. Cooperative agreements generally involve substantial involvement by Federal programmatic staff. The intent here is to assist the investigators during their conducting of the work described in the award. Thus, a cooperative agreement is not a true grant, although the investigators do receive funding support for their research. According to the National Institutes of Health, a cooperative agreement includes characteristics of a research grant and a contract job. With a federal contract, federal managers take a larger role in administrating the contract and directing the investigators.

Request for Proposals (RFP) are focused on awarding a contract to have specific and defined work performed. Just as with a cooperative agreement, which contains a federal contract-like component, federal managers take a more direct and visible role in managing the contract and directing the scientists.

Program Announcements (PA) describe regular, established agency funding programs, using standard criteria for eligibility, review, and regular submission deadlines. The SBIR and STTR programs are prime examples of a PA.

A Notice (NOT) can alert you to changes in an application date for a particular funding opportunity announcement. This mechanism is also used by the NIH to established a list of Frequently Asked Questions (FAQs) and answers for a particular announcement, to announce additional research objectives and funding, and clarification of applicant eligibility, just to name a few. So, it is vital to you and your research and development program that you remain up-to-date with the current programs in the NIH ICO's that most interest you.

Your Company Must Be Qualified to Receive SBIR Awards

Businesses applying to the SBIR program must self-certify at the time an award is made that their company meets the definition of an SBC for the program and is not otherwise ineligible. The primary place of employment for the proposed project's principal investigator must be the small business, and this small business is the prime contractor or grantee. The research space occupied by the business must be available to, and be under the control of, the business for the conduct of its portion of the proposed project. The business must also be federally registered and have an EIN/TIN number. Companies should make certain that they are compliant with the eligibility requirements prior to formally certifying as an SBC. One question that often comes up is whether the company needs to be founded before a proposal can be submitted. While the answer to this question is 'no', the business does need to be established to fulfill an eligibility requirement to receive an award. If your company is not yet founded, to avoid potential complications, a discussion with the procuring agency's contracts or grants officer prior to grant submission may be in order.

The Company Registry is a new element of the SBIR data system and application process that is now in place. All applicants to the SBIR programs must register on the Company Registry. Once your company has registered, an SBIR identification number for that company will be issued. You must register prior to submitting an application to any SBIR agency solicitation since you will be providing a copy of this registration to the agency.

Qualifying as a Principal Investigator (PI) on an SBIR Award

The PI is the person who takes direct responsibility for the scientific and technical direction of the project, completion of the project and reporting to the funding agency. The person in this role is not required to have US citizenship, but the PI must legally reside in the United States and must be available to make sure that the research proposed for the duration of the project is performed. There is no requirement that a PI spend a set or minimum amount of time and effort on a single



It is to your advantage to have the company founded before you apply for an SBIR award.



The PI must be "primarily employed" by the small business during the conduct of the SBIR project, which essentially means that the PI cannot work full time for any other employer. SBIR project. Nor is there a requirement that the PI have an advanced degree such as a Ph.D. or an M.D. What is required of the PI is that they be "primarily employed" by the small business during the conduct of the SBIR project, which essentially means that the PI cannot work full time for any other employer. The PI must also be able to demonstrate that he/she possess the expertise to oversee the project both scientifically and technically.

Planning

Writing a SBIR proposal is much like presenting a business plan to a bank for approval of a loan. Unlike a loan, the difference here is that if you are awarded grant funding, you do not have to pay the money back. It needs to be appreciated that the granting process takes a considerable amount of time from start to completion. A minimum of 2 months is the amount of time that the more successful SBIR award winners spend on their applications. If your research or research and development idea involves animal work or human subjects, add another 2-4 months of time to get the application ready for submission. This extra time will be needed to get the proper protocols and approvals in place. In the best situation, your application fares well during the review process and is awarded funding; it will still take another 3 months or more for you to receive the money. In some cases your proposal may be approved for funding, but due to budget constraints, it is not awarded. With success rates for Phase I SBIR applications at around 15%, most applicants must revise and resubmit their proposals. This translates to an additional 9-12 months, or possibly more, before you may have funding to work on your idea. With SBIR submission dates falling every 4 months during the calendar year, having a game plan for your application is crucial to minimize the time between submission and award.

Determining Your Strategy

SBIR awards are ideal mechanisms to support development of new technologies or to advance existing ones for your business. The length of time for a Phase I award cannot exceed 1 year, and for a Phase II award it is 2 years. Total funding support (direct costs, indirect costs, fees) normally may not exceed \$150,000 for Phase I awards and \$1,000,000 for Phase II awards. As such, this program is clearly not intended to support large-scale research and development efforts that require numerous personnel or significant budgets for equipment or consumables. When assembling your proposal, keep in mind how this project can fit into future and longer-term research and development efforts at your small business. Not only will this help to keep you focused on the main ideas of the current proposal, but once this grant is awarded, you need to be considering what will go into a successful Phase II.

Making Sure that the SBIR Mechanism is Right for You

To be a good match for the SBIR program, make sure that your idea is a novel and innovative technical advance that will likely lead to the development of an enabling technology and advance the state of the art. Also keep in mind the commercialization aspect of the program, so ask yourself if your project will create a business opportunity or fill an unmet need.

Once you have identified the appropriate ICO for your idea, the NIH has other funding mechanisms in addition to the SBIR program for which small businesses are also eligible to apply. There is no prerequisite that a company have prior or current SBIR funding to apply. Here is a summary of the different mechanisms:

Award Mechanism	R01	R03	R21	STTR
Title	Research Project Grant	NIH Small Grant Program	NIH Exploratory / Development Grant Award	Small Business Technology Transfer grant
Scope and Purpose	Supports project performed by the named investiga- tor in an area rep- resenting their specific interests and competencies	Supports: • Pilot or feasi- bility studies • Secondary analysis of exist- ing data • Small, self- contained re- search projects • Development of research methodology • Development of new research technology	Supports: • New research projects early in development • May involve considerable risk • Development of novel tech- niques, agents, methodologies, model, or appli- cations • Breaks new ground or ex- tends previous discoveries in new directions or for new ap- plications	Stimulate techno- logical innovation Foster technology transfer through cooperative R&D between small businesses and research institu- tions Increase private sector commer- cialization of in- novations derived from federal R&D
Award Length (Maximum)	5 years	2 years	2 years	1 year for Phase I 2 years for Phase II
Allowable direct costs (Maximum)	\$500,000/yr unless permis- sion received by agency to exceed this amount	\$50,000/yr	\$275,000 for entire period	\$100, 000 for Phase I \$750,000 for Phase II
Renewability/ Restrictions	Renewable; Competing con- tinuation (Type 2) applications accepted	Non-renewable; No-cost exten- sion for 1 year may be allowed	Non-renewable	Non-renewable, only Phase I awardees are allowed to apply for a Phase II

It needs to be pointed out that while small business are <u>eligible</u> to apply for R01, R03, and R21 grants, these three funding mechanisms are the primary sources of funding to academicians to support their laboratory research efforts. Due most certainly to the number of applying academicians far exceeding the number of small business applicants, the success rate for small businesses is exceptionally low for these mechanisms. This is probably why small companies do not generally make the effort to apply for these types of awards.

In contrast, the STTR program supports opportunities for small businesses and nonprofit research institutions, such as colleges and universities, to work together on joint ventures.

STTR differs from SBIR in three important aspects:

- The SBC and its partnering institution are required to establish an intellectual property agreement detailing the allocation of intellectual property rights and rights to carry out follow-on research, development or commercialization activities.
- 2. STTR requires that the SBC perform at least 40% of the R&D and the single partnering research institution to perform at least 30% of the R&D.
- 3. Unlike the SBIR program, STTR does not require the Principal Investigator to be primarily employed by the SBC.

What this means:

- Intellectual property (Patents), or at least patent filings, are 'have to haves' for many small business concerns (SBC) which are trying to generate value. Make sure that representatives from both the business and the college or university have a discussion on who has rights to any intellectual property developed during the course of the work performed. It is best to have this discussion prior to the start of any laboratory work the project.
- 2. Most of the research and development work must be accomplished by the small business.
- 3. The Principal Investigator can be primarily employed by the academic partner.



Make sure that your idea is a novel and innovative technical advance that will likely lead to development of an enabling technology and advance the state of the art.



TIP:

Many more SBIR awards can be made due to a larger amount of set-aside monies compared to STTR awards. The STTR program, like the SBIR program, is also a practical one for commercial companies as this program also specifically requires small business involvement. The STTR program also has set-aside monies, amounting to 0.4% (for FY 2014) for federal agencies with extramural research and development budgets over \$1 billion. Contrast this with the current 2.8% for the SBIR program, and it should be clear that many more SBIR awards can be made than STTR awards. Nonetheless, should you decide that the STTR program may be a better fit for your proposal, the information contained in this SBIR manual can also be used when applying to the STTR program.

Get the Buy-in from Your Small Company

Unless you are the owner or sole proprietor of a small company, then you are an employee who more than likely has a management team that will have to support your applying to the SBIR program. Here are several questions to consider from the management side of the small business:

- Are the projects in mind a good match with the research, development, and business strategies of the company?
- Does the timing of the funding provided by the SBIR program fit with the company timeline for product research and development?
- Does the company have the capabilities, in terms of a credible PI with experience and expertise, along with the facilities and equipment, to complete the proposed work?
- Are the finances of the SBIR award adequate to complete the project, or will the budget need to be supplemented with company funds? If yes, are these funds available?
- Is the commercial potential of this technology a product or a service?
- Is there a strategy, and a clear pathway, to commercialization?
- Are there issued patents around the technology this company wishes to develop? If so, who holds them? Is there freedom to operate?
- Does this small business need to file patents prior to grant submission so that intellectual property rights will not be jeopardized?

Answers to these questions are a must before doing any actual writing on the grant application.

Deciding on Your Project

Here are some recommendations to aid in your decision making for which proposal idea to submit as an application, with SBIR-specific requirements in mind.

- Play to your research and development strengths. The project needs to be within your area of expertise. Direct knowledge regarding the science and the methodology to accomplish the specific aims in the application are crucial. Any gaps in personal experience can be filled with consultants. Reviewers will be looking to see that your application supports your expertise in the proposed area of investigation.
- **Perform a gap-analysis for your field.** Take a look at your field as it is today and then think about where it can go. Be well versed in the current literature so you understand the challenges while avoiding what has already been undertaken. It is better to not become involved in crowded areas, as distinguishing yourself from others will be much more difficult. Discuss your ideas with trusted colleagues and collaborators.
- Your goal should be to make a big impact on a focused area. Field advancement is something that grant reviewers will be trying to determine from your application, and a focused effort is more likely to be judged feasible. Taken together, these two factors are often the determinants of whether or not your proposal is awarded funding. Keep these questions in mind when picking your research topic:
 - How will this research and development project effect a change?
 For example, will the newly developed technology facilitate new areas of discovery, or perhaps enable new approaches to solve existing problems?
 - How excited will the reviewers be when they finish reading your proposal? While you feel strongly that your research area is of high priority, will the reviewers feel the same way? Have trusted colleagues and collaborators read through it and get their opinions.
 - How will your idea fare against the review criteria for SBIR proposals? We will examine these criteria in later chapters of this manual.



It is better to not become involved in crowded areas, as distinguishing yourself from others will be much more difficult. Discuss your ideas with trusted colleagues and collaborators.



Field advancement is something that grant reviewers will be trying to determine from your application, and a focused effort is more likely to be judged feasible. Taken together, these two factors are often the determinants of whether or not your proposal is awarded funding.

- Your project needs to be achievable. Try composing a sentence or two that demonstrates how your project is keenly-focused, impacts the focused area, and is hypothesis driven or testing feasibility. By limiting yourself to this level of description brevity, this should help you decide if you can truly accomplish your research and development goals within the allotted award period using the resources that you request. Also make sure that your science and technology relates to human health, disease prevention, patient treatment outcomes priorities of the NIH as well as stimulating technological innovation and increasing private-sector commercialization of innovations goals of the SBIR program.
 - Ask for an evaluation of your proposal's merits. Approach the program officer and ask if they would be willing to give you their opinion on your research and development idea. While the officer cannot tell you how to guarantee funding, they will often provide sound advice which you should take advantage of. Also pay close attention to their choice of words during the conversation. For example, while discussing the relevance of your project to the mission of the agency, if the program officer describes your idea as reaching the minimal requirements for submission and funding consideration, you are best advised to figure a way to make your project more appealing. Also see if you can get their insight on the composition of the review panel that will evaluate your proposal; will it be widely focused on multiple areas or narrow focused on just a few? Will there be any experts in your subject area or not? Make sure to enlist any experts and colleagues that you can find to get their input concerning your proposed research's impact. Based on their comments, somehow rate the impact of your topic. If it scores poorly it is best to refine your idea. If is scores very poorly, you may want to consider picking another topic.



Approach the program officer and ask if they would be willing to give you their opinion on your research and development idea and pay close attention to their choice of words.

Put Yourself in the Reviewer's Place – How Does Your Proposed Topic Look

Take a good, hard, objective look at your proposal as a reviewer would, and ask those you have asked to review and evaluate your topic to do the same. Identify the Study Sections that would likely review your area of science and prepare a list of probable reviewers. Familiarize yourself with their work and keep them in mind as you assemble and review your application. This will give you some insight as to how they might view your proposal; anticipate their criticism so you can address it and build their enthusiasm. While those you identify may not turn out to be your actual reviewers, they will probably have similar expertise to those who are.

After working through these recommendations, you should be in a better position to make a final decision on your research and development topic. The next step is to refine your topic into a focused idea so that assembling your application is more efficient. Define the objectives of the proposed work by generating a clear and testable hypothesis, or feasibility study, in the form of specific aims. These aims can then be used to create an outline and a provisional title.

Defining Your Project

As a general rule, when shaping what your research project will involve, the prevailing wisdom is that the most successful grant proposals are hypothesis driven. While this generally holds true for SBIR proposals also, this program specifically states that Phase I grants provide funding for proof-of-concept or feasibility studies. While hypothesis driven research and development and proof-of-concept or feasibility studies all ask and answer questions, how the questions are framed can make a difference.



Phase I grants provide funding for proof-of-concept or feasibility studies.



STRATEGY:

Be sure that your application makes it clear that you will ask and answer questions, not merely collect information, and that the specific aims of your project directly address the hypothesis.

Hypothesis-driven

Your hypothesis should be specific, readily testable, and above all it needs to be clearly stated. If your reviewers have to infer what your hypothesis is, this may create a question in their mind that perhaps you are not certain of the hypothesis, which could dampen their enthusiasm for the proposal. Be sure that your application makes it clear that you will ask and answer questions, not merely collect information, and that the specific aims of your project directly address the hypothesis. There is always the question of which approach is better; to have a general, all-encompassing hypothesis covering the entire proposal, or a specific hypothesis for each specific aim. Given the 1 year maximum length of the Phase I award period, keeping your research proposal tightly focused with a single hypothesis is probably the more sensible approach. Reviewers of SBIR grants often are most enthusiastic about proposals that have the potential to significantly impact future technological development, and a sound, testable hypothesis can provide that impact.

Be careful not to propose vague statements in the hope that they will pass as a hypothesis. For example, a statement such as "we will test the hypothesis that endothelial cells protect against blood clot formation during mechanical blood circulation" adds little to what questions will be asked and addressed. A better statement would be "we will test the hypothesis that a confluent lining of the patients" own endothelial cells will provide a more anti-thrombogenic and biocompatible surface for mechanical circulatory assist devices."

Feasibility Studies

A feasibility study evaluates a system's potential for success, with the goal of objectively testing its strengths, weaknesses, and limitations. Feasibility studies go beyond hypothesis driven research in that they are often technology or tooldriven investigations. As in hypothesis statements, you want to make sure that the feasibility statement in your grant adequately describes what questions you will be asking and addressing. For example, a statement such as "the objective of this proposal is to test the feasibility of using endothelial colony forming cells in a high-throughput assay to detect environmental toxins" sounds like a fishing expedition where you will be gathering data with no clear end-point analysis. A better statement would be "we will determine the feasibility of endothelial colony forming cells as a platform for high-throughput chemical toxicity testing of bisphenol A, perfluorooctanoic acid and cadmium by quantifying the mechanistic effects of these toxicants on cell viability, proliferation, and differentiation."

Descriptive Title of the Project

Enter a brief descriptive title of the project. This field is required (Part I: Instructions for Preparing and Submitting an Application I-47PHS SF424 (R&R) Adobe Forms Version C Application Guide).

A "new" application must have a different title from any other PHS project submitted for the same application due date with the same PD/PI. A "resubmission" or "renewal" application should 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. NIH and other PHS agencies limit title character length to 200 characters, including the spaces between words and punctuation.

What this means

All study section reviewers will read the application title, so it needs to be informative and convey what you will be doing, how it will be done, and what the expected results will be. The title will give reviewers their first impression of your application. So, to have this first impression be the best that it can be, your title needs to communicate imagination, novelty, and inventiveness. A title that will distinguish your proposal from others and makes the reviewers look forward to reading it may give you that additional advantage on the competition. As the SBIR



Many grant-writing experts suggest that you write your Project Summary/ Abstract last as you construct your application materials.



NIH limits your title to 200 characters, including letters, numbers, spaces and any punctuation.


The title will give reviewers their first impression of your application. So, to have this first impression be the best that it can be, your title needs to communicate imagination, novelty, and inventiveness. program is focused on product commercialization, pointing to this aspect in your title is also advised. At the same time, the NIH grant application limits your title to 200 characters, including letters, numbers, spaces and any punctuation.

While this may be small consolation, your colleagues in other departments of your company also have character limits in their writings, particularly those in advertising and communications. These departments are involved in the selling of your business activities or its products; perhaps they can help you with your title because just like them, you are 'selling' something - your research and development project. Your title will become finalized after you complete your application. Up to this point, it is more of a 'work in progress', as it may be adjusted once you have your specific aims in place.

Some tips in developing a descriptive title are as follows:

- Uniqueness. Review published government databases for titles of existing applications, such as those accessible through NIH RePORTER. (http:// projectreporter.nih.gov/reporter.cfm) After reviewing, see to it that your title choice is not the same or closely similar to another.
- **Be succinct.** Include clear and accurate words that emphasize the suitability of your project for the ICO to which you are submitting the application. Be concise. It should also be apparent why your proposal was sent to the ICO which you chose.
- **Be confident.** The reviewers need to be assured that you know what you are writing about.
- Use key words the agency is familiar with. This will help a great deal with getting your proposal to the most appropriate study section. Even though you can suggest that a specific Study Section review your application, it is the NIH's Center for Scientific Review (CSR) staff that makes the final decision, after performing the initial review of your proposal before assigning it to one of its review panels. Guiding them with title language they are used to seeing will help your cause.

- Plain language should be used. This is not the place to use fancy words.
- Your word choices should be results orientated. Stay away from words that refer to your process or experimental approach to the technology. For example, "Hollow Fiber Catheter for Drug Delivery into the Prostate" concisely conveys two pieces of information: the product and problem it addresses.
- Share your title with peers to get their comments. Get input from peer scientists and individuals outside your field, preferably someone with a degree in English or an editor for proofreading and language use. Colleagues with grant-writing experience can be especially helpful.



The following questions were compiled by Dr. Gregory Milman, NIAID, and taken from a slide contained in a presentation he has made to help businesses successfully compete for SBIR and STTR awards. Keep these in mind when you are developing the title for your proposal:

What is the public health problem?

- How large is the problem?
- What are current solutions and their drawbacks?
- What progress is being made?
- What is your product?

Why is it better than what is available?

- What are the requirements to sell it?
- What are the milestones necessary to bring your product to the point of sales?
- What are the estimated time and cost to reach milestone?
- What is your exit strategy along the development pathway?



The Summary should be a faithful, although condensed, replica of the narrative.

Examples of Actual Phase I SBIR Applications Titles (Product, Problem)

Your title should concisely convey two pieces of information: the product and problem it addresses within the title's character limit. The following were also compiled by Dr. Gregory Milman, NIAID, and taken from a slide contained in a presentation he has made to help businesses successfully compete for SBIR and STTR awards.

- "Development of Antimicrobial Peptides" does not identify a pathogen or public health problem.
- 2. "Antigen Detection Assay for the Diagnosis of Visceral Leishmaniasis" states both the product and problem.
- 3. "Enteric-coated Vector Microparticles for Oral Vaccination" describes technology but not a problem.
- 4. "Coupled Enzyme Reporter Assay for Proteases" does not identify a pathogen or public health problem
- 5. "An Immunoadhesin Therapy for Gastrointestinal Anthrax" identifies a product and a problem
- 6. "Proteolytic Antibodies for Treatment of Psoriasis" identifies a product and a problem
- "A Dynamic Web-Based Geospatial Data Visualization and Distribution System". I do not understand this title, do you?
- "Virus-like Particle (VLP) Vaccine for RSV" identifies a product and a problem.
- "Molecular Screen for Antiviral Agents" describes technology but not a specific disease.
- 10. "Multi-antigen Peptide Assay for the Serodiagnosis of Lyme Disease" identifies a product and a problem
- "Rapid, Low Cost, Point-of-Care Diagnostic Device for Group B Streptococcus" identifies a product and a problem
- 12. "Potential Benefits of Personalized Interferons" does not identify a problem.

Finally, remember that the NIH uses your title — as well as your abstract — to assign your application to a study section and institute for review. The agency also uses it to report your research dollars to Congress. So your title plays a vital role not only in the review process, but also throughout the life of your research grant.

When Should You Apply

Deadlines for SBIR applications have fallen on the same dates for a number of years, and the recent re-issue of PHS 2013-02 Omnibus Solicitation of the NIH, CDC, FDA and ACF for Small Business Innovation Research Grant Applications (Parent SBIR [R43/R44]) maintains these same dates of April 5 (Cycle I), August 5 (Cycle II), and December 5 (Cycle II) for all new, resubmissions, and revisions of Phase I and Phase II SBIR applications. Review and award cycles for these dates are as follows:



Your title and abstract play a vital role not only in the review process, but also throughout the life of your research grant.

Review and Award Cycles				
	Cycle I	Cycle II	Cycle III	
Scientific Merit Review	June - July	October - November	February - March	
Advisory Council Round	August or October*	January	May	
Earliest Project Start Date	September or December*	April	July	

The agency asks that you please note:

"The actual date of the Advisory Council may occur in the month before or after the month listed. For example, some ICs may actually hold the January Advisory Council meeting in February or the October Advisory Council meeting in September.

Awarding components may not always be able to honor the requested start date of an application. Before incurring any pre-award obligations or expenditures applicants should be aware of NIH policy governing pre-award costs prior to receiving a Notice of Award. See the NIH Grants Policy Statement.



There are 3 deadlines each year for SBIR submissions; April 5, August 5, and December 5.



TIP:

The time of proposal submission is irrelevant to an outstanding proposal. So, proceed with submitting your application as soon as you are confident that is the best that it will be. *Advisory Council Round for Cycle I applications may be August or October, and their earliest project start date may be September or December respectively."

It is best to anticipate that changes may sometimes occur with these standing deadline schedules. It is safest to reconfirm these deadlines relevant to your anticipated application submission. At the same time, if your proposal is a response to a special request or funding announcement for a specific research topic, there may be a different deadline, or deadlines, than the standing ones above. This information will be provided in the announcement.

There is always a great deal of speculation among applicants that competition for funding may be greater, or less, for particular deadline dates. For instance, some believe that submitting towards the end of the year when the agencies are 'running out of money' due to all of the earlier awards is not a favorable strategy, unless you have a previous submission that scored near the funding cutoff, and the agency wants to make sure that you get funded because you were 'so close'. However, this has yet to translate into a better success rate. The position that the NIH takes is that proposal quality should be the deciding factor for submission, not any supposed difference in successful award rates. The idea here is that time of submission is irrelevant to an outstanding proposal. So, proceed with submitting your application as soon as you are confident that is the best that it will be.

Outlining the Proposal

Creating a basic outline and crafting a provisional title for the proposal is next on your agenda. The goal here is to end up with a workable framework for your writing plan, and to finalize the ICO to which you will submit your proposal. Ideally, this exercise should be relatively straightforward, assuming that you have been discussing research and development topics with colleagues, keeping up-to-date with the literature, and regularly checking with NIH announcements. At its minimum, the project outline needs to clearly state the specific aims, as a hypothesis and/or a feasibility statement, and the basic approach of how you plan on achieving these aims. One way to move ahead is to think about the Project Summary that you will write as you complete the proposal. While this is covered in more detail later in this manual, the Project Summary:

- is meant to serve as a succinct and accurate description of the proposed work containing the application's broad, long-term objectives and specific aims
- make reference to the health relatedness of the project (i.e., relevance to the mission of the agency)
- describe the research design and methods

The proposal outline should also be the theme of at least one meeting with your colleagues who have offered you their help. The outline should be as polished as you can make it, with attention paid to focus, clarity, feasibility, and impact. It should be a page long at is maximum, and perhaps be a bulleted list.

Make a Writing Schedule

Begin with an assumption that two months is the minimum amount of time it will take to put together a successful proposal. Now it may be possible to do so in less time, if your proposal is not very complex, you have very keen abilities, and your schedule is relatively open. For many, at least one of these parameters is lacking, so it may actually take longer than two months. In fact, some previous applicants may suggest that six months is more likely. Also build in at least one month, to be on the safe side, to send your proposal to peers and colleagues and receive their responses. Allow yourself an additional two weeks to integrate any changes you agree with based on their suggestions, as well as final proofreading of the document before submission.

By this time you should have developed your idea to the point of being able to create a writing schedule so that you can track your progress, stay on task while ideally minimizing your stress, and meet the submission deadline you have chosen. Avoid submitting a proposal that does not quite measure up because you were rushed or just ran out of time to do it right; reviewers look for reasons to reject proposals, and they do not need your help by submitting an application that is weak and laden with errors.



The outline should be as polished as you can make it, with attention paid to focus, clarity, feasibility, and impact. It should be a page long at is maximum, and perhaps be a bulleted list. Then, set up a task list with due dates, based on the major components of the application, which will also be discussed in greater detail in later chapters. As you work through each task, do not attempt perfection on your first go-through; view this phase of the writing as fluid and expect changes. Below is a sample task list:

Task Description	Due Date
Focus research and development topic to attainable goals	
Review PHS 2013-02 Omnibus Solicitation of the NIH, CDC, FDA and ACF for Small Business Innovation Research Grant Applications (Parent SBIR [R43/R44])	
Download an copy of SF424 (R&R) SBIR/STTR Application Guide for NIH and Other PHS Agencies and review	
Develop hypothesis/feasibility study statement	
Decide on a provisional title	
Get feedback for peers and colleagues on hypothesis and title	
Prepare Significance and Innovation statements	
Develop specific aims for the proposal	
Etc.	

Writing the proposal is by far the major task, and once that is finished, the last few items you need to attend to is the assembly of all application components and having the entire package reviewed by trusted colleagues. These colleagues should include someone who is an excellent proofreader in addition to those familiar with the science. After you receive all comments, the application is just about ready. What you have left is to make your final review of the entire package, including any last-minute editing and rewriting to ensure that the sections flow as coherently as possible. Finally, and while you may have questioned whether the proposal would ever make it to this stage, submit the completed application before the deadline.

Conclusion

The time and effort you put into clearly defining your research and development project, deciding on a title that will compel the reviewer to read the application, refining your hypothesis/feasibility statements, and sticking to your writing schedule, is time and effort well spent. Having colleagues critique your work prior to actual submission will mean that your ideas have already been vetted and should be competitive with others under study section review with yours. At this stage, you are in the best position you can possibly be for writing and assembling your application for the SBIR program. These grants require considerable amounts of information, time, and effort; careful planning helps you to stay on task and focused.

Chapter 2: Summarizing Your Project and Your Qualifications to Be PI

As part of the SBIR application package, you will be required to summarize your research topic and your plan for execution. The place for this information is in the Project Summary/Abstract section. This section of your application is arguably one of the most important components because all of the reviewers on the study section will read it as it contains information relating to all five review criteria, which will be covered in detail later on. One of the best approaches to help wrap your head around this section is to picture yourself as a storyteller who will take the reviewers on a journey through your project. Success in getting the reviewers hooked on your story is how you will get them to champion your application. Remember that all compelling stories have a resolution at the end; yours will be how your research and development will advance the field and make future investigations possible, particularly the Phase II portion of this project. Since the abstract will be made public once you receive an award, do not include any proprietary information belonging to the company.

More in-depth than a general biography, the principal investigator's (PI) Biographical Sketch will also be covered in this chapter. This sketch must include a personal statement. With some imagination and creativity, there are ways you can use this statement to increase your chances of successfully being awarded funds. Also included in the biosketch is an accounting of the PI's positions and honors, a listing of peer-reviewed publications or manuscripts in press, and research support.

Rounding out this chapter will be an explanation of how letters of support can strengthen your proposal. Suggestions will also be made on the types of people you should approach to provide a letter, and why it is best if you write the first draft for them.



Since the abstract will be made public once you receive an award, do not include any proprietary information belonging to the company.

Make a Writing Schedule

Taken directly from the SBIR/STTR SF424 (R&R) Adobe Forms Version B Application Guide:

Project Summary/Abstract

The Project Summary must contain a summary of the proposed activity suitable for dissemination to the public. It should be a self-contained description of the project and should contain a statement of objectives and methods to be employed. It should be informative to other persons working in the same or related fields and insofar as possible understandable to a scientifically or technically literate lay reader. This Summary must not include any proprietary/confidential information.

The Project Summary 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). 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. Finally, please make every effort to be succinct. This section must be no longer than 30 lines of text, and follow the required font and margin specifications. An abstract which exceeds this allowable length may be flagged.

What this means:

Make sure you describe:

- The public health problem
- Any concerns about current resolutions to the problem
- How you will approach the problem to get better resolution
- The unmet need your technology, and ultimately your product, will address
- Any collaborators, consultants, and what they can provide to strengthen your application
- The specific aims of the proposal
- How the achievements of the Phase I will justify the Phase II and continued product development

Make sure to present your ideas as the solution to the problem, and be specific about your activities and impacts.

The initial review of your application will take place at the Center for Scientific Research (CSR), and they will most certainly use the Project Summary/Abstract to assign your application to a particular Scientific Review Group (SRG) or study section, as well as to the peer reviewers who will examine it in great detail. Using keywords familiar to the agency will ensure that SRG staff can readily assign your application and the NIH computer systems can retrieve it properly. Many times SRG members who are not the primary reviewers will rely on your summary/ abstract almost entirely to comprehend your proposal during the general meeting during which application fundability is discussed.

With so much riding on this Project Summary/Abstract of your proposal, it may be advised to write this section last, after the rest of the application is competed. The rationale here is that you will attain a more comprehensive appreciation of your proposal if you write it last. If you do decide to write this section before others are completed, treat it as conditional and return to it after the other sections are finished.

In contrast, writing the Project Summary/Abstract earlier will help to focus the main ideas for you during the writing of the other sections. Highlighting key words important for understanding your research and development project in the other sections of the grant will make it easier for you to circle back to the project summary and make sure these words are used in correct context.

Storytelling to Engage the Reviewers

Think of the Project Summary/Abstract as the beginning chapter of your story, which provides a glimpse into what the subsequent prose will contain. The reader will expect the abstract to be a mini-version of your story; make sure the story does not contain important ideas that are left out of the abstract, and vice versa.

In speaking with those PI's who have served on study sections, it is not uncommon for reviewers to make a conclusion about your proposal's merit once



It is not uncommon for reviewers to make a conclusion about your proposal's merit once they read the first page or two of your application. They will read the rest of the application to bolster their conclusion. they read the first page or two of your application. They will read the rest of the application to bolster their conclusion. If that conclusion is a positive one, then they will read the remainder of the application to support this view and you now have someone on your side to champion your cause. If that conclusion is negative, they will still read to bolster their conclusion, but now it is to search for weaknesses.

Project Summary/Abstract Examples

The NIH Research Portfolio Online Reporting Tools project (RePORTER) website (<u>http://projectreporter.nih.gov/reporter.cfm</u>) can be queried for abstracts of awarded Phase I SBIR projects. While the exact text for the project description as published on this site is quoted below, the text has been broken up and sub-headings have been inserted to indicate the relevant sections.

Example #1 from NIDDK

Proposal Title: DEVELOPMENT OF CDK4/6 INHIBITORS AS NOVEL RENAL PROTECTANTS

Significance of the proposed research:

Acute kidney injury (AKI) is common, expensive, and highly morbid. There are currently no therapies for AKI, and prevention and treatment represents a \$6.3 billion market opportunity annually in the U.S. Moreover, patients are developing AKI more frequently and the number of patients that survive severe AKI is growing. Between the years of 1988 and 2002, the number of patients who survived AKI requiring dialysis increased from 2.4 to 19.4 per 100,000 population. Although some patients may recover from AKI, many progress to chronic kidney disease (CKD). The proportion of AKI survivors who progress to the most severe form of CKD, end-stage renal disease, has increased over the last two decades, at an enormous societal cost. It has been estimated that caring for patients with CKD accounted for 19% of the Medicare budget in 2002. Novel therapies are urgently needed for the treatment of both AKI and CKD.

Innovation and unique features of the proposal:

G-Zero Therapeutics (GZ) is ready to meet this urgent need for effective renal protectants by leveraging intellectual property surrounding a novel therapeutic approach utilizing proprietary small molecule CDK4/6 inhibitors to induce pharmacological quiescence (PQ). GZ is developing and commercializing their novel Pharmacological Quiescence (PQ) technology. PQ is based on the observation that many cell types are more sensitive to toxic insult when proliferating as opposed to when non-dividing (i.e. quiescent). Crucially, a few specific cell types can be rendered transiently and reversibly quiescent by treatment with small molecule inhibitors of two cyclin dependent kinases (CDK4/6). Thus, certain cells types can be protected by PQ, without the generalized toxicity (e.g. myelosuppression) of non-specific anti-mitotics. GZ has shown that protective PQ can be induced in CDK4/6-dependent cell types at the time of insult (e.g. cytotoxic chemotherapy), and that these cells can then be released to re- enter the cell cycle and proliferate when the insulting exposure has terminated. The PQ approach has been initially used by GZ to afford protection of hematopoietic stem and progenitor cells (HSPC) within the bone marrow from the toxicity of radiation and chemotherapy.

Specific Aims:

The Phase I portion of this proposal will be accomplished in two significant aims: (1) To evaluate the in vitro efficacy and cellular toxicity of GZ proprietary small molecule CDK4/6 inhibitors as novel renal protectants. (2) To evaluate potential GZ lead candidate's ability to induce PQ in vivo in pharmacodynamic (PD) assays predictive of renal protection efficacy.

Re-emphasis of the proposal's innovation:

This proposal capitalizes on the recent discovery from Dr. Sharpless and Dr. Benjamin Humphreys at Harvard Medical School (a consultant on this proposal), that, like HSPC, renal epithelial cells also depend on the catalytic activity of CDK4/6 for proliferation. GZ's preliminary data show that epithelial cells in the kidney can be rendered quiescent transiently by CDK4/6 inhibitors, and that this affords significant protection from renal insults such as chemotherapy and ischemia, thereby ameliorating AKI.

Example #2 from NIEHS

Proposal Title: A FUNCTIONALIZED NANOPARTICLE-BASED HANDHELD DEVICE FOR RAPID AND SENSITIVE DETEC

Significance of the proposed research:

Organophosphate (OP) pesticides are highly toxic compounds used to control insect populations in a number of agricultural and landscaping applications. The widespread use of these toxic chemicals has generated serious environmental health risks. It is vital to sensitively and accurately bio monitoring of environmental exposure to OP pesticides and assessment of its health risk. However, simple, rapid, and quantitative diagnostic technologies and devices for detecting environmental OP exposure are not available.

Innovation and unique features of the proposal:

This Small Business Innovation Research Project is to develop a handheld bio monitoring device incorporating a functionalized nanoparticle and a lateral flow test strip for simple, rapid, cost-effective, and quantitative detection of environmental exposure to OP using a blood sample. This project takes advantage of phosphorylated cholinesterase (OP-ChE) as a biomarker of OP exposure.

Specific Aims:

In phase I, there are three specific aims: (1) Develop Zr (IV)-functionalized fluorescence nanoparticles (Zr-FFNPs) that bind to OP-ChE. (2) Develop a Zr-FFNP-based new immunoassay for detecting OP-ChE. (3) Adapt the Zr-FFNP-based immunoassay to a lateral flow test strip system for detecting OP-ChE. The research will determine the detection limits, response time, dynamic range, and other key performance metrics of the device using blood samples in vitro dosed with three typical pesticides and prove the feasibility of the handheld bio monitoring device for sensitively detecting OP exposure.

Reference to Proposed Phase II:

Phase II will further develop a specialized hand-held bio monitoring device for detecting exposure to OP. The device will be validated with blood in vitro dosed with a wide range of OP pesticides and blood samples from students in schools near farms and family members of workers who involved in the used of OP pesticides.

Re-emphasis of the proposals innovation:

The portable biomonitoring device developed under this program will provide a point-of-care tool for rapid, sensitive, cost-effective, and real-time detection of environmental exposure to OP pesticides.

Notice that in this example, the project title exceeded the 81 character limit (now increased to 200 characters), and abruptly ends in the middle of the word 'detection'.

Example #3 from NIGM

Proposal Title: OPTIMIZATION OF ISORAFT TECHNOLOGY FOR STEM CELL MARKET

Significance of the proposed research:

Cell Microsystems is a North Carolina-based start-up biotechnology company whose mission is to commercialize a novel, yet affordable, platform for the efficient isolation of viable, single cells or colonies from a mixed population while the cell/colony remains adherent or encapsulated to a solid surface. The company's "IsoRaft" technology is based on a unique cell array recently developed at the University of North Carolina (UNC) at Chapel Hill, and represents an ideal opportunity for the translation of an academic technology to the marketplace through the SBIR program. Cell Microsystems has obtained license from UNC to commercialize the technology for a broad market in academic labs, as well as in the biotechnology and pharmaceutical industries.

Innovation and unique features of the proposal:

The products consist of disposable microarray (the IsoRaft Array) for culturing cells and a simple device for isolating the cell/colony of interest. Prototypes of arrays and devices have been completed and are being tested in a number of academic labs as an Early Adoption Program (EPA) at nearby research institutes.

Specific Aims:

In this Phase I SBIR proposal, we will explore the feasibility of using the IsoRaft technology for stem cell research. Particularly we will focus on design and optimize the IsoRaft Array for stem cells, and develop strategies for cell imaging, identification, tracking and retrieval of targeted stem cells/colonies.

Re-emphasis of the proposals innovation:

Our goal is to expand the use of this technology for stem cell research to the large community in the life science market. The studies in Phase I will deliver a 1st generation commercial device and consumables that provide a flexible and powerful means to perform unique stem cell assay and sorting experiments at significant cost and time reduction.

Take note that all of the successfully awarded examples shown follow the same general formula of significance/innovation/specific aims/re-emphasis of innovation; Example #2 also references the Phase II.

Project Narrative

Taken directly from the SBIR/STTR SF424 (R&R) Adobe Forms Version B Application Guide:

Project Narrative

Provide Project Narrative in accordance with the announcement and/or agencyspecific instructions.

For NIH and other PHS agencies applications, this attachment will reflect the Relevance of the proposed project. Using no more than two or three sentences, describe the relevance of this research to public health. In this section, be succinct and use plain language that can be understood by a general, lay audience.

A separate Research Plan form is required for NIH and other PHS agencies applications. Refer to Section 5.4, Research Plan Form, for separate file uploads and instructions.

What this means:

The Project Narrative should summarize the essence of your project's relevance to public health, so that a non-scientist can understand. The NIH RePORTER online grant award reporting tool often refers to the Project Narrative as the "Public Health Relevance Statement." It is included in the RePORTER tool and therefore will become a part of the public record.

Project Narrative Examples

With all this in mind, use the following examples of Project Narratives taken from successful SBIR Phase I grant applications:

Example #1 from NIEHS

Proposal Title: Novel assays for screening the effects of chemical toxicants on cell differentiation

Proposal Narrative: In this study, we propose to test a novel, robust, and comprehensive platform for toxicological risk assessment utilizing donor-specific pluripotent cells. Such platform would be an invaluable tool for the functional analysis of human genetic diversity and identification of population subgroups most vulnerable to toxicants.

Example #2 from NIDDK

Proposal Title: Commercialization of a Human Myocyte and Adipocyte Co-Culture System

Proposal Narrative: At the completion of this project, a commercially available, fully validated human skeletal myocyte system, skeletal myocyte / adipocyte coculture system, and related assay kits will be offered to researchers. The availability of these systems will provide opportunities for new approaches in the investigation of metabolic disease and a unique methodology to examine the complex interaction between these two cell types.

Example # 3 from NCRR

Proposal Title: Commercialization of Human Omental Mesothelial Cells for Research

Proposal Narrative: At the completion of this project, a commercially available, fully characterized primary human mesothelial cell system and support reagents will be offered to researchers. The accessibility of this currently unavailable system will provide wider opportunity to investigate novel methods to inhibit ovarian tumor attachment, prolong the utility of peritoneal dialysis, and treat peritonitis.

The Biographical Sketch

The NIH Application Guides states, which is reiterated in the SBIR/STTR SF424 (R&R) Adobe Forms Version B Application Guide:

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.

What this means:

The Biographical Sketch, also referred to as the Biosketch, is limited to a maximum of four pages per person, and this information must be contained in the form provided for presenting this information. Your application must include a complete Biosketch for all Senior/ Key Personnel and Other Significant Contributors.

NIH defines Senior/Key Personnel as the Project Director (PD)/Principal Investigator (PI) "and other individuals who contribute to the scientific development or execution of the project in a substantive, measureable way, whether or not salaries or compensation are requested under the grant." Usually, these Senior/Key Personnel have doctoral or other professional degrees, NIH says, adding that you should also include those with master's and baccalaureate degrees if their involvement meets the above definition.

You will also need a Biosketch for any Other Significant Contributors, those who commit to contribute to the project's scientific development or execution, NIH states. They are usually listed as presenting "effort of zero person months" or "as needed" on your application. Consultants likely will be in this category.

The Biosketch is your opportunity to detail your knowledge, skills and ability to carry out and manage the proposed research. Demonstrate that you are the



TIP:

Reviewers scrutinize this section to ensure that you and other investigators and proposed staff have the proper experience with the proposed techniques. individual most qualified to do it. Reviewers scrutinize this section to ensure that you and other investigators and proposed staff have the proper experience with the proposed techniques.

The form for the biosketch is only the first page and provides space for only the key personnel's education. There is no template for the additional three pages to complete the individual's Biographical Sketch. The educational information should begin with baccalaureate or other initial professional education, moving forward to doctorate, postdoctoral training, residency training, etc. as applicable.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2. Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITL	POSITION TITLE		
eRA COMMONS USER NAME (credential, e.g., agency login)				
EDUCATION/TRAINING (Begin with baccalaureate or other initial pro residency training if applicable.)	ofessional education,	such as nursing, incl	lude postdoctoral training and	
INSTITUTION AND LOCATION	DEGREE (if applicable)	MM/YY	FIELD OF STUDY	

Please refer to the application instructions in order to complete sections A, B, C, and D of the Biographical Sketch.

What Should Be Included in Your Biosketch:

The NIH Application Guides states:

Following the educational block, complete sections A, B, C, and D as described below.

A. Personal Statement. Briefly describe why your experience and qualifications make you particularly well-suited for your role (e.g., PD/PI, mentor) in the project that is the subject of the application.

- B. Positions and Honors. List in chronological order previous positions, concluding with your present position. List any honors. Include present membership on any Federal Government public advisory committee.
- C. Selected Peer-reviewed Publication and Patent Citations (in chronological order). NIH encourages applicants to limit the list of selected peer-reviewed publications, manuscripts in press, and patent citations to no more than 15. Do not include manuscripts submitted or in preparation. The individual may choose to include selected publications based on recency, importance to the field, and/or relevance to the proposed research. When citing articles that fall under the Public Access Policy, were authored or co-authored by the applicant and arose from NIH support, provide the NIH Manuscript Submission reference number (e.g., NIHMS97531) or the Pubmed Central (PMC) reference number (e.g., PMCID234567) for each article. If the PMCID is not yet available because the Journal submits articles directly to PMC on behalf of their authors, indicate "PMC Journal - In Process." A list of these journals is posted at: <u>http://publicaccess.nih.gov/submit</u> process journals.htm. Citations that are not covered by the Public Access Policy, but are publicly available in a free, online format may include URLs or PMCID numbers along with the full reference (note that copies of publicly available publications are not acceptable as appendix material).
- D. Research Support. List both selected ongoing and completed (during the last three years) research projects (Federal or non-Federal support). Begin with the projects that are most relevant to the research proposed in this application. Briefly indicate the overall goals of the projects and responsibilities of the Senior/Key Person identified on the Biographical Sketch. Do not include number of person months or direct costs.

What this means:

The sections below must be included in the Biosketch, but remember that the Biosketch cannot exceed four pages in total length:

 Personal Statement — Briefly describe why your experience and qualifications make you ideally suited for your role on this project, as PI, mentor, etc.

- Positions and Honors List your previous positions in chronological order, concluding with your present one. Include any honors and list any memberships on federal government public advisory committees.
- Peer-Reviewed Publications and Manuscripts in Press (in chronological order) NIH suggests that you limit the list of selected peer-reviewed publications or manuscripts in press, and patent citations to no more than 15. You should not include manuscripts submitted or in preparation, but you may include selected publications based upon most recent release, importance in the field, relevance to the proposed research and development effort. If the article happens to fall under the Public Access Policy, was authored or co-authored by the applicant and arose from NIH support, you need to provide only the NIH Manuscript Submission reference number or the PubMed Central (PMC) reference number.
- Research Support List both selected ongoing and completed (during the last three years) research projects. Begin with the most relevant to your current application, and briefly state the overall goals of the project and the responsibilities of the Senior/Key Personnel. Do not include the number of person months or direct costs.

In the next section, we will go into more detail for each of the Biosketch features and their relevance to your application.

Personal Statement

This is the section where you get to detail why you are the best individual for a chosen role in the project. Reviewers will carefully consider the information you include here when they examine your qualifications. You may include your pedigree, research experience, management experience, mentoring, or your track record of product and technology research and development. Indicate specifically why you feel that you are the most qualified person to lead this proposed project. You need to avoid sounding boastful, so point to specific objectives and criteria in your background, grant funding you have previously received, and publications resulting from those grants. If you have been employed with a company for a significant length of time during your career, you may not have had the opportunity to publish or compete for grants to the same level as an academician. Since company value often relies on intellectual property, it would be appropriate here to describe any intellectual property you have contributed to, such as trade secrets, patent filings or patents awarded. You may also include here any previous products you have developed, product testing in clinical trials, or contracts awarded to you and your company.

Within this section you may, at your discretion, briefly describe factors such as family care responsibilities, illness, disability, and active duty military service that may have affected your scientific advancement or productivity. You may also reference presentations you made, or address changing fields of study.

The idea here is that the personal statement will provide an overview of your research and product development capabilities, and why it is worth the reviewer's time to read your proposal and award the SBIR program's money. It should contain your objectives for wanting to conduct the work. It would explain your personal motivations for wanting the award and why you deserve it. Your personal statement can give a good first impression to the study section that will review your application.

Here is an example of a personal statement from a recently awarded Phase I SBIR:

The goal of the proposed research is to test the feasibility of human endothelial progenitor cells or endothelial colony forming cells (ECFCs), a population of CD31+/CD34+ pluripotent cells found in circulation, for toxicological risk assessment. I have expertise in cellular and molecular biology. For the past 8 years, my scientific interest has been associated regulation of cell signaling, cell-cell, and cell environment communication. I also interested in finding efficient ways to conduct biological research and I founded [Company Name] in 2010 with an



Personal Statement is where you may describe your contributions to your company's intellectual property portfolio. idea to capitalize on and advance novel technologies associated with human stem/ progenitor cells. Our company focuses on research and manufacturing of barrier tissues, i.e.,endothelium and epithelium. We see a value in stem/progenitor cells, which can be isolated from any person, especially in the area of diagnostics. Together with [Academic Institution Name], we concluded a study where we identified the first biomarker for low-dose ionizing radiation (LDIR). We found that human endothelial progenitor, or endothelial colony-forming cells (ECFCs) are highly sensitive to LDIR. ECFCs can be (a) isolated in a noninvasive manner, (b) easily expanded in culture, and (c) cryopreserved without loss of viability. We realize that ECFC can be valuable for high-throughput analysis of environmental hazards. The overall goal of this research is to evaluate the effect of chemical toxicants on viability, proliferation, and differentiation of ECFCs derived from different individuals.

Notice the following features:

- The statement begins by identifying the main point for the research and helps to keep the rest of the statement focused and on track.
- Objectives are identified describe why you want your application to be approved and how your research will benefit the field. You have to make the reviewers understand why this study is significant and that it addresses and unmet commercial need.
- Personal statement is in essay form Come straight to the point and envision that you are straightforwardly answering a question as to why your proposal should be considered and that you are doing it in full detail.
- Specific discussion of background Covers past relevant work, and your role, that lead up to this proposed study.
- Uses the first person perspective This is a personal statement so you need to use "I". It is here where you have an opportunity to say something about yourself and the personal significance of the grant. This is your chance to include pertinent details that were not included in the application forms.

Positions and Honors

This is the section where you list your employment history. Include the dates, places, and nature of the position. For SBIR applications, this listing is in chronological order, concluding with your present position. Include any honors and memberships to organizations that you hold, as well as present membership on any Federal Government public advisory committee.

The NIH provides this example:

B. Positions and Honors

Positions and Employment

1998-2000	Fellow, Division of Intramural Research, National Institute
	of Drug Abuse, Bethesda, MD
2000-2002	Lecturer, Department of Psychology, Middlebury College,
	Middlebury, VT
2001-	Consultant, Coastal Psychological Services, San Francisco, CA
2002-2005	Assistant Professor, Department of Psychology, Washington
	University, St. Louis, MO
2007-	Associate Professor, Department of Psychology, Washington
	University, St. Louis, MO

Other Experience and Professional Memberships

1995-	Member, American Psychological Association
1998-	Member, Gerontological Society of America
1998-	Member, American Geriatrics Society
2000-	Associate Editor, Psychology and Aging
2003-	Board of Advisors, Senior Services of Eastern Missouri
2003-05	NIH Peer Review Committee: Psychobiology of Aging, ad
	hoc reviewer
2007-11	NIH Risk, Adult Addictions Study Section, member Honors
2003	Outstanding Young Faculty Award, Washington University, St.
	Louis, MO
2004	Excellence in Teaching, Washington University, St. Louis, MO
2009	Award for Best in Interdisciplinary Ethnography, International
	Ethnographic Society



While you application won't be tossed out if you provide more than 15 publications, don't irritate the reviewers by having them go through a long list of your papers to try and find the ones relevant to your application – highlight them for ease of identification.

Peer-Reviewed Publications and Manuscripts in Press

The publications list allows you to demonstrate that you have a track record of success as researcher. Applicants are encouraged to list no more than 15 selected peer-reviewed publications or manuscripts in press, do not include any submitted manuscripts, manuscripts not published, or manuscripts in preparation. While your application won't be tossed out if you provide more than 15 publications, don't irritate the reviewers by having them go through a long list of your papers to try and find the ones relevant to your application – highlight them for ease of identification.

One approach in selecting these 15 is to pick the five most recent, the five most important to your field, and five which are most relevant to your proposed research and development project. Most reviewers will be focused on what you have done during the last five years, regardless of whether this can be covered in 5 or 10 papers. If the majority of your recent publications are directly relevant to your current proposal, then you may be able to use your most recent 15 papers to satisfy all of the aforementioned areas. In contrast, if your most recent 15 do not give an accurate picture of your strength and ability as an investigator, you may go back to five or six older publications showing that you have worked in the field, you have a track record of accomplishments, and you have made an impact. Another approach towards indicating to the reviewers that you have an extensive publication record is to make a statement such as 'selected publications from the last 10 years', or 'selected publications out of 90' before listing your papers.

Below is an example, provided by the NIH, of the Peer-Reviewed Publications or Manuscripts in Press portion of the Biosketch.

C. Selected Peer-reviewed Publications (Selected from 42 peer-reviewed publications)

Most relevant to the current application

 Merryle, R.J. & Hunt, M.C. (2004). Independent living, physical disability and substance abuse among the elderly. Psychology and Aging, 23(4), 10-22.

- Hunt, M.C., Jensen, J.L. & Crenshaw, W. (2007). Substance abuse and mental health among community-dwelling elderly. International Journal of Geriatric Psychiatry, 24(9), 1124-1135.
- Hunt, M.C., Wiechelt, S.A. & Merryle, R. (2008). Predicting the substanceabuse treatment needs of an aging population. American Journal of Public Health, 45(2), 236-245. PMCID: PMC9162292
- Hunt,M.C., Newlin, D.B. & Fishbein, D. (2009). Brain imaging in methamphetamine abusers across the life-span. Gerontology, 46(3), 122-145.
- Hunt, M.C. & Sher, K.A. (2009). Successful intervention models for older drug-abusers: Research across the life-span. American Psychologist, in press. NIHMSID: NIHMS99135

Additional recent publications of importance to the field (in chronological order)

- Gryczynski, J., Shaft, B.M., Merryle, R., & Hunt, M.C. (2002). Community based participatory research with late-life addicts. American Journal of Alcohol and Drug Abuse, 15(3), 222-238.
- Shaft, B.M., Hunt, M.C., Merryle, R., & Venturi, R. (2003). Policy implications of genetic transmission of alcohol and drug abuse in female nonusers. International Journal of Drug Policy, 30(5), 46-58.
- Hunt, M.C., Marks, A.E., Shaft, B.M., Merryle, R., & Jensen, J.L. (2004). Early-life family and community characteristics and late-life substance abuse. Journal of Applied Gerontology, 28(2),26-37.
- Hunt, M.C., Merryle, R. & Jensen, J.L. (2005). The effect of social support networks on morbidity among elderly substance abusers. Journal of the American Geriatrics Society, 57(4), 15-23.
- Hunt, M.C., Pour, B., Marks, A.E., Merryle, R. & Jensen, J.L. (2005). Aging out of methadone treatment. American Journal of Alcohol and Drug Abuse, 15(6), 134-149.
- Hunt, M.C., Marks, A.E., Venturi, R., Crenshaw, W. & Ratonian, A. (2007). Community-based intervention strategies for reducing alcohol and drug abuse in the elderly. Addiction, 104(9), 1436-1606. PMCID: PMC9000292

- Merryle, R. & Hunt, M.C. (2007). Randomized clinical trial of cotinine in older nicotine addicts. Age and Ageing, 38(2), 9-23. PMCID: PMC9002364
- Hunt, M.C., Jensen, J.L. & Merryle, R. (2008). The aging addict: ethnographic profiles of the elderly drug user. NY, NY: W. W. Norton & Company.
- Hunt, M.C. (2009). Contrasting ethnicity with race in the older alcoholic. The Journals of Gerontology Series B: Psychological Sciences and Social Sciences, in press. PMCID: PMC Journal – In Process.
- Hunt, M.C. (2009). Intervening successfully with the older methadone patient. Journal of Applied Gerontology, 13(4), 67-79.

Take note that this applicant chose to divide their 15 publications into two distinct groups (most relevant and importance to the field) and that these choices were selected from a much larger group (42).

Upcoming Changes to the Biosketch Format

NIH's plan to modify the current biosketch format is scheduled to roll out for all grant applications received for FY 2016 funding and beyond (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-14-091.html). In practice, this means that applications submitted in early 2015 will use this new format which is described on the SF424 (R&R) Applications and Electronic Submission Page (http://grants.nih.gov/grants/funding/424/index.htm). Until this time, read any RFAs you plan to apply for very carefully, since they may be part of the pilot phase of the implementation that requires use of the new biosketch format. In summary, these changes include:

- Increasing the total biosketch length to five pages, instead of two or four.
- There is a new Section C Contributions to Science. This section will succeed the Selected Peer-Reviewed Publications section. In this new section C, applicants will briefly describe up to five of their most significant contributions to science. Each description should be no longer than one half page, including figures and citations. For each contribution, the applicant

will reference up to four peer-reviewed publications relevant to that specific contribution. Be sure to provide a URL to a full list of your published work as found in a publicly available digital database such as PubMed or My Bibliography.

OMB No. 0925-0046 (Approved Through 5/31/2016)

BIOGRAPHICAL SKETCH— <i>Pilot Format (To Be Used for Specific FOAs only)</i> Provide the following information for the Senior/key personnel and other significant contributors. Follow this format for each person. DO NOT EXCEED FIVE PAGES.				
NAME	POSITION TITI	E		
eRA COMMONS USER NAME (credential, e.g., agency login)				
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)				
INSTITUTION AND LOCATION	DEGREE (if applicable)	MM/YY	FIELD OF STUDY	

Why change the format?

The purpose of these changes has best been summarized by Dr. Sally Rockey, NIH's Deputy Director for Extramural Research. Her complete web posting on this subject may be found at <u>http://nexus.od.nih.gov/all/2014/05/22/changes-to-the-biosketch/</u>:

The primary focus of the new NIH biosketch will be the magnitude and significance of the scientific advances associated with a researcher's discoveries and the specific role the researcher played in those findings. This change will help reviewers evaluate you not by where you've published or how many times, but instead by what you've accomplished. Hopefully, this change will redirect the focus of reviewers and the scientific community more generally from widely questioned metrics, like the number of published papers, the number of citations received by those papers, or one of several statistical approaches used to normalize citations.

We strongly believe that allowing a researcher to generate an account of his or her own work will provide a clearer picture of each individual's contributions and capabilities. But one might question whether this new biosketch will have a negative impact on younger investigators whose body of work may not be as robust as more established investigators. I believe the contrary is true; this new format will give early career investigators a platform for describing and framing the significance of their contributions, which should help reviewers better understand their accomplishments without having to rely simply on a list of publications.

The NIH provides the following example of the new Section C:

C. Contributions to Science

- My early publications directly addressed the fact that substance abuse is
 often overlooked in older adults. However, because many older adults were
 raised during an era of increased drug and alcohol use, there are reasons to
 believe that this will become an increasing issue as the population ages. These
 publications found that older adults appear in a variety of primary care settings
 or seek mental health providers to deal with emerging addiction problems.
 These publications document this emerging problem but guide primary care
 providers and geriatric mental health providers to recognize symptoms, assess
 the nature of the problem and apply the necessary interventions. By providing
 evidence and simple clinical approaches, this body of work has changed
 the standards of care for addicted older adults and will continue to provide
 assistance in relevant medical settings well into the future. I served as the
 primary investigator or co-investigator in all of these studies.
 - a. Gryczynski, J., Shaft, B.M., Merryle, R., & Hunt, M.C. (2002).
 Community based participatory research with late-life addicts.
 American Journal of Alcohol and Drug Abuse, 15(3), 222-238.
 - b. Shaft, B.M., Hunt, M.C., Merryle, R., & Venturi, R. (2003). Policy implications of genetic transmission of alcohol and drug abuse in female nonusers. International Journal of Drug Policy, 30(5), 46-58.

- c. Hunt, M.C., Marks, A.E., Shaft, B.M., Merryle, R., & Jensen, J.L. (2004). Early-life family and community characteristics and late-life substance abuse. Journal of Applied Gerontology, 28(2),26-37.
- Hunt, M.C., Marks, A.E., Venturi, R., Crenshaw, W. & Ratonian, A. (2007). Community-based intervention strategies for reducing alcohol and drug abuse in the elderly. Addiction, 104(9), 1436-1606. PMCID: PMC9000292
- 2. In addition to the contributions described above, with a team of collaborators, I directly documented the effectiveness of various intervention models for older substance abusers and demonstrated the importance of social support networks. These studies emphasized contextual factors in the etiology and maintenance of addictive disorders and the disruptive potential of networks in substance abuse treatment. This body of work also discusses the prevalence of alcohol, amphetamine, and opioid abuse in older adults and how networking approaches can be used to mitigate the effects of these disorders.
 - a. Hunt, M.C., Merryle, R. & Jensen, J.L. (2005). The effect of social support networks on morbidity among elderly substance abusers. Journal of the American Geriatrics Society, 57(4), 15-23.
 - b Hunt, M.C., Pour, B., Marks, A.E., Merryle, R. & Jensen, J.L. (2005).
 Aging out of methadone treatment. American Journal of Alcohol and Drug Abuse, 15(6), 134-149.
 - c. Merryle, R. & Hunt, M.C. (2007). Randomized clinical trial of cotinine in older nicotine addicts. Age and Ageing, 38(2), 9-23. PMCID: PMC9002364.
- 3. Methadone maintenance has been used to treat narcotics addicts for many years but I led research that has shown that over the long-term, those in methadone treatment view themselves negatively and they gradually begin to view treatment as an intrusion into normal life. Elderly narcotics users were shown in carefully constructed ethnographic studies to be especially responsive to tailored social support networks that allow them to eventually reduce their maintenance doses and move into other forms of therapy. These studies also

demonstrate the policy and commercial implications associated with these findings.

- a. Hunt, M.C. & Jensen, J.L. (2003). Morbidity among elderly substance abusers. Journal of the Geriatrics, 60(4), 45-61.
- Hunt, M.C. & Pour, B. (2004). Methadone treatment and personal assessment. Journal Drug Abuse, 45(5), 15-26.
- c. Merryle, R. & Hunt, M.C. (2005). The use of various nicotine delivery systems by older nicotine addicts. Journal of Ageing, 54(1), 24-41.
 PMCID: PMC9112304
- Hunt, M.C., Jensen, J.L. & Merryle, R. (2008). The aging addict: ethnographic profiles of the elderly drug user. NY, NY: W. W. Norton & Company.

Complete List of Published Work in My Bibliography: <u>http://www.ncbi.nlm.nih.</u> gov/sites/myncbi/collections/public/1PgT7IEFIAJBtGMRDdWFmjWAO/?sort=dat e&direction=ascending

When writing this section, keep the following in mind:

- What do you consider your most significant contributions to science? This can be contributions to science in general, to a specific scientific discipline, or a combination.
- The background for the scientific question or problem you are highlighting in each contribution
- A recap of the critical findings for each
- How these findings were used to guide future progress in addressing healthrelated problems or advancing technology
- What was your specific role in the described work?

Sections A, B, and D, (Personal Statement, Positions and Honors, and Research Support, respectively) have remained the same.

Research Support

In this section, list any ongoing and completed projects which received funding from outside of your company. This is typically limited to federal sources for an SBIR application, since non-federal sources of funding (i.e. private foundations) for small companies is generally scarce. Do not include any research and development contract work funded by another company.

Begin with any projects that are most relevant to the current application and indicate their overall goals in addition to the responsibilities of the Senior/Key Personnel involved in the current proposal. This section, however, is not the place to detail the personnel time and effort or the direct costs. "Research Support" and "Other Support" are different and not interchangeable. The Biosketch's Research Support section highlights your scientific accomplishments and your role in selected awards. This information will be used by reviewers to assess each individual's qualifications for a specific role in the project, as well as their roles within the research group.

The Other Support section includes information required for all applications that are selected to receive awards. NIH staff will request complete and up-todate Other Support information from awarded researchers after peer review and then check this information to make certain that the proposed research has not already been federally funded.

NIH provides the following example of the Research Support portion of the Biosketch:

D. Research Support

Ongoing Research Support

R01 DA942367-03Hunt (PI)09/01/08-08/31/13Health trajectories and behavioral interventions among older substance abusersThe goal of this study is to compare the effects of two substance abuseinterventions on health outcomes in an urban population of older opiate addicts.

Role: PI

R01 MH922731-05 Merryle (PI) 12/15/07-11/30/12 Physical disability, depression and substance abuse in the elderly The goal of this study is to identify disability and depression trajectories and demographic factors associated with substance abuse in an independently-living elderly population.

Role: Co-Investigator

Faculty Resources Grant, Washington University08/15/09-08/14/11Opiate Addiction Database

The goal of this project is to create an integrated database of demographic, social and biomedical information for homeless opiate abusers in two urban Missouri locations, using a number of state and local data sources.

Completed Research Support

K02 AG442898Hunt (PI)02/01/02-01/31/05Drug Abuse in the ElderlyIndependent Scientist Award: to develop a drug addiction research program with
a focus on substance abuse among the elderly.Role: PI

R21 AA998075Hunt (PI)01/01/02-12/31/04Community-based intervention for alcohol abuseThe goal of this project was to assess a community-based strategy for reducingalcohol abuse among older individuals.Role: PI

Letters of Support (e.g., Consultants)

Directly from the SBIR/STTR SF424 (R&R) Adobe Forms Version B Application Guide:

Attach all appropriate letters of support, including any letters necessary to demonstrate the support of consortium participants and collaborators such as Senior/Key Personnel and Other Significant Contributors included in the grant application. Letters are not required for personnel (such as research assistants) not contributing in a substantive, measurable way to the scientific development or execution of the project. Letters should stipulate expectations for co-authorship, and whether cell lines, samples or other resources promised in the letter are freely available to other investigators in the scientific community or will be provided to the particular investigators only. For consultants, letters should include rate/charge for consulting services and level of effort/number of hours per year anticipated. In addition, letters ensuring access to core facilities and resources should stipulate whether access will be provided as a fee-for-service. Do not place these letters in the Appendix. Consultant biographical sketches should be in the Biographical Sketch section.

Phase I, Phase II, Phase IIB, and Fast-Track SBIR/STTR Applications: Involvement of consultants and collaborators in the planning and research stages of the project is permitted. Include with the application letters from each individual and/or collaborator confirming their role(s) in the project. Following is guidance for such documentation: The letter(s) should be prepared on the consultant or collaborator's letterhead and addressed to the Small Business Concern (SBC). One page is recommended.

At a minimum, each consultant and collaborator letter should (1) verify their commitment to the project; (2) refer to the specific project by name, acknowledging the PD/PI as the lead on the project; and (3) specify what services /tasks the consultant or collaborator will contribute (e.g. expertise, number of hours/ percent of effort, summary of tasks to be completed). For consultants, the letter should also
include the rate/charge for consulting services. Also include biographical sketches for each consultant.

For STTR projects, the single "partnering" research institution must provide a letter to the applicant small business concern certifying that at least 30% of the work of the STTR project will be performed by the research institution.

Letters of interest from potential commercial partners or investors and letters of commitment of funds or other resources that will enhance the likelihood of commercialization should be placed following the letters of support for consultants and collaborators.

What this means:

Letters of support from consultants will fill in any capability gaps that may exist in your Biographical Sketch. Since these letters do not fall within the application page limitations, you are free to include as many as you feel are necessary. You will need a strong, specific letter of support from that individual, or a representative from a collaborating company, declaring exactly what will be provided to the project and demonstrating enthusiasm for it. It works to your advantage if you can write a draft for each consultant to review and sign, after making sure you determine what aspects of your proposal would be most interesting and relevant to each of your consultants. No one knows your grant application strategy better than you do. Describing to your consultant precisely what your needs are and what you need them to cover can be challenging and take up a lot of time. If you draft it for them, you can get what you need in a timely fashion, since editing your letter is much easier than having them craft it from scratch. Remember to make each of your supporting letters look different.

Tips to Writing Strong Letters of Support

When you write a letter of support, here are a few tips to keep in mind:

- **Clearly define duties and timelines.** Be specific with your expectations and any deadlines. This will sidestep any confusion between you and the consultant. Be sure that the letter draws the reviewer's attention to you, the applicant, and what you have achieved relevant to the SBIR requirements.
- Write it from the consultant's point of view. Craft each letter as if the consultant wrote it, tailoring it to their specific duties. Use unique language for each consultant letter.
- **Display enthusiasm.** The letter needs to effectively communicate the consultant's enthusiasm for the project. This can be achieved by summarizing specifics like resource and time commitment, as well as interest in the project's details.
- Get the standard details correct. Address the letter according to the grant's guidelines. The final written version needs to be on the consultant's letterhead and it needs to be signed.

REMEMBER:

Letters of support from consultants will fill in any capability gaps that may exist in you Biographical Sketch.

A suggested structure for these letters is as follows:

- **Statement of support** Using no more than three sentences, demonstrate enthusiasm and identify the specific project by name.
- Supporting paragraphs Describe how the consultant's expertise and technical skills will support the applicant. Detail the consultant's relevant experience and past performance on similar projects. If there has been a previous working relationship, describe the project and the results. Lastly, explain specific responsibilities.
- **Cordial closing** The closing's formality will depend on the relationship between the applicant and the consultant who is supporting them. If the two have a previous productive working relationship, it can be less formal. If that relationship is more limited, the closing should be more formal.

Multiple Program Directors/Principle Investigators

Taken from the SBIR/STTR SF424 (R&R) Adobe Forms Version B Application Guide :

Multiple PD/PI Leadership Plan

For applications designating multiple PD/PIs, a leadership plan must be included. For applications designating multiple PD/PIs, all such individuals must be assigned the PD/PI role on the Senior/Key Profile form, even those at organizations other than the applicant organization. A rationale for choosing a multiple PD/PI approach should be described. The governance and organizational structure of the leadership team and the research project should be described, including communication plans, process for making decisions on scientific direction, and procedures for resolving conflicts. The roles and administrative, technical, and scientific responsibilities for the project or program should be delineated for the PD/PIs and other collaborators. Do not submit a leadership plan if you are not submitting a Multiple PD/PI application.

If budget allocation is planned, the distribution of resources to specific components of the project or the individual PD/PIs should be delineated in the Leadership Plan. In the event of an award, the requested allocations may be reflected in a footnote on the Notice of Grant Award.

What this means:

While there is no page limit on this document, it should include the following:

- A. The reason for choosing a multiple PD/PI approach to lead the proposed research.
- B. The governance and organization structure of the leadership team and the research project, including:
 - Communication plans;
 - Process for making decisions regarding scientific direction; and
 - Procedures for resolving conflict.

C. The roles and administrative, technical and scientific responsibilities for the project or program for each of the PDs/PIs and other collaborators.

If you have planned the budget allocation, your Leadership Plan should detail resource distribution to specific project components or individual PDs/PIs.

NIH offers the following examples of Leadership Plans, noting that applications should follow any special instructions offered by individual ICOs:

Example 1

Principal Investigator #1 and Principal Investigator #2 will provide oversight of the entire Program and development and implementation of all policies, procedures and processes. In these roles, PI#1 and PI#2 will be responsible for the implementation of the Scientific Agenda, the Leadership Plan and the specific aims and ensure that systems are in place to guarantee institutional compliance with US laws, DHHS and NIH policies including biosafety, human and animal research, data and facilities.

Specifically, PI#1 will oversee aim 1 and be responsible for all animal research approvals. PI#2 is responsible for aims 2, 3, and 4 including the implementation of all human subjects research and approvals. PI#1 will serve as contact PI and will assume fiscal and administrative management including maintaining communication among PI s and key personnel through monthly meetings. He will be responsible for communication with NIH and submission of annual reports. The responsibilities of the contact PI will be rotated to PI #2 in even years of the grant award. Publication authorship will be based on the relative scientific contributions of the PIs and key personnel.

Example 2

Principal Investigator #1 at Institution A will be responsible for the oversight and coordination of project management for aim 1 involving the molecular design and production of vectors expressing tumor specific antigens. Principal Investigator #2 at Institution B will be responsible for aims 2 and 3 including the in vivo and in vitro testing of vaccines. Each PI will be responsible for his own fiscal and research administration.

The PIs will communicate weekly, either by phone, e-mail, or in person, to discuss experimental design, data analysis, and all administrative responsibilities. All PIs will share their respective research results with other PIs, key personnel, and consultants. They will work together to discuss any changes in the direction of the research projects and the reprogramming of funds, if necessary. A publication policy will be established based on the relative scientific contributions of the PIs and key personnel.

PI#1 will serve as contact PI and be responsible for submission of progress reports to NIH and all communication.

Intellectual Property

The Technology Transfer Offices at Institutions A and B will be responsible for preparing and negotiating an agreement for the conduct of the research, including any intellectual property. An Intellectual Property Committee composed of representatives from each institution that is part of the grant award, will be formed to work together to ensure the intellectually property developed by the PIs is protected according to the policies established in the agreement.

Conflict Resolution

If a potential conflict develops, the PIs shall meet and attempt to resolve the dispute. If they fail to resolve the dispute, the disagreement shall be referred to an arbitration committee consisting of one impartial senior executive from each PI's institution and a third impartial senior executive mutually agreed upon by both PIs. No members of the arbitration committee will be directly involved in the research grant or disagreement.

Change in PI Location

If a PI moves to a new institution, attempts will be made to transfer the relevant portion of the grant to the new institution. In the event that a PI cannot carry out his/her duties, a new PI will be recruited as a replacement at one of the participating institutions.

Example 3

Principal Investigator #1, Principal Investigator #2, and Principal Investigator #3 will serve as PIs for the project. PI#1 will be responsible for the gene expression studies. He will supervise Technician #1 for all microarrays. PI#2 will be responsible for the endothelial cell studies and flow cytometry studies proposed in the grant. She will supervise the Technician #2 at 50% effort for the flow cytometry studies and the post Doc for the endothelial cell studies. PI#3 will oversee all bioinformatics work in the gene expression and flow cytometry studies and will work with PI#1 and PI#2 on all data analysis.

The PIs will form a Steering Committee (membership may include PIs, key personnel, consultants, etc.) that will manage the oversight and coordination of project management, research administration, publications and data sharing, and integration of all resources needed for the project. The Institution will subdivide the award funds and each PI will be responsible for his own budget.

The Steering Committee will oversee decisions on minor changes in research direction and have the authority to reallocate funds and resources between PIs. PI#1 will serve as Chair of the Steering Committee and be responsible for communication among PIs, including meeting schedules and agendas. The position of Chair will rotate among the PIs on a yearly basis. PI#2 will be designated the contact PI and be responsible for submitting all necessary documents to NIH, including IRB approvals, and annual progress reports.

Intellectual Property

The PIs will grant necessary access rights to the pre-existing patents and or the patents potentially generated within the frame of this project for the purpose of this research project to all the other PIs and key personnel on a non-exclusive royalty-free basis. Each PI shall take appropriate measures to ensure that he/she can grant these access rights. Right in any pre-existing intellectual property will remain the property of the party that created and/or controls it.

Conflict Resolution

If a potential conflict develops, the appropriate Departmental administrators representing the PIs shall meet and attempt in good faith to settle any dispute, claim or controversy arising out of or relating to the interpretation, performance or breach of this disagreement. However, if the Departmental administrators fail to resolve the disagreement within thirty business days, then such disagreement shall be referred for resolution to a designated senior executive of the parties who has the authority to settle the disagreement but who is not directly involved in the disagreement.

Change in PI Location

If one of the PIs moves to a new institution, attempts will be made to transfer the relevant portion of the grant to the new institution. In the event that a PI cannot carry out his/her duties, a new PI will be recruited as a replacement, subject to the approval of the Steering Committee and the Institution.

CONCLUSION

Clear, focused, and enthusiastic writing of your abstract will be the hook to get the reviewers interested in reading your proposal. Your Biographic Sketch will be the place where the reviewers will make their determination of whether or not you have the background, ability, and expertise to accomplish the research and development goal you propose. These sections have limited space with which you can get your points across to prove that your proposal is worth funding. Use these sections to help the reviewer become your ally.

Chapter 3: Small Company Resources and Commitment

Reviewers will pay close attention to the environment in which you plan to execute the research and development proposal. They need to determine that you will have adequate resources, in terms of company support, equipment, and physical items needed to successfully complete the work. This section of the grant will be scored and is arguably the easiest section to receive a high mark in. Any unique features of your scientific environment or consulting and collaborative arrangements will benefit your project. These elements are detailed in the Facilities and Other Resources and Equipment sections of the application.

Showcase Your Facilities and Other Resources

Taken directly from the SBIR/STTR SF424 (R&R) Adobe Forms Version B Application Guide:

Facilities & Other Resources

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.

The research to be performed by the applicant small business concern and its collaborators must be in United States facilities (i.e., foreign sites must be approved by the funding officer) that are available to and under the control of each party for the conduct of each party's portion of the proposed project.



Reviewers will pay close attention to the environment in which you plan to execute the research and development proposal; any unique features of your scientific environment or consulting and collaborative arrangements will benefit your project. No special form is required but this section must be completed and attached for submissions to NIH and other PHS agencies unless otherwise noted in an FOA. Describe how the scientific environment in which the research will be done contributes to the probability of success (e.g., institutional support, physical resources, and intellectual rapport). In describing the scientific environment in which the work will be done, discuss ways in which the proposed studies will benefit from unique features of the scientific environment or subject populations or will employ useful collaborative arrangements.

For Early Stage Investigators, describe institutional investment in the success of the investigator, e.g., resources for classes, travel, training; collegial support such as career enrichment programs, assistance and guidance in the supervision of trainees involved with the ESI's project, and availability of organized peer groups; logistical support such as administrative management and oversight and best practices training; and financial support such as protected time for research with salary support.

If there are multiple performance sites, describe the resources available at each site.

Describe any special facilities used for working with biohazards or other potentially dangerous substances. Note: Information about select agents must be described in the Research Plan, Section 11 (Select Agent Research).

What this means:

As you compose the Facilities and Other Resources section, keep these questions in mind:

- What facilities will you be using? Break this question into subheadings and describe the capacities (including square footage), relevant capabilities, proximity and extent of availability of each to your project:
 - Laboratory
 - Clinical
 - Animal
 - Computer
 - Office
 - Other, such as machine shop, electronic shop, etc.

- How do you see this environment promoting your success? This section is also best described using subheadings. Explain how your work will benefit from any unique features of the scientific environment, subject populations, and useful collaborative arrangement:
 - Institutional support
 - Physical resources
 - Intellectual support
- 3. If your research and development will be performed at more than one site, include a description of the available resources at each site.
- 4. Provide information on any special facilities you plan to use for working with biohazards or other potentially dangerous substances. If you are working with something classified as a Select Agent, make sure to describe any special facilities used for working with these materials. Here, you list any unique features, which may include the following:
 - A distinctive set of technical capabilities
 - Access to an unusual human populations for tissue or blood samples
 - The collaborative nature of interactions between you and your consultants
 - Emphasis in a particular area, such as high-throughput screening

This section has a two-fold purpose; by informing reviewers how your institution will support your proposed project, it also underscores your qualifications as the best person to conduct this research and development project. While there is no limitation on this section's length, make sure the information you provide only relates to your available facilities and resources. Elements you should consider including, if applicable to your project, are:

- A description of any collaborations that you may have with colleagues within the company who can impact your research and development project; intellectual support is invaluable.
- Matching the budget request section of the proposal with the Facilities and Other Resources section.
- Leveraging appropriate adjectives when describing your resources, such as "cutting- edge technology", "state-of-the-art equipment", "centralized core facility"



While there is no limitation on this section's length, make sure the information you provide only relates to your available facilities and resources. For projects involving live vertebrate animals, your company must ensure that all Project/Performance Sites hold an OLAW-approved Animal Welfare Assurance. In the likely event that your company does not have an animal facility on-site, and the animal work will be conducted at an institution with an Animal Welfare Assurance, you must obtain an Inter-institutional Assurance from OLAW prior to an award.

List Your Available Equipment

Here is an example of a Facilities and Other Resources section from a successful SBIR Phase I grant application:

Facilities and Other Resources available at [Company Name].

The laboratory for [Company Name] is located in [City and State] in close proximity to [Academic and Commercial Institutions] and other research institutions facilitating collaborative efforts and exchange of expertise. The laboratory facilities occupy 2600 square feet and contain all the necessary equipment for tissue culture, biochemistry, and molecular biology including: positive pressure HEPA filtered air system, chemical fume hood, 7, 6 foot laminar flow biological safety cabinets, 2, 4 foot laminar flow biological safety cabinets, 11 CO2 cell incubators, 5 Zeiss inverted microscopes, a Leica DM IRB fluorescence microscope, an Agilent 2100 Bioanalyzer, and a Nanodrop ND-1000 spectrophotometer. The laboratory is also equipped with a BD FACSCalibur flow cytometer with cell sorting capabilities, an Accuri C6 flow cytometer, 2 COBE Cell Processors, Kodak imaging system, 4 microplate readers, 2 CBS isothermal V-3000 liquid nitrogen vapor storage systems with automatic fill/ monitoring, and 6 additional liquid phase cryogenic storage containers.

[Company Name] is also equipped for laboratory automation with a Matrix PlateMate 2x3 workstation, 2 Multidrop 384 machines, an AutoMACS Pro Cell Separator, and a Biotek ELx405 Cell Washer. Our scientists are skilled in the use of robotics to miniaturize cell based assays to 384-well format for compound screening. We have successfully incorporated robotics into our contract assay services and have processed tens of thousands of compounds through our human primary cell based systems. Other Equipment Available for use includes a BioRad ChemiDoc, a Shimadzu Prominence HPLC system, a Flexcell FX5000 Tension system, 2 refrigerated ultra centrifuges, 3 refrigerated table top centrifuges, 3 balances, an ABI 7900HT real time PCR machine, an Eppendorf Mastercycler PCR machine, Perkin Elmer scintillation counter/luminometer, an MVE Cryogenics CRF2000 liquid nitrogen step down freezer.

Additional equipment includes refrigeration, freezers, 3 -80°C freezers, a radiation license, and back-up power capable of running all systems.

The equipment listed is also utilized for [Company Name] other manufacturing and production activities. However, there is ample time available for the equipment to be used on this project.

[Company Name] has office and meeting room space of approximately 2600 square feet. Finance personnel have managed Phase I and Phase II SBIR grants in addition to over \$15 million in financial transactions over the company's history.

In this particular case, the writer chose not to use subheadings, and instead used a more integrated prose, while still describing the laboratory space and the available equipment. While there is no special form required by the agency for this document, the following outline may be helpful in your own writing process. In fact, you may find that subheadings are again useful in organizing the requested information, whose content is based on the information asked for by the SBIR program:

- **Company:** Describe the general scientific environment in which you will carry out your research and development work, and how your company will contribute to successful outcomes.
- **Research Population:** If you are using tissue or blood specimens from human subjects, include this section and describe how your research and development will benefit from the subject populations.
- **Research Facilities:** Signify how your company's resources will support your proposed research and development. Convey any specific divisions that will be available, such as a machine shop, electronic shop, etc., and the extent to which they will be available. If there are multiple research sites, describe the resources available at each site.

- **Biohazard Facility:** If your project involves the use of biohazards or other potentially dangerous substances, you must describe any special facilities for working with them.
- Collaborative Arrangements/Intellectual Connection: Detail any collaborative relationships with your company colleagues and consultants
- **Company Support:** As discussed previously, indicating your company's support for you and your research and development efforts is key for reviewers, and you should use this section for this purpose.
- Laboratory: Explain your laboratory space, including the location(s), number of rooms, dimensions and equipment available.
- Animal: If your work will involve test animals, use this section to note AAALAC accreditation or, if that is lacking, provide information regarding animal care resources.
- **Computer:** Here, you should indicate the computers, databases, servers and other data storage/computing equipment available for your project.
- Office: Will office space be provided by your company for you and your consultants? If yes, provide a brief description, including location(s), number of office(s) and square footage.

Resources Sharing Plan

Taken directly from the SBIR/STTR SF424 (R&R) Adobe Forms Version B Application Guide:

NIH considers the sharing of unique research resources developed through NIH-sponsored research an important means to enhance the value and further the advancement of the research. When resources have been developed with NIH funds and the associated research findings published or provided to NIH, it is important that they be made readily available for research purposes to qualified individuals within the scientific community. See Part III, 1.5 Sharing Research Resources.

Supplemental Instructions:

- Data-Sharing Policy or http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-032.html. Data Sharing Plan: Investigators seeking \$500,000 or more in direct costs (exclusive of consortium F&A) in any year are expected to include a brief 1-paragraph description of how final research data will be shared, or explain why data-sharing is not possible (for example human subject concerns, the Small Business Innovation Development Act provisions, etc.). Specific funding opportunity announcements may require that all applications include this information regardless of the dollar level. Applicants are encouraged to read the specific opportunity carefully and discuss their data-sharing plan with their program contact at the time they negotiate an agreement with the Institute/Center (IC) staff to accept assignment of their application. See Data-Sharing Policy or http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-032.html.
- 2. Sharing Model Organisms Policy, and NIH Guide NOT-OD-04-042. Sharing Model Organisms: Regardless of the amount requested, all applications where the development of model organisms is anticipated are expected to include a description of a specific plan for sharing and distributing unique model organisms or state why such sharing is restricted or not possible. See Sharing Model Organisms Policy, and NIH Guide NOT-OD-04-042.
- 3. Genome Wide Association Studies (GWAS): Applicants seeking funding for a genome-wide association study are expected to provide a plan for submission of GWAS data to the NIH-designated GWAS data repository, or an appropriate explanation why submission to the repository is not possible. GWAS is defined as any study of genetic variation across the entire genome that is designed to identify genetic associations with observable traits (such as blood pressure or weight) or the presence or absence of a disease or condition. For further information see Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-Wide Association Studies, NIH Guide NOT-OD-07-088, and <u>http://gds.nih.gov/</u>.



TIP:

As a small business, specific nature of the data you collect will determine whether or not you decide to share the final dataset. If the final data are not open to sharing, if they are proprietary for instance, then you need to explain this in your application.

What this means:

These are separate documents that you upload as part of your application, but they do not count toward the application page limit. The reviewers will comment on your resource sharing plans; if you argue that your resources should not be shared, they will scrutinize any rationale you propose as well.

As a small business, the specific nature of the data you collect will determine whether or not you decide to share the final dataset. If the final data are not open to sharing, if they are proprietary for instance, then you need to explain this in your application. Under the Small Business Act, SBIR awardees may withhold their data for four years after the end of the award. The Small Business Act provides authority for NIH to protect from disclosure and nongovernmental use of all SBIR data developed from work performed under an SBIR funding agreement for a period of four years after the closeout of either a Phase I or Phase II grant, unless NIH obtains permission from the awardee to disclose these data. The data rights protection period lapses only upon expiration of the protection period applicable to the SBIR award, or by agreement between the small business concern and NIH.

Here is an example of a Data Sharing Plan from a funded SBIR Phase I application:

Data sharing and other inventions that are developed as part of NIH-funded research work will be assessed on a case-by-case basis to determine the best strategy possible in order to meet the NIH guidelines for sharing of research tools.

If intellectual property protection is not appropriate, data will be shared with the research community at the end of the project period through several mechanisms, which could include NIH-based sites and mechanisms to promote sharing of inventions and technologies. Additionally, we will publish results in peer-reviewed journals, present our findings at research conferences.

Where it is appropriate to proceed with patent protection for the development of a research tool as a potential product for sale and distribution to the research community, such protection will be pursued. Following appropriate protection, the data will be shared with the research community as described above. Licensing of inventions to a manufacturer or distributor for the further development of a research tool is consistent with the goals of the Bayh-Dole Act and might be most appropriate. If so, once proper protection of intellectual property rights has occurred, sharing detailed information and other inventions with the research community will be implemented in a timely manner.

[Award Company Name] and [Collaborating Company Name] internal monitoring of all intellectual property and material transfer activities includes oversight of potential relationships with third-parties interested in commercializing biomaterials or other research tools from NIH-funded research. As a result, the possibility of inappropriate "reach-through" requirements regarding the transfer of biomaterials that might be encouraged by for-profit third-parties and are addressed at the outset of negotiations. These third-parties are informed that such requirements are inconsistent with NIH-funded research tools and are not appropriate as part of any research, material transfer, or commercialization agreements involving these biomaterials or research tools.

As this example illustrates, protecting the small business's intellectual property position is of paramount importance, and is a legitimate reason for not sharing data until this protection has been realized. Unless you are absolutely certain that you will have data to share, it may be best to take the position of assessing the work *"on a case-by-case basis to determine the best strategy possible in order to meet the NIH guidelines for sharing of research tools"*, as in the above example. Remember, if you do submit a data-sharing plan, the agency will expect you to follow through with that plan. Failure to comply may result in unpleasant consequences for you and your small company, as the NIH, and perhaps the SBA, will act to protect their interests.

If you do decide to provide a plan, the precise content will be dependent upon the type of data you generate and how you plan to share it. For example, your datasharing plan might be as simple as describing:

- Anticipated data-sharing schedule
- Final format of the data
- Documentation to be shared



Remember, if you do submit a datasharing plan, the agency will expect you to follow through with that plan. Failure to comply may result in unpleasant consequences for you and your small company, as the NIH, and perhaps the SBA, will act to protect their interests.

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- Any analytic tools
- A brief description of the data-share agreement, if needed
- Mode of data sharing.

Model Organisms and GWAS

Model organisms are defined as new, genetically modified organisms developed for research. In these organisms, genetic modifications include those which have been induced by chemicals, irradiation, transposons or transgenesis, as well as spontaneous mutations and congenic or consomic strains. They may be shared as mature organisms, sperm, eggs, embryos or vectors used to generate transgenic or knockout organisms. Model organisms can include mammalian models, such as mice and rats, and non-mammalian models, like budding yeast, social amoebae, roundworm, Arabidopsis, fruit fly, zebra fish and frog. The NIH provides examples of model organisms on the Model Organism for Biomedical Research Web site at <u>www.nih.gov/science/models</u>.

A genome-wide association study (GWAS) involves scanning markers across the complete sets of DNA of multiple individuals looking for genetic variations which can be associated with a particular disease state. Upon identification of new genetic associations, the information can be used to develop more effective strategies to detect, treat and prevent the disease. Such studies are extremely valuable in elucidating genetic variations contributing to common, complex diseases including asthma, cancer, diabetes, heart disease and mental illnesses.

This same rationale for your Data Sharing Plan is applicable for both the Sharing Model Organisms Plan and the Genome Wide Association Studies (GWAS) requirement; state in your application that you will assess the work on a case-by-case-basis and decide the best course or action to meet the agency's sharing guidelines.

CONCLUSION

The facilities in which you will perform your research and development studies is one of the core criteria that reviewers will use to assess your SBIR grant application. As such, do not skimp on your discussion in your Facilities and Other Resources section. While important, providing merely a list of lab equipment and supplies that you will have access to is not sufficient. You also have to convince the reviewers that your small business supports you and your research and development endeavors. With regards to the agency requirement for you to disclose plans for data, model organisms and GWAS sharing, the plans you put forth will be part of the materials reviewers will examine and use to evaluate your application. Describe these plans carefully, especially if you chose not to initially share your data, as is the case for many small businesses.

Chapter 4: Describing Your Proposed Research

There is perhaps nothing more important to your SBIR application than describing your proposed research and development project. This information will be conveyed to the reviewers in both the Specific Aims and Research Strategy sections of the application. It is in these sections that you will address the Significance and Innovation of your project, as well as the Approach you will take towards successfully achieving the project's objectives. These three criteria are included in the five that will be used to score your application.

To put a finer point on this, we are specifically referring to the Specific Aims and Research Strategy sections. They address your project's Significance, Innovation and Approach, which are three of the five scored grant criteria that reviewers will use to grade your application (the other two being the Investigator(s) and environment, covered in the previous chapter). Your application's Impact Score will depend heavily on how the reviewers perceive your specific aims and research strategy. While there is no specific section or template to detail the overall impact of your proposal, the agency wants you to clearly describe your project's "impact" as you see fit. In this chapter, we will examine how you can use the Specific Aims and Research Strategy sections to satisfy the Significance, Innovation, and Approach criteria, as well as support the Overall Impact of your research and development.

While composing these sections, be conscious of your use of the words "goals", "objectives" and "aims". Goals are strategic and high-level views. For instance, "The overall goal of this research is to evaluate the effect of chemical toxicants on viability, proliferation, and differentiation of ECFCs derived from different individuals." Objectives are more mid-level views, and will address a more focused aspect of the goal, such as, "to delineate the pathway and functional role of TAK1 in ECFC differentiation." Finally, Aims are close-up views, and will outline your tactical approach towards the work to be performed. For example, "Aim 1: To analyze the dose-effect relationship between toxicants and ECFC's viability, proliferation, and differentiation."



Goals are strategic and high-level views, objectives are mid-level views, and aims are close-up views.

The Specific Aims Section

Taken directly from SF424 (R&R) SBIR/STTR Application Guide for NIH and Other PHS Agencies (updated November 1, 2013):

Specific Aims

The Specific Aims attachment is required unless otherwise specified in the FOA.

Phase I Applications: State the specific objectives of the Phase I research and development effort, including the technical questions you will try to answer to determine the Phase I feasibility of the proposed approach and the impact that the results of the proposed research will exert on the research field(s) involved. State concisely and realistically what the proposed research is intended to accomplish in terms of its potential for technological innovation and commercial application. Define the proposed product, process or service to ultimately be developed. Include milestones for each of the aims as these will be used in the evaluation process.

What this means:

In this section, the FOA directs that you should briefly list the specific objectives of your research and development, which may include:

- Solving a specific technical challenge
- Addressing an unmet commercial need
- Developing new technology
- Developing a new commercial product

Milestones are stages in the project at which something is completed, usually a key deliverable; they mark an important decision point which can affect the future course of the project. Think of them as a pausing point in the project where you will make an assessment of what has been accomplished and determine if any adjustments need to be made to your overall project plan. Reviewers tend to look more favorably upon a smaller focused project than they do upon a larger spread-out project. If they like what they see, they will most likely read the rest of the proposal for details to support their initial impression and you will have a chance at being funded. If they do not like what they see, they will perhaps look for flaws in the remaining document to justify their negative impression, thus putting you out of funding consideration.

Keep in mind that the Specific Aims section will quite likely be the only section that others in the study section will look at to grasp your Approach, Innovation, and Overall Impact. While not your primary reviewers, giving the other members of your study section a favorable view of your project may help sway a funding decision during their discussions. The Specific Aims is a one-page document that you will upload in the Research Plan Attachments area of the application.

Pitfalls to Steer Clear Of

With so much riding on the Specific Aims section, two common pitfalls that you should work toward avoiding are as follows:

- What if your reviewer likes your Specific Aims but is on the fence regarding their enthusiasm for the project? More than likely they will read the remainder of the application and come to a conclusion regarding the project's feasibility. Assuming they decide that it is indeed feasible, they will next look to the impact of the project – so spell it out for them; if they have to work to find it, their enthusiasm may diminish. For example, "This proposal describes an approach to the discovery of new drugs with novel chemistries that will activate AMPK and modulate cellular energy utilization for the treatment of metabolic disease".
- 2. What if reviewers see the aims as interdependent, and are left with the impression that if Aim 1 doesn't work, then Aim 2 is also a bust? The best grant applications are those with interconnected but not interdependent aims. Reviewers look for those experiments where the results do not particularly matter because the various outcomes are equally interesting. Thus, your aims should be interconnected but not dependent on the successful outcome of another aim.



Milestones are pausing points in the project where you will make an assessment of what has been accomplished and determine if any adjustments need to be made to your overall project plan.



TIP:

Avoid interdependent specific aims at all costs.



TIP:

Two or three specific aims is about all that may be accomplished in the 6-12 month time frame of a Phase I SBIR. EXAMPLE:

- Bad– Aim 2 cannot proceed until the studies in Aim 1 are completed.
- Good– Aim 2 proceeds in parallel with Aim 1 and findings from Aim 1 might direct future studies in Aim 2 or possibly Aim 3.

Crafting Your Specific Aims

While there is no rule on how many specific aims your proposal can or should have, given the maximum award length of one year for a Phase I SBIR award, 2-3 specific aims seems to be the popular number for many applicants. Some applications will have four. A word of caution: four specific aims may be viewed as not feasible within the time period of the award. In addition, space limitations will not easily permit you to convincingly describe four aims, leading the reviewers to suspect that you have not fully developed your plan. The Specific Aims will comprise the bulk of your research and development plan; think of them as the power source for your proposal.

Advice from Someone on the Inside

Dr. Gregory Milman, NIAID, has made several presentations to help businesses successfully compete for SBIR and STTR awards. For the specific aims section, he suggests the following:

Begin your Specific Aims section with a paragraph briefly describing the problem and why it is significant. Then, briefly describe the current status of solutions and unmet public health needs. Check the ICO's WebPages for background information that may help you.

Describe your product in the next paragraph. Hypothesize why your product is an innovative solution to the problem.

Present your Specific Aims in bullet format. Describe two to four measurable Specific Aims for Phase I research and for each, the criteria by which success will be judged. Make your Specific Aims "end points" as opposed to a "best effort." Your Specific Aims may be milestones, or if appropriate, each of your Specific Aims may be subdivided into milestones.

A review committee should easily be able to determine if your Specific Aims have been achieved and agree that successfully accomplishing them justifies Phase II funding. Propose a timeline for achieving your Specific Aims in table or graphic format. Do not propose more work than reviewers would think reasonable to achieve in Phase I. Estimate the additional time and funding necessary to bring your product to market after the completion of Phase I.

Example from a Funded Phase I Application

Keep in mind that as originally submitted, this section takes up just one page:

A. Specific Aims

The majority of breast cancers originate in the lobular or ductal cells of the milk-producing glands. In these structures, there are two main cell types: the inner luminal cells surrounded by basal myoepithelium. These cell types are the precursors to various forms of breast cancer making it important to study them independently and in co-culture systems. Current methods for culturing human mammary epithelial cells select for those of a basal phenotype. Thus, there are no commercial sources of quality-controlled, matched basal and luminal cells (from individual donors) in the U.S. forcing researchers to isolate and characterize the cells on their own. This process is time consuming, requires access to human tissue, and introduces variation in the preparation and characterization of the cells. Primary cultured human mammary-derived cells are an ideal model currently used to investigate the genesis and understanding of human breast cancer. Currently there is no consistent commercial source of primary human cultured breast-derived luminal and basal cells.

[Company Name] will address this need by providing a well characterized system to the research community. [Company Name] is a small biotechnology company that specializes in providing primary human cells and support products to researchers worldwide. The company is uniquely positioned to undertake this project with an already well-established breast tissue procurement network and twelve-plus years of human primary cell isolation experience. [Company Name] is a leading commercial source for human primary cell systems and has the existing infrastructure to successfully bring new products to the market. Phase I of this proposal is focused on optimizing the isolation, propagation, and characterization of primary human luminal and basal epithelium cells from breast tissue to establish a robust primary cell product. Extensions of this product and further characterization of the cells will be undertaken in Phase II resulting in additional products and services provided by [Company Name].

The goal of this proposal is to solicit SBIR Phase I funding to commercially provide quality controlled human primary cells to the breast cancer research community in a cost effective manner. Accordingly, the Specific Aims of this project are:

- Identify an effective method for isolation of primary luminal and basal cells from human breast tissue. This will involve assessment of two contemporary approaches for establishing luminal and basal cell cultures. Several biomarkers specific for luminal or basal cells will be used to determine cell purity. We will also employ a trans-differentiation assay as an additional index of specific cellular activity. The main criteria will be a method that can reproducibly provide homogeneous cell populations while maintaining sufficient cell yields for commercialization.
- 2. Optimize growth conditions during initial expansion phase. From our experience in commercial development of primary cell lines, at least 20 x 106 cells per tissue isolation (after the second passage) are required. While our preliminary data suggest this can be accomplished we would like to further optimize the conditions during the initial propagation and expansion phase in order to increase initial yields while minimizing the number of passages.
- 3. Determine lifespan of basal and luminal cells in culture and optimize freezing and storage conditions. In order to provide a quality commercially available primary cell line we will need to determine the lifespan of the luminal and basal cell lines in culture. In addition, we will also establish optimal conditions for cryopreservation.

Successful completion of Phase I will generate standard operating procedures required to provide well characterized human primary breast-derived basal and luminal cells and support products to researchers in a variety of areas. This will provide a platform with which to further investigate the mechanisms that lead to the formation of breast tumors as well as for use in drug screening programs.

Research Strategy

Taken directly from SF424 (R&R) SBIR/STTR Application Guide for NIH and Other PHS Agencies (updated November 1, 2013):

Organize the Research Strategy in the specified order and using the instructions provided below. Start each section with the appropriate section heading – Significance, Innovation, Approach. Cite published experimental details in the Research Strategy section and provide the full reference in the Bibliography and References Cited section (Part I Section 4.4.9).

Follow the page limits for the Research Strategy in the table of page limits (Table 2.6-1), unless specified otherwise in the FOA. Note that the page limit for this attachment will be validated as a single file.

(a) Significance

- Explain the importance of the problem or critical barrier to progress in the field that the proposed project addresses.
- Explain how the proposed project will improve scientific knowledge, technical capability, and/or clinical practice in one or more broad fields.
- Describe how the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field will be changed if the proposed aims are achieved.
- Explain the project's potential to lead to a marketable product, process or service.
- For Phase II, Fast-Track, and Phase IIB Competing Renewals, explain how the commercialization plan demonstrates a high probability of commercialization.

(b) Innovation

- Explain how the application challenges and seeks to shift current research or clinical practice paradigms.
- Describe any novel theoretical concepts, approaches or methodologies, instrumentation or interventions to be developed or used, and any advantage over existing methodologies, instrumentation, or interventions.
- Explain any refinements, improvements, or new applications of theoretical concepts, approaches or methodologies, instrumentation, or interventions.

(c) Approach

- Describe the overall strategy, methodology, and analyses to be used to accomplish the specific aims of the project. Provide a tentative sequence or timetable for the project. Unless addressed separately in Item 15 (Resource Sharing Plan), include how the data will be collected, analyzed, and interpreted as well as any resource sharing plans as appropriate.
- Discuss potential problems, alternative strategies, and benchmarks for success anticipated to achieve the aims.
- If the project is in the early stages of development, describe any strategy to establish feasibility, and address the management of any high risk aspects of the proposed work.
- Point out any procedures, situations, or materials that may be hazardous to personnel and precautions to be exercised. A full discussion on the use of select agents should appear in Item 11, below.
- If research on Human Embryonic Stem Cells (hESCs) is proposed but an approved cell line from the NIH hESC Registry cannot be identified, provide a strong justification for why an appropriate cell line cannot be chosen from the Registry at this time.

If an applicant has multiple Specific Aims, then the applicant may address Significance, Innovation and Approach for each Specific Aim individually, or may address Significance, Innovation and Approach for all of the Specific Aims collectively.

As applicable, also include the following information as part of the Research Strategy, keeping within the three sections listed above: Significance, Innovation, and Approach. **Preliminary Studies for Phase I Applications:** Preliminary data are not required for Phase I applications; however, such results may assist reviewers in assessing the likelihood of success of the proposed project and may be included in the Research Strategy section.

What this means:

Your 6-page Research Strategy section will have three main parts:

- 1. Significance
- 2. Innovation
- 3. Approach

These correspond to three primary criteria reviewers use to evaluate and score your proposal, and you should begin each section with the corresponding subheading.

In addition, although not required for submission, your Research Strategy should also include a Preliminary Studies section. You can address this by including the appropriate subheading — Preliminary Studies - within one of the main sections listed above.

Preliminary data may best be placed at the end of the Approach section, as this serves as a good segue into the description of how you will address the specific aims. Wherever you decide to include your preliminary data, reviewers seem to prefer these data being in a separate, headed section. If you feel that, while you are describing a specific aim in the Specific Aim Section you need to disclose some preliminary data to make your point, you can always reference the specific aim in the separate, headed, preliminary data section.

You may find that you need more room for one section over another, and must take the needed space from another section. When making this choice, remember that your Approach and Significance sections often make up the heart and soul of your proposal, so you may not want to take space from them.

Significance

Dr. Gregory Milman, NIAID, suggests the following:

Describe the significance of the public health problem. My advice is to appeal to reviewers by focusing on a single disease even if your technology has multiple applications. Describe the number and composition of the population affected. Give references to supporting statistical data. Provide background on the current solutions to the problem, their limitations, and the discoveries needed. Show reviewers you know the field by the breadth of your knowledge of both published and unpublished work by others, some of whom could be your reviewers.

Here is an example from a funded Phase I SBIR, illustrating Dr. Milman's points:

Significance

A decline in the quality of skeletal muscle tissue and its capacity for regeneration is prevalent in the aging population and in a number of specific diseases [1-2]. This is usually accompanied by replacement of muscle tissue with adipose and fibrous tissues. The resulting decrease in muscle function is associated with an increase in the number of falls and injury, loss of independence and a reduced quality of life [3]. This leads to a health care burden in the aged population reported to cost \$18.5 billion in the year 2000. By the year 2025, the Census Bureau estimates an 80% increase in the geriatric population [4]. Currently, there are no small molecule therapeutics that target skeletal muscle maintenance or regeneration.

In addition to sarcopenia associated with aging, there are a number of other specific diseases that have muscle wasting as part of their pathophysiology. COPD is among the most prominent followed by cachexia, end-stage renal disease and disuse atrophy [5-8]; all of which would benefit from new medicines that improve skeletal muscle function. There is a major unmet medical need to keep the elderly independent from nursing homes or other caretakers and, importantly, able to function in a positive manner that contributes to society rather than being a burden.

A major factor that promotes this is the physical ability to independently manage one's day-to-day activities. Overall, novel therapies that can improve or extend the health of muscle tissue will be essential to extend the productive life of seniors.

It is clear that aging has a significant effect on the ability of satellite cells to regenerate, and this serves as an appropriate model system with which to apply a drug discovery program. The majority of data accumulated to date that address potential mechanisms by which aging alters satellite cell growth are derived from rodent studies. Based on these studies, proposed mechanisms leading to a decline in satellite cell regenerative capacity fall into two major categories. First, age-associated changes in the stem cell niche (i.e. local environment) have been shown to be responsible for the decline in cell growth. Second, other studies have shown that changes develop in the aged cell itself. Interestingly, this change can be reversed by (poorly characterized) circulating factors from young animals [9-10]. Our preliminary data are supportive of this hypothesis and show that there is a difference in proliferative capacity between satellite cells isolated from young and elderly human skeletal muscle biopsies. These results are also in agreement with those from a recent publication [11]. Our studies will provide additional insight into the age-dependent mechanisms that reduce satellite cell proliferative activity, as well as establish a human cell-based system that can be applied to a high throughput drug discovery program.

Be aware that reviewers do use this section to guide them in assigning your application to an institute for possible funding; the words you choose in describing this section will affect that assignment decision. You may also consider writing the Approach section before facing the Significance section, because you will have a clearer overall picture of your proposal if you do so in this order.

Significance is Not the Same as Impact

Direct from NIH:

Significance: Does the project address an important problem or critical barrier to progress in the field? If the aims of the project are achieved, how will scientific knowledge, technical capability, and/or clinical practice be improved? How will successful completion of the aims change the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field?



TIP:

Be aware that reviewers do use this section to guide them in assigning your application to an institute for possible funding; the words you choose in describing this section will affect that assignment decision. *Overall Impact:* Reviewers will provide an overall impact/priority score to reflect their assessment of the likelihood for the project to exert a sustained, powerful influence on the research field(s) involved, in consideration of the following five core review criteria, and additional review criteria (as applicable for the project proposed).

What this means:

In short, if the project is worth doing, then it is "significance"; what the agency gets in return for its monetary investment is the "impact."

The NIH also provides the following details for clarification:

Significance is one of the five scored review criteria. It is only one of the elements that will be taken into consideration when deciding the Overall Impact of the application.

Significance:

- Is used for applications for research grants and cooperative agreements, among other programs.
- Is evaluated and scored independently of the evaluation and scoring of investigator(s), innovation, approach and environment.
- Assumes that the "aims of the project are achieved" and/or will be "successfully completed."
- Reviewers should evaluate the significance of the project within the context of a (research) field(s). For example, autism is a significant field of study but not all studies (projects) of autism are significant.
- Research field(s) may vary widely, so reviewers should identify in their reviews the research field(s) within which the project addresses an important problem or critical barrier to progress.
- For more guidance on Impact and Significance, refer to <u>Guide Notice</u> <u>NOT-OD-09-025</u> and the Overall Impact versus Significance document.

Overall Impact

- Takes into consideration, but is distinct from, the core review criteria (significance, investigator(s), innovation, approach and environment).
- Is not an additional review criterion.
- Is not necessarily the arithmetic mean of the scores for the five scored review criteria.
- Is the synthesis/integration of the five core review criteria that are scored individually and the additional review criteria, which are not scored individually.

Writing Your Significance Section

Make sure that you use plain, uncomplicated language when you write; the reviewer needs to be told upfront what you are going to attain that is different. Keep these questions in mind while composing this section:

- 1. Why are the results from my studies so important?
- 2. How will this work change the field?
- 3. Will patient lives be saved, or their quality of life made better? If yes, how?
- 4. Will this work lead to better treatment strategies?

When composing your Significance section, you should be able to describe all of your main points in 3-4 four paragraphs. The following are examples from funded SBIR awards:

1. Introduction to the problem: "Metabolic diseases such as type 2 diabetes (T2D), obesity and their related co-morbidities have reached epidemic proportions worldwide. According to a statement from the Centers for Disease Control, if current trends continue, as many as 1 in 3 adults are predicted to have diabetes by 2050. A significant component in this predicted value is related to the increase in the prevalence of obesity. Diabetes and obesity are already an enormous burden to our healthcare system. While progress continues to be made into the molecular mechanisms involved in both obesity and T2D, the identification and development of safe, efficacious therapeutic modalities is significantly limited. This is exemplified by the fact that two-thirds of patients receiving medication for T2D in the US and

Europe do not achieve their therapeutic goals (1-3). Similarly there are no effective drug treatments for obesity. There is an urgent need for innovative medicines to combat both obesity and diabetes".

2. Additional background: "AMPK is a key regulator of metabolic activity in cells. Activation of AMPK drives an increase in fatty acid uptake and oxidation, glucose uptake and glycolysis, as well as mitochondrial biogenesis (4). In addition, activation of AMPK reduces fatty acid-, cholesterol- and protein biosynthesis, as well as switching off gluconeogensis (4, 5). This shift to a catabolic state occurs, at least in part, in response to raised cellular levels of AMP/ATP in the presence of LKB1, the protein kinase that phosphorylates and activates AMPK. Metformin, the most prescribed oral anti-diabetic agent in the US and Europe, works in part through activation of AMPK (6). However, the efficacy of metformin is limited by low potency, GI tolerability (~25% of patients stop treatment because of GI disturbance) and 36% of patients are poor responders because they express a less active form of the organic cation transporter 1 which transports metformin into hepatocytes (7)".

3. Describe the approach that will be used: "This proposal describes an approach to the discovery of new drugs with novel chemistries that will activate AMPK and modulate cellular energy utilization for the treatment of metabolic disease. Fyn is a tyrosine protein kinase and has recently been shown to phosphorylate LKB1 at Y261 and Y365, and to regulate the LKB1-AMPK pathway, resulting in a major impact on cellular energy metabolism (8, 9). Phosphorylation of LKB1 blocks its translocation to the cytoplasm, thereby reducing access of LKB1 to its substrate, AMPK. Thus, phosphorylation of LKB1 effectively inhibits activation of AMPK by LKB1. Fyn knockout mice (Fyn KO) have been generated (8, 9). These mice display increased cytoplasmic levels of LKB1 (a constitutively active Ser/ Thr kinase), which then activate AMPK and deliver profound metabolic advantages of reduced body weight, reduced adiposity and improved insulin sensitivity. When compared with WT controls, Fyn KO mice had 20% less body weight at birth, which is maintained at this level throughout life, and which was shown to be a consequence of reduced white fat. White adipose tissue (WAT) mass was reduced by 70% in Fyn KO, even when adjusted for body weight. Importantly, Fyn KO mice have the

hallmarks of increased insulin sensitivity, with reduced fasting plasma levels of glucose (30% \downarrow) and insulin (60% \downarrow), when compared with WT animals. Furthermore, glucose excursions following an IPGTT were significantly lower in both Fyn null mice, and heterozygous (Fyn+/-) mice. This latter finding suggests a gene titration effect, since the body weight of Fyn+/- mice was only 5% less than WT controls, an effect that might be mimicked by a 50% pharmacological inhibition of the enzyme. In addition, fasting plasma triglyceride (TG) and non-esterified fatty acid (NEFA) levels were reduced by ~40%; this was accompanied by 55-75% reductions of TG and NEFA levels in tissues. Bastie et al (8) found that Fyn null mice exhibit increased Akt phosphorylation (2-fold in WAT), a key event in insulin signaling; as well as increased oxygen consumption (10%) and energy expenditure (40%). Loss of Fyn resulted in a tissue specific increase in fatty acid uptake (WAT 2-fold and muscle \sim 1.5-fold) and in fatty acid oxidation (WAT 4-fold and muscle \sim 2.5-fold). The authors also established a link between the increased fatty acid oxidation observed in Fyn KO mice and increased mitochondrial content in WAT, BAT and skeletal muscle, but not in liver. These data strongly suggest that pharmacological intervention of Fyn would provide an excellent target for the discovery of novel drugs to treat metabolic disease. Indeed, Yamada et al (9) have shown that the non-specific Fyn kinase inhibitor, SU6656, was able to reduce WAT weight in mice following a single 4mg/kg injection, without affecting lean mass. These findings were consistent with increases in fatty acid oxidation, energy expenditure and respiratory quotient (RQ) observed with SU6656. It is also important to note that the reduced RQ in Fyn KO mice is not reduced further by administration of SU6656".

4. Emphasize the commercial significance in a broader context: "Diabetes and obesity major worldwide health issues. Novel, safe and effective treatments are needed. Recent evidence lends strong support to Fyn kinase as a novel drug target for metabolic disease. Our phase 1 goal is to identify an effective and highly selective inhibitor of Fyn kinase. Even as a small biotech company, we realize the enormous physical and financial effort required to get a small molecule therapy to market. Our phase 2 efforts will provide additional in vivo data necessary for an initial IND. At this stage we will identify a larger pharmaceutical partner to help drive additional pre-clinical and clinical research".

Innovation

In the NIH's instructions to grant writers regarding innovation, they state:

(b) Innovation

- Explain how the application challenges and seeks to shift current research or clinical practice paradigms.
- Describe any novel theoretical concepts, approaches or methodologies, instrumentation or intervention(s) to be developed or used, and any advantage over existing methodologies, instrumentation or intervention(s).
- Explain any refinements, improvements, or new applications of theoretical concepts, approaches or methodologies, instrumentation or interventions.

It must be appreciated that "innovation" does not necessarily mean "new". There are plenty of awarded SBIRs that have taken existing ideas and technology, then applied them to a different problem that itself was or was not new, and that was innovative. Innovation solves a problem in a manner that has not been previously demonstrated. To convince the reviewer that you are breaking new ground, present your project in the context of what is already known and what the problems are. Be clear – make your background section brief but concise, state what is new and revolutionary about your proposal, and use the word "innovative" in your writing. The bullet points above are good guidelines, you do not have to break the section up into subheadings. To be confident that you have a thorough Innovation section, make sure you cover all three points. Here is an example from a funded SBIR grant. Note that a narrative approach was taken:

"The innovation of the project has both a conceptual and a technical aspect. Conceptually, the use of autologous cells for regenerative medicine has been envisioned by others. However, the use of donor-specific cells for multiple cell-based assays is innovative. The population-based approach in developing the platform for toxicological testing is also novel. The main technical innovation is the development of a proprietary cell growth supplement allowing us to derive ECFCs from small volumes of blood." Remember that what you propose in your application must be possible; being too creative can make reviewers skeptical. The best way to fend off this skepticism is the content of your Preliminary Data section, which supports your innovation, and your track record as a scientist, illustrating that your creativity has paid off. Ultimately, how your reviewers respond to your Innovation section depends on how much novelty and risk they are willing to tolerate.

Approach

The Approach section is the heart of your Research Strategy. Here you will provide the details of your research and development to convince reviewers that you know what work needs to be done and that you have the resources and expertise to conduct the investigation.

From the NIH Quick Guide to Grant Applications:

Purpose: The purpose of the approach section is to describe how the research will be carried out. This section is crucial to how favorably an application is reviewed.

Content: The research design and methods section should include the following:

- PI's preliminary studies, data, and experience relevant to the application and the experimental design;
- the overview of the experimental design;
- a description of methods and analyses to be used to accomplish the specific aims of the project;
- a discussion of potential difficulties and limitations and how these will be overcome or mitigated;
- expected results, and alternative approaches that will be used if unexpected results are found;
- a projected sequence or timetable (work plan);
- if the project is in the early stages of development, describe any strategy to establish feasibility, and address the management of any high risk aspects of the proposed work;



"Innovation" does not necessarily mean "new"; innovation solves a problem in a manner that has not been previously demonstrated.
- a detailed discussion of the way in which the results will be collected, analyzed, and interpreted;
- a description of any new methodology used and why it represents an improvement over the existing ones;

Suggestions

Number the sections in this part of the application to correspond to the numbers of the Specific Aims.

- Preliminary data, or a progress report, may be included before the Specific Aims sections. Alternatively, integrate preliminary data with the methods description for each Specific Aim. Preliminary data can be an essential part of a research grant application and helps establish the likelihood of success of the proposed project.
- 2. Avoid excessive experimental detail by referring to publications that describe the methods to be employed. Publications cited should be by the applicants, if at all possible. Citing someone else's publication establishes that you know what method to use, but citing your own (or that of a collaborator) establishes that the applicant personnel are experienced with the necessary techniques.
- 3. If relevant, explain why one approach or method will be used in preference to others. This establishes that the alternatives were not simply overlooked. Give not only the "how" but the "why."
- If employing a complex technology for the first time, take extra care to demonstrate familiarity with the experimental details and potential pitfalls. Add a co-investigator or consultant experienced with the technology, if necessary.
- 5. Explain how the research data will be collected, analyzed, and interpreted as well as any resource sharing plans as appropriate.
- 6. Develop alternative strategies for potential problems.
- 7. Document proposed collaborations and offers of materials or reagents of restricted availability with letters from the individuals involved.
- 8. Point out any procedures, situations, or materials that may be hazardous to personnel and precautions to be exercised (i.e., use of Select Agents).

Since the Approach is so vital to your Research Strategy section, you will end up spending more of your writing time on it compared to the other sections. In turn, this is the section that reviewers will spend most of their time assessing. Potential problems, alternative strategies, and milestones are key elements they will be on the lookout for. Take the time to explain the rationale of each aim, stating why you are doing it and outlining the experiment related to each one. Including a figure or a table is a good idea; it will convey to the reviewer a sense of confidence that you are indeed the expert capable of successfully executing this project. Be sure to relate the different areas of your proposal together, as this will better support your overall application.

Reviewers want to make sure of the following:

- How thorough were you in thinking through the problem you want to solve?
- What is your first action to deal with the problem you want to solve?
- What is the likelihood that this action will work?
- What are the possible things that could go wrong?
- What is your plan for dealing with things that go wrong?

Keeping these questions in mind, and pre-emptively addressing them in your writing, should help you to avoid negative impressions from reviewers such as "applicant is overambitious", "aims are unfocused", "inadequate description of results", and the ultimate show-stopper, "aims are too risky and not supported". You can also use your Approach section to provide details regarding novel aspects of your work.

Regarding the Research Design section, Dr. Gregory Milman, NIAID, goes on to say:

The Research Design section of your Research Plan should spell out in detail what you are going to do, how you are going to do it, and your criteria for success. Reviewers will use this section to evaluate your approach and innovation. Make it easy for reviewers by organizing this section by Specific Aims and include a timeline in table or diagram format to quickly convey your entire project to reviewers. Give a rationale for each set of experiments. Convince reviewers that your methods are appropriate to your Specific Aims. If your methods are innovative, show how you have changed existing or proven methods while avoiding technical problems. Provide supporting data and references.

Describe the kinds of results you expect and how they will support continuation of your project. Present other possible outcomes and contingency plans.

Define the criteria for evaluating the success or failure of each set of experiments. If possible, include statistical analysis as reviewers are impressed by statistics.

Describe hazards anticipated and precautions you propose. Spell out your sources of important reagents and equipment, and details of any use of animals or human subjects. Be sure to follow NIH guidelines.

Explain how credible collaborators will participate in your proposed research

You should include letters that describe collaborators agreements with you, including their role on the project and hours to be committed.

Here is an example from a funded SBIR Phase I application. This is not a full section due to its length, but what is excerpted here should give you a feel for the structure and content. In this case, the applicant has described the overall approach in the opening paragraph, followed it with preliminary data, and then broke the section down addressing each Specific Aim. In this example, only two sections of the first aim are detailed.

Example 1.

Approach

The overall goal of this application is to establish and validate a human satellite cell system for use in a drug discovery program. These Phase 1 efforts will focus on enrichment of the satellite cell population, determining assay parameters and validating the platform by screening a well-annotated chemical library. Successful completion of these studies will be followed by Phase 2 studies that will focus on significantly expanding the screening efforts and a more detailed elucidation\ validation of the pathways involved in muscle regeneration. As described in more

detail below, we have compared the proliferative capacity of satellite cells isolated from elderly subjects (age 65 - 80) with those obtained from young subjects (age 21-30). Our preliminary data show significant differences between the two groups. These observations point to a site of action of at least one mechanism to explain, in part, the differences in regenerative ability between young and elderly muscle tissue. We expect to better understand these molecular mechanisms in the "older" cell population by assessing their response to highly annotated agents that have been shown to act at specific control points in important signaling pathways. Along with prior knowledge from muscle regeneration studies in rodent models, we should be able to pinpoint the pathways most suitable for therapeutic intervention. Overall, this therapeutic area in regenerative medicine is poised for major advancements. A robust human assay system that can measure the effects of agents on aged skeletal muscle progenitor cells will be essential in the search for new drugs to treat muscle wasting conditions.

Aim 1: Optimize the isolation of progenitor satellite cells from human skeletal muscle and create a cell-based assay system to measure proliferation.

Analysis of satellite cell growth. Using the isolation procedures described above, the satellite cells from both young and old donors displayed greater than 90% purity. As shown in Table 2, an increase in the doubling time was observed with satellite cells from old subjects when compared to cells from young subjects. These preliminary data are highly suggestive that a difference exists in proliferative capacity between satellite cells isolated from young vs. elderly donors, and that this defect would most likely be a component in the overall mechanism responsible for decreased skeletal muscle regeneration in elderly subjects. These data were obtained using the CellTiter-Blue assay. While this is an effective method it does not allow us to analyze the potential effects of test agents on commitment of the satellite cells to myoblast differentiation. Thus we will employ high throughput cell imaging that allows us to directly count live cells, and concomitantly analyze transitional states of cell commitment to differentiation (see below) in one assay platform. [Company Name] is a biotech company offering high throughput cell imaging hardware, software and services. We have previously worked with [Dr. PM] in successfully establishing imaging solutions for human adipocytes [14]. Under the current proposal we will extend our collaboration (see letter of support) with [Company Name] to utilize their systems for assessing cell growth and satellite cell commitment. As described in detail above in Preliminary Results, the automated microscopy will be used for counting cells positive for DAPI staining as well as specific antibody staining. In brief, following incubation with test agents (see Aim 2) the cells will be fixed and stained with DAPI. Imaging of the stained cells is performed using a Beckman Coulter IC1000 image cytometer with a 10x objective and a digital camera using 2x2 binning [14]. Multiple images will be taken per well and then stitched together using Vala's CytSeer software. The same software determines the number of positively stained nuclei per well using a specific counting algorithm. This high content screening application can acquire images from 140,000 wells/day; reading over 350 384-well plates.

As can be seen from the example above, this applicant included Preliminary Data, which was included immediately after the paragraph explaining the overall approach, just before diving into the Specific Aims. Dr. Gregory Milman, NIAID, who has made several presentations to help businesses successfully compete for SBIR and STTR awards, offers another suggestion for the Approach section:

Although the SBIR/STTR solicitation states that "Preliminary data are not required," most applications include preliminary data. Review committees are likely to have greater enthusiasm for proposals with good preliminary data. Poorly presented or poorly interpreted preliminary data can hurt your score.

Include preliminary studies that support the feasibility of your project. They may consist of your own publications and those of others, as well as unpublished data from your laboratory. To improve your "Investigator" score, emphasize work you have accomplished that indicates you can direct the proposed research and achieve your Specific Aims. Interpret results critically and evaluate alternative meanings but do not over interpret. You can be assured that critical members of the review committee will look for explanations other than the ones you propose.

The preliminary studies section of your Research Plan should convince reviewers that your approach could work. Reviewers may also use your work described in this section to assess the investigator criterion.

Be aware that the Phase I progress report in your Phase II application will list the milestones proposed and achieved in Phase I.

What this means:

Include preliminary data. More than likely you will be fighting a losing battle to convince the reviewers that you have something worth funding if you do not show them anything to support your approach.

Here is an example of Preliminary Data from the same grant example above:



TIP:

Although not required, review committees are likely to have greater enthusiasm for proposals that include good preliminary data.

Preliminary Data.

Enrichment of CD56+ cells. Based on modifications of our existing protocols [12], we have established procedures to enrich the isolation of satellite cells from skeletal muscle tissue. In this procedure, one gram of skeletal muscle tissue was used as a source of CD56+ satellite cells. The donor tissue is washed, minced, and digested with 0.2% trypsin / 0.1% collagenase in HBSS + 1% BSA. Following digestion, the liberated cells are pelleted by centrifugation, washed extensively and resuspended in a minimal amount of PBS/BSA and blocked with human FcR blocking reagent (Miltenyi Biotec). After a round of filtration to remove any remaining cellular debris, the single cell suspension is incubated with a mouse monoclonal anti-CD56. A separate small aliquot of the cell suspension is incubated in parallel with mouse IgG as a control. Following incubation at 4°C, unbound antibody is removed by washing and rat antimouse IgG-coupled magnetic Microbeads (Miltenyi Biotec) are added to the cell suspensions. After a brief incubation, the microbeads are isolated by magnetic separation and washed following manufacturer's protocols. CD56+ cells are retained on the beads and washed as the unbound cells passed through the separation column. Retained cells are collected by removing the magnetic field and resuspending in PBS/ BSA. Following a typical isolation, 1-2% of the total cell population in the tissue digest can be specifically isolated by the CD56 antibody under these conditions (Table 1).

Table 1. CD56+ Cell Enrichment

Skeletal Muscle Tissue in Grams	1.0 g
Total cells liberated by enzymatic digestion	~10 million
Cells specifically isolated using CD56 antibody	176,000
Percent CD56+ population	1-2%

As per Dr. Milner's suggestion regarding a timeline in a table format, an example is provided below:

Timeline:

Study Event	Month 1-2	Month 3-9	Month 6-11	Month 9-12
Protocol Set up	Х			
Experiments		Х		
Data Analysis			Х	
Report Preparation				X

Overall Impact Ties Everything Together

Taken from NOT-OD-09-025:

- Overall Impact is the synthesis/integration of the five core review criteria that are scored individual and the additional review criteria which are not scored individually.
- To evaluate, the reviewer(s) make an assessment of the likelihood for the project to exert a sustained, powerful influence on the research field(s) involved, in consideration of the scored review criteria, and additional review criteria (as applicable for the project proposed).
 - o Likelihood (i.e., probability) is primarily derived from the investigator(s), approach and environment criteria.
 - o Sustained powerful influence is primarily derived from the significance and innovation criteria.
 - Research field(s) may vary widely, so it would be helpful if reviewers identify in their reviews the research field(s) they believe will be influenced by each project.

What this means:

Reviewers have been tasked to determine the probability that the experiments you propose will succeed. If they do not succeed, there will be no impact, regardless of whether the research is highly significant.

The NIH provides the following case study to illustrate the difference between Significance and Overall Impact:

Case Study #1:

An investigator proposes using a novel method of viral vector-mediated siRNA delivery to knock-down the gene for a particular CNS receptor subtype in specific brain regions he/she hypothesizes to be involved in cognitive aspects of a rare mental illness. He/she proposes to use this method to examine disruption of this receptor subtype on cognitive performance in three animal models of the illness.

Scenario 1:

A. Reviewer 1 is an expert on research of the rare mental illness. He argues that the PI has previously confirmed the proposed hypothesis using pharmacological and genetic approaches. This reviewer felt that the successful accomplishment of the proposed aims would very minimally advance knowledge in the field of study devoted to the rare mental illness. Thus, Reviewer 1 feels the application is of low significance. Reviewer 1 notes that the proposed method is highly innovative, that the models used are appropriate, and that the investigator and environment are strong. Nevertheless, in light of the low Significance of the proposal, Reviewer 1 feels the Overall Impact would be modest and scores accordingly.

B. Reviewer 2 is an expert on viral vector-mediated siRNA delivery methods. He disagrees that the project's significance is low. He concedes that the proposed hypothesis has already been confirmed in the investigator's previous work. He argues, however, that the proposed technique is highly innovative and if successful, has the potential not only to transform the way scientists manipulate receptor function in the laboratory, but also has potential to provide the foundation for clinical application for many diseases. He suggests that the proposed replication of previous findings is actually a strength because it would confirm the successful implementation of the highly innovative methods. Thus, on the basis of the work's potential to transform technical capability and shape clinical practice in the future, Reviewer 2 argues that the application has high Significance. On the basis of high Significance and strengths in the other review criteria, Reviewer 2 believes the Overall Impact should be rated as high.

Scenario 2:

Both reviewers agree that the application addresses an important problem and that the hypothesis and methods are highly innovative. They believe that if the proposed aims were achieved, the project would significantly advance knowledge in the field and promote substantially new research directions in research on the rare mental illness as well as the broader field of mental health. Therefore, they rate Significance as high. They have strong reservations, however, about the application relative to other review criteria. The investigator and his/her colleagues do not appear to have the relevant training and expertise to successfully accomplish the work and there are some flaws in the approach that may reflect their inexperience with critical methods. Therefore, they rate the Overall Impact as moderate.

There is no set or standard rule that reviewers use to equate your individual criterion scores to your overall impact score. It is likely that each reviewer will rate each criterion somewhat differently. Your impact score can be based almost entirely on your experimental approach, or on Innovation and Significance, it all depends on the reviewer's preferences.



TIP:

You might want to include an "impact statement" somewhere in each of the five scored criteria sections.

Impact Should 'Come Through' When Reading the Proposal

Impact should be clearly described throughout the application. Use whatever terms are relevant to your proposed project. Reviewers want to be sure that you are tackling an opportune and critical problem that can be completed in the time period of the award with the available resources and those requested. You might want to include an "impact statement" somewhere in each of the five scored criteria sections. For example, in the innovative section, for developing a new drug delivery device, you may say "To our knowledge, this device has not been used as a means to promote the transient, non-invasive, and targeted delivery of therapeutic compounds in human patients. Using localized/site-directed treatment, as described in this proposal, there is an extraordinary opportunity to control biodistribution and enhance the effect of chemotherapeutic drugs by increasing tissue penetration and subsequent cell permeability".

Likewise, the Project Summary/Abstract section is also a good place, since it is one of the first elements of your application reviewers will read. For example: "Successful completion of these specific aims will establish proof-of concept to justify moving forward with the design and manufacture of a novel drug delivery device for the clinic, capable of locally directing biodistribution of cellimpermeable molecules to tumor areas."

Bibliography and References

Directly from SF424 (R&R) SBIR/STTR Application Guide for NIH and Other PHS Agencies (updated November 1, 2013):

Bibliography & References Cited

Provide a bibliography of any references cited in the Project Narrative. Each reference must include the names of all authors (in the same sequence in which they appear in the publication), the article and journal title, book title, volume number, page numbers, and year of publication. Include only bibliographic citations. Applicants should be especially careful to follow scholarly practices in providing citations for source materials relied upon when preparing any section of the application.

Unless otherwise noted in an FOA, this section is required for submissions to NIH and other PHS agencies. This section (formerly "Literature Cited") should include any references cited in the PHS 398 Research Plan form (see Section 5.4 for details on completing that form). When citing articles that fall under the Public Access Policy, were authored or co-authored by the applicant and arose from NIH support, provide the NIH Manuscript Submission reference number (e.g., NIHMS97531) or the PubMed Central (PMC) reference number (e.g., PMCID234567) for each article. If the PMCID is not yet available because the Journal submits articles directly to PMC on behalf of their authors, indicate "PMC Journal – In Process." A list of these journals is posted at: http://publicaccess.nih.gov/submit_process_journals.htm.

Citations that are not covered by the Public Access Policy, but are publicly available in a free, online format may include URLs or PubMed ID (PMID) numbers along with the full reference (note that copies of publicly available publications are not accepted as appendix material). The references should be limited to relevant and current literature. While there is not a page limitation, it is important to be concise and to select only those literature references pertinent to the proposed research.

What this means:

Full references are provided so that reviewers can access them on online. Do not include any copies of publications whether they are available on line or not; Phase I SBIR applications are not to include appended materials unless specifically asked for by the agency.

Here is an abbreviated example of a Bibliography from a funded SBIR application:

- Bauer, J.M. and C.C. Sieber, Sarcopenia and frailty: a clinician's controversial point of view. Exp Gerontol, 2008. 43(7): p. 674-8.
- 2. Morley, J.E., D.R. Thomas, and M.M. Wilson, Cachexia: pathophysiology and clinical relevance. Am J Clin Nutr, 2006. 83(4): p. 735-43.
- Rantanen, T., R. Sakari-Rantala, and E. Heikkinen, Muscle strength before and mortality after a bone fracture in older people. Scand J Med Sci Sports, 2002. 12(5): p. 296-300.
- Janssen, I., et al., The healthcare costs of sarcopenia in the United States. J Am Geriatr Soc, 2004. 52(1): p. 80-5.
- Inui, A., Cancer anorexia-cachexia syndrome: current issues in research and management. CA Cancer J Clin, 2002. 52(2): p. 72-91.
- McKinnell, I.W. and M.A. Rudnicki, Molecular mechanisms of muscle atrophy. Cell, 2004. 119(7): p. 907-10.

CONCLUSION

Take the time and effort needed to write the Research Strategy section of your proposal. Significance, Innovation and Approach are all scored criteria the reviewers will use to decide the fundability of your project and its value to your scientific field, technology development, and commercialization. In addition, your project's Overall Impact score will likely depend heavily on what you write in these sections.

Chapter 5: Special Considerations

The SBIR program does not generally support human clinical studies, especially in a Phase I application. Exceptions to this generality may be found in funding opportunity announcements, and even then funding for clinical studies is usually restricted to Phase II projects, nonetheless, your project may still involve samples or data from human subjects. If so, you must inform the agency by completing specific portions of the application regarding this use. Similarly, if your work involves the use of vertebrate animals, in this case as actual test subjects or as a source of tissue samples, there are a different set of forms that need to be filled out. Both you and your company must assure the NIH that human and animal test subjects will be protected. NIH cannot award any grant until such assurances are on file with the agency.

In reading over the guidelines, it seems apparent that they were developed with academic institutions in mind. This makes sense, as most of the extramural NIH funding awards are made to academic scientists. Unlike large universities, small companies eligible for the SBIR program seldom if ever have the resources to conduct human clinical studies on their own; they would subcontract that work to another vendor, perhaps even a university. The same holds true for animal studies; the expense and infrastructure involved to have an animal facility is almost always too steep for a small company to invest resources in, so this work would be contracted out. Nonetheless, any company engaged in non-exempt human subjects research conducted or supported by the NIH must submit a written assurance of compliance to the Office of Human Research Protections (OHRP). The Federalwide Assurance (FWA) is the only type of assurance of compliance accepted and approved by OHRP. (See http://www.hhs.gov/ohrp for further information.) If your project includes vertebrate animal work at a subcontractor site, and the subcontractor has an Institutional Animal Care and Use Committee (IACUC) approval for the animal work, you will need an Interinstitutional Agreement before an award can be made. The NIH's Office of Laboratory Animal Welfare (OLAW) negotiates



The SBIR program does not generally support human clinical studies. Interinstitutional Agreement Assurances of Compliance when an awardee institution, in this case your company, without an animal care and use program will rely on a research partner to conduct the animal work. This agreement insures that all involved parties are aware of their responsibilities regarding animal use and proper procedures are followed.

This chapter will cover your responsibilities with respect to informing the agency about your use of human subjects and vertebrate animals. As mentioned above, since SBIR awards do not support clinical trials, the main purpose for the human subjects' forms in the application, what you have to provide to the agency for an SBIR is abbreviated compared to other NIH grant applications. The same is true for SBIR projects that propose to use vertebrate animals.

Human Subjects

According to the DHHS IRB Guidebook, conducting a controlled study involving human subjects, designed to evaluate prospectively the safety and effectiveness of new drugs or devices or of behavioral interventions, is a clinical trial. Regarding human subjects, the Code of Federal Regulations (45 CFR 46.102(f) states "Human subject means a living individual about whom an investigator (whether professional or student) conducting research obtains:

- (1) data through intervention or interaction with the individual, or
- (2) identifiable private information." (45 CFR 46.102(f))

What it means:

Intervention includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. Interaction includes communication or interpersonal contact between investigator and subject. Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.

What is meant by "publicly available sources"?

This language in the regulation was intended to apply to public sources of data, such as census data. Its meaning with respect to human tissue specimens is widely debated, and to date there is no firm position by the agency. This question comes about because there are organizations that make human cells and tissues broadly accessible to the research community, yet these materials are not usually available to the public at large and are not generally considered to be publicly available.

Deciding Whether You Have Human Subjects in Your Research Plan or Not

Supplemental SF-424 (R&R) Instructions for Preparing the Human Subjects Section of the Research Plan provides the following scenarios, and how to address them in the application:

Scenario A. No Human Subjects Research

If no human subjects research is proposed in the application, you will have designated **No** in Item 1 on the SF424 R&R Other Project Information page. If your proposed research involves the use of human data and/or biological specimens, you must provide a justification for your claim that no human subjects are involved in the Protection of Human Subjects section of the Research Plan. See the <u>instructions for Scenario A</u>. Unless you are providing a special justification as described above, no additional information is necessary if no human subjects are involved.

What it means:

(Instructions for Scenario A) If you are planning on using human data or human tissue, you need to provide a justification as to why you state that no human subjects are involved. The justification could include a description of the source of the data/ biological specimens; whether any intervention or interaction with the subjects took place by you to obtain the specimens and data; what identifiers will be associated and who will have access to them; the role(s) of providers of the data/biological specimens in the proposed research; and the manner by which the privacy of research participants and confidentiality of data will be protected.

Research that does not involve intervention or interaction with living individuals, or identifiable private information, is not human subjects research.

Research involving the use of coded private information or biological specimens may not constitute human subjects research if the conditions of the OHRP Guidance on Research Involving Coded Private Information or Biological Specimens have been met (http://www.hhs.gov/ohrp/policy/cdebiol.html), whereby access to this private information is controlled and secure.

Research that only proposes the use of cadaver specimens is not human subjects research because human subjects are defined as "living individuals." The use of cadaver specimens is not regulated by 45 CFR part 46, but may be governed by other Federal, State or local laws.

This scenario seems to be the most common one for SBIRs, involving tissue samples or data from a third party, not the awardee. In such cases, the third party has to assure you, the awardee that human subjects are not involved, based on the agency's definition above. However, it is still your responsibility as the awardee to verify this information that no human subjects are involved.

Scenario B. Non-Exempt Human Subjects Research

If research involving human subjects is anticipated to take place under the award, you will have designated **Yes** in Item 1 on the SF424 R&R Other Project Information page and entered your OHRP assurance number in Item 1a. In the Protection of Human Subjects section of the Research Plan, you must provide sufficient information for reviewers to determine that the proposed research meets (1) the requirements of the DHHS regulations to protect human subjects from research risks (45 CFR part 46), and (2) the requirements of PHS policies on inclusion of women, minorities, and children. See the instructions for Scenario B.



Research that only proposes the use of cadaver specimens is not human subjects research because human subjects are defined as "living individuals."

What it means:

(Instructions for Scenario B). In the application narrative, provide the required information for each of the following topics below.

- Protections of Human Subjects
- Inclusion of Women and Minorities
- Targeted/Planned Enrollment
- Inclusion of Children

If your project involves collaborating sites or subprojects, this information needs to be included for each participating site.

Clinical studies fall under this category, and remember, the SBIR program does not generally support clinical studies. However, your proposed project may meet the NIH definition of "Clinical Research":

Research with human subjects that is:

1. Patient-oriented research. Research conducted with human subjects (or on material of human origin such as tissues, specimens, and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. Excluded from this definition are in vitro studies that utilize human tissues that cannot be linked to a living individual. It includes:

- mechanisms of human disease
- therapeutic interventions
- clinical trials
- development of new technologies
- 2. Epidemiological and behavioral studies.
- 3. Outcomes research and health services research.

Studies falling under 45 CFR part 46.101(b) (4) (Exemption 4) are not considered clinical research by this definition.

If your work falls into this category, below is an example from a funded SBIR on how to address the requested information:

Protection of Human Subjects

1. RISKS TO THE SUBJECT

A. Human Subjects Involvement and Characteristics

- When subjects undergo elective surgery they will be asked if a small sample of breast tissue removed during the course of the surgery could be used in this study. If they say yes and sign the consent form, the sample is removed, placed in a container and relevant medical information such as type of surgery, patient demographics, current medications, and medical history is included with the sample. The patient has no further involvement with the PI or any part of this study. No information about the patient's identity is passed to the PI by the surgeon. At no time is information such as case numbers, social security numbers, insurance information, names, or addresses passed on to the PI. The PI can in no way contact the patient, request additional information from the patient, or interact with the patient in any way.
- The subject population will be drawn from subjects undergoing volunteer surgery. We anticipate that over the period of research a minimum of 30 subjects will be involved. The age range is difficult to predict though we will be accepting tissue from patients as young as 18. We anticipate the age characteristics to closely mirror those that we have received over a randomly selected 4 months in 2004. They are: age range 21-66 with a mean age of 42.65 modal age of 40 and median age of 41 with 51 samples from females and 15 samples from males. Of those samples, 3 were African American, 2 were Hispanic, 3 were unknown, and 58 were Caucasian. The health status is variable and may be influenced by being obese.
- All patients who are undergoing elective surgery with our participating surgery groups will be given the opportunity to participate in this study. People under the age of 18 are excluded as explained in the inclusion of children section below. Additionally, we will remove tissue that tests positive for HIV1, HIV 2, HTLV 1, HTLV 2, HBV, or HVC. The reason for excluding these patients is the unknown affect these disease states have on the

proliferation of mesothelial cells. Those studies should be undertaken under a separate research program once parameters for normal growth parameters are determined.

• There are no classes of subjects that will be specifically included or excluded as a part of this research with the exception of those under the age of 18 addressed elsewhere.

B. Sources of Materials

- The materials obtained from living human beings are breast tissue samples
- removed during the course of elective breast-reduction surgery. The samples are expected to range in size from 50-100 grams. Data will be recorded about the type of surgery along with information about the patient.
- Data to be received and recorded by [Company Name] about patients
 is limited to the following: age, race, gender, height, weight, smoking /
 non-smoking, diabetic / nondiabetic, current medication(s). Additional
 information about the sample will be recorded including specimen size, the
 location it was removed from, surgeon who performed the surgery, date of the
 surgery, date the sample was processed, and the results of pathogen testing
 once it is completed.
- There is no easy or established way to link a tissue lot number back to a patient. No personally identifiable patient information is stored at [Company Name] which will associate a particular patient with a particular [Company Name] issued tissue lot number. The surgical groups working with [Company Name] have no information about [Company Name] tissue lot numbers or any way to connect an individual patient with a tissue lot number. It is extremely unlikely, but within the realm of possibility, that a patient may be able to be linked with a tissue sample. To do that, a person would have to have the willing participation of both [Company Name] and the surgical group. Patients have been warned about this potential loss of confidentiality in IRB approved patient consent forms. Additionally, in the 12 years [Company Name] has been collecting tissue samples using this protocol, no patient has lost confidentiality.

• A consented patient will have a sample of breast tissue removed during voluntary surgery ranging in size from approximately 50-100 grams. The surgeon will remove this tissue, place it in a specimen cup with media and then send it to the PI for research. The sample is surgical waste tissue and would otherwise be discarded. Data about the patient will be recorded as outlined in bullet point 2 above. This information has already been collected from the surgeon prior to surgery as a regular part of the procedure and is being provided to the PI in order to better understand how different factors influence the growth of human cells in culture.

C. Potential Risks

 Risks to patients as a result of participating in this study are minimal. No health risks in addition to the ones already assumed for the elective surgery have been experienced or identified as possibilities. Breast samples removed generally aren't large and in all cases are, in point of fact, surgical remnants. There are no reasonably anticipated social, psychological, legal, ethical, or other risks identified with participating in this study.

a. Recruitment and Informed Consent

- Subjects are recruited from patients undergoing elective surgery. Written
- consent will be obtained by a Registered Nurse (RN) during the course of completing surgical paperwork. The RN will go through the consent form and ask the patient if they have any questions about the research. The patient is then given the opportunity to review the form, ask any additional questions and sign the form if they so desire. No patients except for those under the age of 18 will be excluded from the study.
- Consent will be obtained by a RN working with the surgical group and documented by the patient's signature on the consent form. The forms are maintained by the surgical group and the PI will at no time have access to the forms. Information to be provided includes: Purpose of the study, procedures to be followed, risks associated with the study, how to withdraw consent if the patient changes their mind, the fact that there is no financial or diagnostic

benefit to the patient, alternatives to participation in the study, how to contact the MD with any questions about the study, the fact that there are no costs to the patient for the study, and that [Company Name] pays for the costs the hospital or surgery group may incur while participating in the study.

b. Protection Against Risk

 No additional reasonable risks beyond loss of confidentiality have been identified. While the risk of losing confidentiality exists it has been minimized by not maintaining patient information at [Company Name] or maintaining [Company Name] tissue lot numbers at the surgical center's site. There is no established protocol for the patient to be identified utilizing only the information possessed by [Company Name] or only the information at the surgical center site. Additionally [Company Name] has been collecting tissue from voluntary surgery patients using this protocol for over 12 years and has not had any issues with loss of confidentiality.

2. POTENTIAL BENEFITS OF THE PROPOSED RESEARCH TO THE SUBJECTS AND OTHERS

- The patient is not expected to benefit directly from participation in the study. The information gained from the study will not be used in the diagnosis or treatment of their current problem. There is no payment or reimbursement paid to the patient for their participation in the study. [Company Name] pays for costs the hospital or surgery group may incur while participating in the study.
- The risk of loss of confidentiality is the only identified risk for participation in the study. The patient, with full knowledge of that risk, chooses to donate the tissue without any financial compensation. One can only guess at the otivation of the patient to participate. However, it is presumed that many participants are well informed about breast cancer and the importance of research in its prevention. Therefore, this research may be personally important enough to them to take on the risk of losing confidentiality.

3. IMPORTANCE OF THE KNOWLEDGE TO BE GAINED

- The outcomes of study will be a robust, well characterized human-based platform for discovering the causes of and treatments for various forms of breast cancer.
- The patient has accepted the risk of loss of confidentiality as being reasonable for participation in the study. [Company Name] and the PI have taken steps to minimize that risk and believe that the likelihood of the loss of confidentiality has been successfully mitigated. The importance of a well validated human mammary-derived basal/luminal cell discovery platform cannot be understated. The value of being able to validate or eliminate compounds in a cultured human primary cell model is both economic and health related. There is currently no human primary basal/luminal culture system on the market in the U.S. The development and availability of this system will provide advancements in existing research and establish new areas of research.

Inclusion of Women and Minorities

Tissue samples taken for this set of protocols will be from elective surgery patients. Due to the nature of elective surgery, we are unable to accurately predict the percentages of women or minorities that will participate in this study. However, no tissue samples will be rejected based on gender or minority status. The expected patient demographics are discussed in the human subjects section of this application.

Targeted/Planned Enrollment

Tissue will be procured from elective surgeries with no targeted population for the study. No tissue samples will be rejected based on donor demographics.

Inclusion of Children

We are including children in this study for the following reasons. The current protocols involve taking human material while receiving an elective surgical procedure. As this is an elective procedure and the tissue is surgical waste tissue we there should be no health risks associated with participating in the study. Only children from 18 - 21 will be included in this study since our surgical practices do not routinely have patients under 18 undergoing breast reduction surgeries.

Scenario C. Exempt Human Subjects Research

If **all** of the proposed human subjects research meets the criteria for one or more of the exemptions from the requirements in the DHHS regulations (46.101(b)), Yes should be designated in Item 1 on the SF424 R&R Other Project Information page, the appropriate exemption number checked in Item 1a, and "NA" entered for the Human Subject Assurance Number since no OHRP assurance number is required for exempt research. In the section on Protection of Human Subjects in the Research Plan, provide a justification for the exemption(s) containing sufficient information about the involvement of the human subjects to allow a determination by peer reviewers and HRSA staff that claimed exemption(s) is/are appropriate.

The PHS will make a final determination as to whether the proposed activities are covered by the regulations or are in an exempt category, based on the information provided in the Research Plan. When in doubt, consult with the Office for Human Research Protections (OHRP), Department of Health and Human Services by accessing their Web site <u>http://www.hhs.gov/ohrp/</u> for guidance and further information. The six categories of research exempt from the DHHS human subjects regulations are found at the end of this document. Please note: If the proposed research involves only the use of human data or biological specimens, you should first determine whether the research involves human subjects. The exemptions do not apply if the research does not involve human subjects. See the instructions for Scenario C.

The exemptions are:

Exemption 1: Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

Exemption 2: Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior, unless: (i) information obtained is recorded in such a manner that human subjects can be identified directly or through identifiers linked to the subjects and (ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

Exemption 2 for research involving survey or interview procedures or observation of public behavior, does not apply to research with children (see <u>45</u> <u>CFR part 46</u>, <u>Subpart D</u>), except for research involving observations of public behavior when the investigator(s) do not participate in the activities being observed.

Exemption 3: Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (b)(2) of this section if: (i) the human subjects are elected or appointed public officials or candidates for public office; or (ii) Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

Exemption 4: Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

The humans subjects regulations decision charts (<u>http://www.hhs.gov/ohrp/</u> <u>policy/checklists/decisioncharts.html</u>) of the Office for Human Research Protection (OHRP) will determine whether the research falls under the human subjects regulations and if so, whether it meets the criteria for Exemption 4. Research that meets the criteria for Exemption 4 is not considered "clinical research" as defined by PHS. Therefore the PHS policies for inclusion of women, minorities and children in clinical research, do not apply to research projects covered by Exemption 4.*SF*-424 (*R*&*R*) Supplemental Instructions Human Subjects 21.

Exemption 5: Research and demonstration projects that are conducted by or subject to the approval of Department or Agency heads and that are designed to study, evaluate, or otherwise examine: (i) public benefit or service programs (ii) procedures for obtaining benefits or services under those programs (iii) possible changes in or alternatives to those programs or procedures or (iv) possible changes in methods or levels of payment for benefits or services under those programs. Note: It is uncommon for investigators applying for a PHS grant to qualify for this exemption. Please seek guidance from HRSA staff if you think your project is eligible for Exemption 5.

Exemption 6: Taste and food quality evaluation and consumer acceptance studies (i) if wholesome foods without additives are consumed or (ii) if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural, chemical, or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

What it means:

While there is no specific page limitation for this section of the application, be brief. While your research may be exempt from the DHHS regulatory requirements, it is still research which involves human subjects, and the application must follow the instructions for each of the following topics and provide the information that is requested. In the application narrative, provide the required information for each of the following topics below: Protections for Human Subjects – Include the following statement: 'This Human Subjects Research falls under Exemption(s)' Clearly identify which exemption(s) (1, 2, 3, 4, 5, 6) you are claiming, and justify why the research meets the criteria for exemption that you have claimed.

For SBIR applications claiming Exempt Human Research Studies, Exemption 4 is the most appropriate for those studies using human tissue specimens.

Additional Form

If, however, your project includes women and minorities, and if you answered "Yes" to the question "Are human subjects involved, and your research and development project does not fall under Exemption 4, you will need to complete the Planned Enrollment Report illustrated below.

Planned Enrollment Report

This report format should NOT be used for collecting data from study participants.

Study Title:

Domestic/Foreign: Domestic

Comments:

	Ethnic Categories				
Racial Categories	Not Hispanic or Latino		Hispanic or Latino		Total
	Female	Male	Female	Male	
American Indian/ Alaska Native					0
Asian					0
Native Hawaiian or Other Pacific Islander					0
Black or African American					0
White					0
More Than One Race					0
Total	0	0	0	0	0

PHS 398 / PHS 2590 (Rev. 08/12 Approved Through 8/31/2015) Page OMB No. 0925-0001/0002 Planned Enrollment Report

Use of Vertebrate Animals

If you propose the use of live vertebrate animal in your research and development plan, reviewers will need to evaluate how you will involve them. To adequately do so, you must provide additional documentation to support using the animals. This information will be provided as a separate document to upload when completing your application.

Direct from NIH:

This section is required for applicants answering "Yes" to the question "Are vertebrate animals involved?" on the R&R Other Project Information form. If Vertebrate Animals are involved in the project, address each of the five points below. This section should be a concise, complete description of the animals and proposed procedures. While additional details may be included in the Research Strategy, the responses to the five required points below must be cohesive and include sufficient detail to allow evaluation by peer reviewers and NIH staff. If all or part of the proposed research involving vertebrate animals will take place at alternate sites (such as project/performance or collaborating site(s)), identify those sites and describe the activities at those locations. Although no specific page limitation applies to this section of the application, be succinct. Failure to address the following five points will result in the application being designated as incomplete and will be grounds for the PHS to defer the application from the peer review round. Alternatively, the application's impact/priority score may be negatively affected.

If the involvement of animals is indefinite, provide an explanation and indicate when it is anticipated that animals will be used. If an award is made, prior to the involvement of animals the grantee must submit to the NIH awarding office detailed information as required in points 1-5 below and verification of IACUC approval. If the grantee does not have an Animal Welfare Assurance, then an applicable Animal Welfare Assurance will be required (see Part III Section 2.2 Vertebrate Animals for more information). The five points are as follows:

- 1. Provide a detailed description of the proposed use of the animals in the work outlined in the Research Strategy section. Identify the species, strains, ages, sex, and numbers of animals to be used in the proposed work.
- 2. Justify the use of animals, the choice of species, and the numbers to be used. If animals are in short supply, costly, or to be used in large numbers, provide an additional rationale for their selection and numbers.
- 3. Provide information on the veterinary care of the animals involved.
- 4. Describe the procedures for ensuring that discomfort, distress, pain, and injury will be limited to that which is unavoidable in the conduct of scientifically sound research. Describe the use of analgesic, anesthetic, and tranquilizing drugs and/or comfortable restraining devices, where appropriate, to minimize discomfort, distress, pain, and injury.
- 5. Describe any method of euthanasia to be used and the reasons for its selection. State whether this method is consistent with the recommendations of the American Veterinary Medical Association (AVMA) Guidelines on Euthanasia. If not, include a scientific justification for not following the recommendations.

Do not use the vertebrate animal section to circumvent the page limits of the Research Strategy.

What it means:

This section should be a brief, yet complete, description of the animals and proposed procedures they will be subjected to. The agency wants you to address the following five points:

1. A detailed description of how you propose to use the animals, complete with identification of the species, strains, ages, sex, and numbers of animals planned to be used.

Here is an example of how this may read:

"Cultured glioma cells will be used to induce tumors in the brains of adult Fischer rats. Blood brain barrier (BBB) impermeable cisplatinum, administered systemically followed by localized microwave irradiation, will be used to test microwave-assisted delivery of the drug across the BBB and its effect on glioma mass in vivo. The microwave procedure and duration used does not generate heat, thus adding no additional discomfort to the animal. Standard procedures for generating glioma tumors in rats will be followed. A total of 12 rats will be used for this study. Control group will have 3 males and 3 females, experimental group will consist of the same".

2. Justification for animal usage, choice of species and the numbers you plan to use. If animals are not abundant, expensive, or to be used in large numbers, provide an additional rationale regarding why you selected them and at the numbers you indicate.

Here is an example of how this may read:

"Experimental animals are needed because there are no mathematical, computer or *in vitro* biological models that can simulate the BBB permeability to compounds. Rats are the standard model for gliomas. The scope of the proposed work requires this modest number of rats for the planned assays".

3. Veterinary care of the animals

For example:

"Rats will be housed in the pathogen-free animal care facility at [University Name]. The facility is an approved facility of the State University system. The animals will be cared for following the procedures for adequate maintenance and veterinary care as described in "Guide for the Care and Use of Laboratory Animals," HHS, NIH Pub. No. 86-23, 1985".

4. Describe the procedures for ensuring that discomfort, distress, pain, and injury will be limited to that which is unavoidable in the conduct of scientifically sound research.

Here is an example:

"Animals will be comfortably restrained in a stereotactic device for cell injections into the cranium, as well as injections of compound into the femoral vein. Animals will be placed in a comfortable shielding tube so that microwave energy, which does not generate heat at the wattage and duration used, is localized to the tumor-containing area only".

Animals will be sedated as indicated below:

MATERIAL	Ketamine	Xylazine
FREQUENCY	Once, PRN	Once, PRN
DOSE (mg/kg)	100 mg/kg* with supple- mental doses of 30 mg/ kg**	3 mg/kg* with supple- mental doses of 1 mg/ kg**
ROUTE	IP	IP
CONCENTRATION	33.3 mg/ml	3.3 mg/ml

*initial dosing

**Supplemental dosing every 15 to 20 minutes to maintain anesthesia

5. Describe any method of euthanasia to be used and the reasons for its selection.

Please see following example:

"All rats to be used for the experiments described in this proposal will be sacrificed by methods consistent with the recommendations of the Panel on Euthanasia of the American Veterinary Medical Association". Be aware that if you choose not to address these five points, your application may be considered incomplete and therefore removed from its scheduled round of peer review. Alternatively, your impact/priority score could be negatively affected. If you are unsure whether your research will require the use of vertebrate animals, you must still complete this additional document. Include an explanation, and indicate when you anticipate you will use animals. If your grant is awarded, you must submit to the awarding office detailed information covering the five points above and verify approval by your IACUC — all before you may involve animals in your research.

What About the Use of "Select Agents"?

As in the case of using human or animal test subjects, you must create additional documentation — which you will upload as a separate document — if your research involves using "Select Agents." These are hazardous biological agents and toxins that the U.S. Department of Health and Human Services (HHS) and Department of Agriculture (USDA) identify as having the potential to pose a severe threat to public health and safety, to animal and plant health, or to animal and plant products. You can find a list of these agents, at the National Select Agent Registry website (<u>http://www.selectagents.gov/SelectAgentsandToxinsList.html</u>).

Direct from NIH:

Select Agents are hazardous biological agents and toxins that have been identified by DHHS or USDA as having the potential to pose a severe threat to public health and safety, to animal and plant health, or to animal and plant products. CDC maintains a list of these agents. See <u>http://www.selectagents.gov/</u><u>SelectAgentsandToxinsList.html</u>

If the activities proposed in the application involve only the use of a strain(s) of Select Agents which has been excluded from the list of select agents and toxins

as per 42 CFR 73.3, the Select Agent requirements do not apply. Use this section to identify the strain(s) of the Select Agent that will be used and note that it has been excluded from this list. The CDC maintains a list of exclusions at http://www.selectagents.gov/SelectAgentsandToxinsExclusions.html

If the strain(s) is not currently excluded from the list of select agents and toxins but you have applied or intend to apply to DHHS for an exclusion from the list, use this section to indicate the status of your request or your intent to apply for an exclusion and provide a brief justification for the exclusion.

If any of the activities proposed in your application involve the use of Select Agents at any time during the proposed project period, either at the applicant organization or at any other performance site, address the following three points for each site at which Select Agent research will take place. Although no specific page limitation applies to this section, be succinct.

- 1. Identify the Select Agent(s) to be used in the proposed research.
- Provide the registration status of all entities* where Select Agent(s) will be used.
 - If the performance site(s) is a foreign institution, provide the name(s) of the country or countries where Select Agent research will be performed. *An "entity" is defined in 42 CFR 73.1 as "any government agency (Federal, State, or local), academic institution, corporation, company, partnership, society, association, firm, sole proprietorship, or other legal entity."
- 3. Provide a description of all facilities where the Select Agent(s) will be used.
 - Describe the procedures that will be used to monitor possession, use and transfer of the Select Agent(s).
 - Describe plans for appropriate biosafety, biocontainment, and security of the Select Agent(s).
 - Describe the biocontainment resources available at all performance sites.
 - If you are responding to a specific funding opportunity announcement (e.g., PA or RFA), address any requirements specified by the FOA.
Reviewers will assess the information provided in this Section, and any questions associated with Select Agent research will need to be addressed prior to award.

What it means:

Check this document to see if what you plan to use is on the excluded list. If so, this section does not apply to you, so you do not need to provide the requested information. The exclusions list can be found at: http://www.selectagents.gov/ SelectAgentsandToxinsExclusions.html. If the strain(s) is not currently excluded from the Select Agent list but you have applied or intend to apply to HHS for an exclusion from the list, use this document to indicate your request's status or your intent to apply for an exclusion and provide a brief justification for the exclusion. If Select Agents are going to be used at any time during execution of the project, by your lab or in a contractors lab, you must address the following three points for each research site where Select Agent research will take place:

- 1. Identify the Select Agent(s) planned for use.
- 2. Provide the registration status of all entities which the agency defines as "any government agency (Federal, State, or local), academic institution, corporation, company, partnership, society, association, firm, sole proprietorship, or other legal entity" where you will use Select Agent(s). Even if the performance site(s) is a foreign institution, provide the name(s) of the country(ies) where Select Agent research will be performed.
- Provide a description of all facilities where the Select Agent(s) will be used, including:
 - Procedures for monitoring Select Agent(s) possession, use and transfer.
 - Your plans for biosafety, biocontainment and Select Agent(s) security.
 - The available biocontainment resources at all performance sites.

Here is an example of a select agent section from a successful grant application (Developing small molecule therapeutics for Ebola hemorrhagic fever virus):

Select Agent							
Select Agent to be used:							
In vitro:							
Ebola	Zaire	Mayinga					
Ebola	Sudan	Boniface					
Marburg	Angola						
In vivo:							
Mouse	Adapted	Ebola	Zaire				
Guinea Pig	Adapted	Ebola	Zaire				
Organization Name registration status:							

The foundation is a select agent registered entity with Health and Human Services, Centers for Disease Control and Prevention (CDC) and U.S. Department of Agriculture, Animal Plant Health Inspection Service, National Select Agent Program. The foundation has been inspected by the CDC National Select Agent Program for use of HHS Select Agents and Toxins, Overlap Select Agents and Toxins and USDA Select Agents and Toxins. Per the requirements of 42 CFR 73, is approved for use of select agents at BioSafety Level 2, 3, and 4 and Animal Biosafety Level 3 and 4.

Description of Facilities:

Procedures used to monitor possession, use and transfer of Select Agent(s) The foundation maintains an experienced and trained staff of scientists, veterinarians, research technicians and veterinary technicians available to perform studies at high biocontainment and maximum containment. These individuals have demonstrated proficiency at conducting nonhuman primate studies with the agents identified in the proposal. The BSL3, ABSL3 and BSL4 Operations and Safety Manuals specify policies, procedures, and standard operating procedures (SOP) for the safe handling of biological materials in biosafety laboratories. The policies, procedures, and SOPs comply with application federal, state, and municipal regulations and with the guidelines "Biosafety in Microbiological and Biomedical Laboratories" issued by the Centers for Disease Control and Prevention (CDC) and the National Institutes of Health (NIH). Employees are trained from these manuals on each facility's mechanical systems, biosafety, biocontainment and security. Employees are also trained according to project specific and departmental standard operating procedures.

These procedures apply to all foundation employees and visitors that use, generate, store, or dispose of potentially infectious materials in foundation biosafety laboratories and to persons who must enter those laboratories to perform services. Prior to conducting experiments in the foundation biosafety laboratories, staff members must read and be trained in the requirements outlined in this manual and applicable task-specific safety plans.

At the present time, the director is the CDC designated Responsible Official (RO). Select agent use, transfer or possession is forbidden without the permission of the Responsible Official or Alternate Responsible Official, the required forms filed, and written approval received from the CDC Select Agent Program.

Upon approval, the BSK-3/4 Committee will consider select agents proposals for work in the BSL-3/4 laboratory. BSL-3/4-qualified investigators desiring to work on a BSL4 project must also submit a Biohazard Application to the Biohazards and Safety committee. The foundation Biosafety Committee has a key role in the foundation's overall biosafety program. The committee is responsible for evaluating the foundation's facility, equipment, and staff capabilities for performing work in a safe manner. The committee is also responsible for:

- Reviewing protocols and risk assessments submitted by principal investigators for work involving biological materials or toxins.
- Meeting with PIs prior to the implementation of projects involving biological materials or biological-derived toxins.
- Evaluating the foundation's staff, facility and equipment for their ability to provide the appropriate containment for handling biological materials.
- Assessing the foundation's compliance with existing federal, state and localenvironmental regulations.

Committee membership consists of representatives from technical departments, management, and administrative staff, among others. The committee communicates by e-mail with face-to-face meetings at least quarterly and/or more frequently if necessary.

Plans for appropriate biosafety, biocontainment, and security of the Select <u>Agent(s)</u>

Infectious cultures, inventory stocks or toxic materials are stored inside the BSL4 laboratory in refrigerators, incubators or freezers that are marked with the universal biohazard sign. Principal investigators maintain inventories of infectious agents stocks. A master list of select agents is securely kept by Virology and Immunology in the BSL4 Scientific Manager's office. A computerize and bar code inventory system has been selected for the select agent inventory. All issues relating to select agent inventory or tracking must be directed to the Responsible Official. All infectious or toxic materials stored in refrigerators or freezers are properly labeled and stored in containers capable of withstanding thermal shock of freezing and thawing. Each container is labeled with the identity of the infectious agents, the date of the preparation, the initials or name of the responsible laboratorian and a reference number that links the material to the more inclusive information contained in the inventory database.

When work is completed, all infectious cultures and toxins are removed from workbenches and cabinets and stored in a designated refrigerator or freezer. Materials to be discarded are placed in a sealable container filled with a suitable disinfectant. The container is placed in a discard pan containing the disinfectant. Discard pans are placed in a cart and transported to the autoclave. Labware containing infectious liquids are stored and transported in leak-proof containers large enough to contain the fluid in case of leakage.

CONCLUSION

The agency will need you to provide additional specific information if you plan on using human subjects, vertebrate animals, and/or select agents. This information will focus on need and safety. This information will be uploaded as part of your SBIR application. But remember you cannot use these documents to bypass the Research Strategy page limitation.

Chapter 6: Your Proposal's Budget

In addition to a description of your research and development project, your SBIR application also needs to have a projection of the amount of money needed to successfully perform the work. The budget and associated justifications that you provide are very important in conveying to the reviewer what your plan is for the funds they are investing. Reviewers will consider whether the budget and the requested period of support are fully justified and reasonable in relation to the proposed research.

The NIH has two types of budget formats they will accept:

- 1. Modular Budget
- 2. Detailed Budgets

For SBIR (and STTR, for that matter) applications, the modular format was excluded beginning with the 2005 Omnibus Solicitation (2006 Solicitation available at (http://grants.nih.gov/grants/funding/sbirsttr1/2006-2_SBIR-STTR-topics.pdf). So, you have no choice but to submit the Detailed Budgets — also called Research and Related (R&R) Budgets. This involves filling out three separate data entry screens, comprised of 11 different sections as part of the application process. Also, a separate detailed budget is required. Be forewarned — this will take you some time to complete. The justification documents will detail where you propose to spend your award money and why you are spending it in this manner.



Reviewers will consider whether the budget and the requested period of support are fully justified and reasonable in relation to the proposed research.

The Difference Between Direct and Indirect Costs

According to the NIH:



Unless previously negotiated, do not propose an F&A rate above 40% of the total direct costs. **Direct Costs** are those that can be identified specifically with a particular sponsored project, an instructional activity, or any other institutional activity, or that can be directly assigned to such activities relatively easily with a high degree of accuracy.

Indirect Costs include Facilities and Administrative (F&A) Costs that are incurred by a grantee for common or joint objectives and cannot be identified specifically with a particular project or program.

When putting your detailed budget together, include both direct and indirect costs. It is customary for a company to have previously established a single, negotiated contracted percentage rate to represent F&A costs for all SBIR grants received. For Phase I applicants who do not have a negotiated rate with a Federal agency, you should not propose an estimated rate above 40% of the total direct costs. If you have a subcontract or consulting agreements, any associated costs are considered "direct," including the subcontracted organization's indirect costs.

What is the "Fee"?

SBIR awardees are permitted to charge a fee for performing the work, which is explained this way by the NIH:

A reasonable fee, not to exceed 7% of total costs (direct and indirect) for each project, is available to small businesses receiving awards under the SBIR/STTR program. The fee is intended to be a reasonable profit factor available to for-profit organizations, consistent with normal profit margins provided to profit-making firms for research and development work. The amount requested for the fee should be based on the following guidelines:

- it must be consistent with that paid under contracts by the PHS for similar research conducted under similar conditions of risk;
- (2) it must take into account the complexity and innovativeness of the research to be conducted under the SBIR/STTR project; and
- (3) it must recognize the extent of the expenditures for the grant project for equipment and for performance by other than the grantee organization through consultant and subaward agreements.

The fee is not a direct or indirect "cost" item and may be used by the small business concern for any purpose, including additional effort under the SBIR/STTR award. The fee applies solely to the small business concern receiving the award and not to any other participant in the project. However, the grantee may pay a profit/ fee to a contractor providing routine goods or services in accordance with normal commercial practice.

How About "Program Income"?

As a commercial entity, your small business may have an opportunity to generate some cash under the awarded program. The agency will certainly allow this, but they ask that you provide an estimate of the amount of income you foresee. According to the SF424 (R&R) SBIR/STTR Application Guide for NIH and Other PHS Agencies:

NIH policy requires applicants for research grants to include in their grant applications an estimate of the amount and source of program income (defined below) expected to be generated as a result of the project for which funding is being sought. The specific policies that govern the treatment of program income under research grants are set forth in the NIH Grants Policy Statement (http://grants.nih.gov/grants/policy/policy.htm#gps).

Program Income is defined as gross income earned by the applicant organization that is directly generated by a supported activity or earned as a result of the award. The PHS Grants Policy Statement or NIH Grants Policy Statement contains a detailed explanation of program income, the ways in which it may be generated and accounted for, and the various options for its use and disposition.

Examples of program income include:

- Fees earned from services performed under the grant, such as those resulting from laboratory drug testing;
- Rental or usage fees, such as those earned from fees charged for use of computer equipment purchased with grant funds;
- Third party patient reimbursement for hospital or other medical services, such as insurance payments for patients when such reimbursement occurs because of the grant-supported activity;
- Funds generated by the sale of commodities, such as tissue cultures, cell lines, or research animals;
- Patent or copyright royalties (exempt from reporting requirements); and
- Registration fees generated from grant-supported conferences.

What this means:

If your company earns income under the award of the program, such income can be added to the grant account and used to further the objectives of the research project under the expanded authorities stated in the Notice of Award.

Fees generated from services provided under the award or from the sale of commodities as described above are real possibilities under a Phase I award given the focus of the program on technology development. If so, report your best estimate in the application. If you do not expect to have any program income, indicate this also.

Budget Limits

Unlike R01 and other types of NIH grants, the SBIR program has limits to the budget that you may request in your application. The agency states that SBIR Phase I awards may not exceed \$150,000 in total costs (direct costs, facilities and administrative (F&A/indirect costs, and fee) for a period typically not to exceed six months. Can you submit a larger budget and ask for a longer award period, say, up to one year? Absolutely. According to the SF424 (R&R) SBIR/STTR Application Guide for NIH and Other PHS Agencies:

Deviations from the indicated statutory award amount and project period guidelines are acceptable, but must be well justified and should be discussed with NIH Program Staff prior to submission of the application. (CDC, FDA, and ACF do not make awards greater than the stated guidelines.) The budgets of SBIR and STTR applications will be evaluated to assess the appropriateness of the budget to the timeliness of the research goals and may be reduced on a case-by-case basis as recommended by peer reviewers, Institute/Center Advisory Board/Council, or program staff. When making awards, NIH reserves the right to withhold or reduce grant funding on applications at any ranking based on program priority.

The Application guide goes on to say:

According to statutory guidelines, total funding support (direct costs, indirect costs, and fee) normally may not exceed \$150,000 for Phase I awards and \$1,000,000 for Phase II awards. With appropriate justification from the applicant, Congress will allow awards to exceed these amounts by up to 50% (\$225,000 for Phase I and \$1,500,000 for Phase II, a hard cap). As written in the statute and under appropriate circumstances, NIH can apply for a waiver from SBA to issue an award exceeding \$225,000 for Phase I or \$1,500,000 for Phase II, if this hard cap will interfere with NIH's ability to meet its mission. Award waivers from the SBA are not guaranteed and may delay the release of funds. Applicants are strongly



You can negotiate funding support exceeding the \$150,000 limit for Phase I awards. encouraged to contact NIH program officials prior to submitting any award in excess of the guidelines. In all cases, applicants should propose a budget that is reasonable and appropriate for completion of the research project.

What this means:

With appropriate justification on your part, Congress will allow awards to exceed this amount by up to 50% (\$225,000 for Phase I). Consult the appropriate Institute's or Center's topic section for additional budget guidance. Also, you should first contact program officials prior to submitting any application. Regardless of your budget or award length requests, propose a budget and time line that is both reasonable and appropriate for completion of the research and development project.

One additional observation – regardless of the amount of funding requested, many Phase I applications request an award length of one year. This observation suggests that many applicants feel six months is too short a time frame to complete the project or to get it to a place where they can confidently apply for a Phase II SBIR award.

Budget Strategy

Without a doubt, the more complete your budget justification is, the better your application will be viewed. Also, there are parameters for what is appropriate to be charged to a grant. The NIH provides the following guidance:

An allowable cost is one which is:

 reasonable for the performance of the award, meaning any fiscally responsible person would do so under the circumstances when the decision to spend the funds was made

- allocable, meaning that the cost was incurred for work performed under the award
- in conformance with any limitations or exclusions set forth in the Federal cost principles applicable to the organization incurring the cost or in the Notice of Award (NoA) as to the type or amount of cost;
- consistent with regulations, policies, and procedures of the recipient that are applied uniformly to both federally supported and other activities of the organization;
- 5. accorded consistent treatment as a direct or indirect cost;
- determined in accordance with generally accepted accounting principles; and
- not included as a cost in any other federally supported award (unless specifically authorized by statute).

What this means:

As the PI, you are responsible to make sure all costs are assigned appropriately and consistently. Although seldom actually occur, be confident that your project cost assignments can pass an accounting audit by the agency if need be.

What Else Should You Consider Before Actually Creating Your Budget?

Given the budget limitations of the SBIR award program, many budgets will focus their requests on salary for personnel to perform the work, and money for goods and services to fulfill the specific aims. Be careful with requests for equipment purchases; large pieces are just not realistic for a Phase I. Small equipment can seem reasonable at first, but at the expense of personnel or goods and services, this may jeopardize your ability to accomplish the proposed aims. Reviewers will be looking for reasonable costs and form opinions based on how well the Specific Aims and Methods support your request. As a check to make



Be careful with requests for equipment purchases; large pieces are just not realistic for a Phase I.



Asking for too little funding will be perceived as lack of experience and misjudgment on your part for what it will take to actually get the project completed, which can lower enthusiasm and be reflected in your overall score. sure you have included everything in your financial plan that you should, have a colleague review it to search for anything that you may have missed.

Although your budget is not one of the five scored review criteria, the reality is that reviewers will look at your budget and it will play a role in their scoring of these other five sections. Make sure that you ask for the correct amount of funding to get the job done; overinflating the budget is not advised. Asking for too little funding will be perceived as lack of experience and misjudgment on your part for what it will take to actually get the project completed, which can lower enthusiasm and be reflected in your overall score, thus putting you out of award range.

Budget Creation

As mentioned above, SBIR applicants must follow the Detailed Budget format, using the R&R budget component forms (Application Sections A-K). From the SF424 (R&R) SBIR/STTR Application Guide for NIH and Other PHS Agencies:

The R&R Budget form includes three separate data entry screens: (1) Sections A and B; (2) Sections C through E; and (3) Sections F through K. To navigate between the various screens, use the Previous and Next buttons at the top of the form or use the scroll bar on the side of the screen. Complete the R&R Budget form following the instructions provided. You must complete a separate detailed budget for each year of support requested. The form will generate a cumulative budget for the total project period. You must complete all the required information (i.e., those fields that are highlighted in yellow, outlined in red and noted with an "*") before the Next Period button is activated. If no funds are requested for a required field, enter "0."

While the dollar fields allow cents to be entered, all dollar fields should be presented in whole numbers. Please round to the nearest whole number.

NIH and other PHS agencies use the concept of person months as a metric for determining percent of effort. To assist applicants unfamiliar with this concept,

resources are available on the web at: <u>http://grants.nih.gov/grants/policy/person_</u> <u>months_faqs.htm</u>. Frequently asked questions and a conversion calculator are available.

What this means:

These are the sections that must be filled out:

- A: Senior/Key Person
- B: Other Personnel
- C: Equipment Description
- D: Travel
- E: Participant/Trainee Support Costs
- F: Other Direct Costs
- G: Total Direct Costs (A through F)
- H: Indirect Costs
- I: Total Direct and Indirect Institutional Costs (G+H)
- J: Fee
- K: Budget Justification

Start With Personnel

From the SF424 (R&R) SBIR/STTR Application Guide for NIH and Other PHS Agencies:

Senior/Key Person

This section should include the names of all senior/key persons at the applicant organization who are involved on the project in a particular budget year. Include all collaborating investigators, and other individuals meeting the senior/key person definition if they are from the applicant organization. Details of collaborators at other institutions will be provided in the Subaward budget for each subaward/

consortium organization. Personnel listed as Other Significant Contributors who are not committing any specific measurable effort to the project should not be included in the Personnel section of the budget since no associated salary and/or fringe benefits should be requested for their contribution. Consultants designated as senior/key persons in the Senior/Key Person Profile Form can be included in Budget Section A only if they are also employees of the applicant organization. Otherwise, consultant costs should be included in F.3 Consultant Services.

What this means:

There are a series of data fields for each Senior/Key Person which needs to be populated:

- First, middle and last name, along with any prefixes or suffixes
- Project role identify each Senior/Key Person, including Project Directors/ Principal Investigators, Postdoctoral Associates and other professionals
- Base salary enter the annual compensation paid by the employer
- Calendar, Academic or Summer months indicate the number of person months devoted to the project for each individual (based upon the appropriate calendar, academic or summer designations)
- Requested salary regardless of the number of months each Senior/Key Person devotes to the project, you must identify only the salary amount you are requesting for this budget period
- Fringe benefits enter the cash value of any applicable fringe benefits for each person (This is a rate based upon your institution's policy, and NIH states these are "allowable as part of overall compensation to employees in proportion to the amount of time or effort employees devote to the grant-supported project, provided such costs are incurred under formally established and consistently applied policies of the organization.")
- Funds requested here, note the requested salary and fringe benefits.
- Total Funds requested for all senior/key persons in the attached file enter total funds requested for all senior/key persons. This is required information

Total Senior/Key Persons - enter total funds requested for all senior/key persons.

For Section B (Other Personnel), you will identify only the number of people in each project role, not their names. Section B includes the following data fields for each role:

- Number of personnel identify the number of people you are proposing for each project role category
- Project role the form already lists Post-Doctoral Associates, Graduate Students, Undergraduate Students and Secretarial/Clerical, and you should count only those not already listed in Section A. You can list additional project roles in the additional data fields provided.
- Calendar, Academic or Summer months indicate the number of person months devoted to the project for each project role category (based upon the calendar, academic or summer designations)
- Requested salary show the amount of salary/wages you are requesting for each project role
- Fringe benefits enter the cash value of any applicable fringe benefits for each project role
- Funds requested note the requested salary and fringe benefits for each project role
- Total Number of Other Personnel This total will auto-calculate. Total Salary, Wages and Fringe Benefits (A+B).
- Total Other Personnel Total funds requested for all other Personnel

Equipment

Section C is where you will separately list any equipment costing more than \$5,000. NIH defines equipment as "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 agency will allow items limited

to research and development equipment and apparati that is not currently available to you for conducting the work. General-use equipment such as lap top computers are not allowed, unless they are used exclusively or primarily for conducting your proposed project. You need to list the estimated cost of each equipment item, including shipping and any maintenance costs and agreements.

Travel:

In Section D, you have an opportunity to outline your travel costs. Separate data fields exist for domestic and foreign travel, which NIH breaks down as follows:

- Domestic travel total requested funds for travel within the United States, Canada, Mexico and U.S. possessions.
- Foreign travel —total requested funds for travel outside of North America and U.S. possessions.

Make sure that you describe in your budget justification section the purpose, destination, anticipated travel dates (if possible) and number of individuals for each trip. If you are not certain when the travel will take place, make sure that you estimate the duration of the trip (i.e. five days).

Participant/Trainee Support Costs

NIH states the following:

Unless specifically stated otherwise in an announcement, NIH and other PHS agencies applicants should leave blank Section E. Note: Tuition remission for graduate students should continue to be included in Section F. Other Direct Costs when applicable.

In the unlikely event that you do need to fill out this section, the SF424 (R&R) SBIR/STTR Application Guide for NIH and Other PHS Agencies provides a list of what information is needed (i.e. Tuition/Fees/Health Insurance, stipends, travel, to name just a few of the categories).

Other Direct Costs

Section F is where you will request Other Direct Costs:

- Materials and supplies List general categories, unless the category is under \$1,000
- Publication costs
- Consultant services
- Computer services
- Subawards/consortium/contractual costs
- Equipment or facility rental/user fees
- Alterations and renovations
- Other, which might include technical assistance

Total Direct Costs

In Section G, the project's Total Direct Costs, you add the totals for Sections A-F and report this number.

Indirect Costs

Section H is the place to provide Indirect Costs information, grouping by type, such as salaries and wages.

Total Direct and Indirect Costs

For Section I, Total Direct and Indirect Costs, add the totals for Sections G and H and record this number.

Fees

Remember, the fee is neither a direct or indirect "cost" item and may be used by the small business concern for any purpose. Note: The electronic system automatically rounds up. If you get an error "The fee must be less than 7%," try using 6.99% as the rate.

Budget Justification

Direct from NIH:

Use the budget justification to provide the additional information requested in each budget category identified above and any other information the applicant wishes to submit to support the budget request. The following budget categories must be justified, where applicable: equipment, travel, participant/trainee support and other direct cost categories. Only one file may be attached.

Use this section to list the names, role (e.g., PostDoc or Graduate Student), associated months, salary and fringe benefits for all Postdoctoral Associates and Graduate Students included in Budget Section B. Other Personnel.

Include a justification for any significant increases or decreases from the initial year budget. Justify budgets with more than a standard escalation from the initial to the future year(s) of support. Also use this section to explain any exclusions applied to the F&A base calculation.

If the application includes a subaward/consortium budget, a separate budget justification is submitted for that budget. See Section 4.7 Special Instructions for Preparing Applications with a Subaward/Consortium.

What this means:

Section K is where you will upload your justification to support the need for the requested funds detailed in Sections A-J. Remember to address each cost individually. The budget justification section is your chance to show the reviewers that your project is well thought-out. With this in mind, make certain that there is nothing in the budget that was not mentioned previously in the research strategy section. For example, funds requested for microarray analysis in the budget section, when this was not described a part of your research and development work in the research strategy section.

Here is a sample of Section K, which was combined from two successful SBIR Phase I grants. The reason for the combination is that each grant alone did not illustrate all of the sections needed to be justified.

Senior/Key personnel

[AB], Ph.D., will serve as Co-PI on this new Phase I SBIR proposal. He will devote 10% of his effort to the execution, oversight, and coordination of all components of the study and will be responsible coordinating outside fee-for-service efforts. He will be responsible for the design and organization of all experiments and analysis of their outcomes in coordination with Dr. [AK].

[AK], PhD, Co-PI will be responsible for setting the experimental strategies, interacting with collaborators and consultants, will oversee the project, manage the laboratory personnel, and evaluate data. He will also lead the writing of manuscripts for publication and progress reports. He will devote 12 calendar months to this effort coordinating efforts with Dr. [AB].

[MP], PhD, Senior Scientist will be responsible for purchasing reagents, execution of the experiments, data evaluation, and preparation of visual and written presentation of obtained results. Dr. [MP] will devote 12 calendar months to this work.



The budget justification section is your chance to show the reviewers that your project is well thought-out.

Other Significant Contributors

[DI], Ph.D., consultant, will provide support to this project as a population scientist. Dr. [DI] is an epidemiologist with extensive training in basic science that is required for this interdisciplinary project. She has been instrumental for the development of this proposal. The proposed study is a next step in our collaboration Dr. [DI] on studying individual responses to low-dose ionizing radiation. She will participate in meetings twice a month and will conduct statistical analysis.

[SS], PhD, consultant. Dr. [SS] is an expert in the field of vascular biology and angiogenesis with for more than 20 years of experience. He has special interest in neovascularization of bioengineered and regenerating tissues using angiogenic growth factors and vascular cells, including endothelial progenitor cells. Dr. [SS] will participate in monthly meeting and in the discussion of the results.

[RS], PhD, consultant on toxicological risk assessment. Dr. [RS] has the perspective and expertise and will consult on the issues of integration of toxicological testing with population based approach. The proposed project is an extension of our collaboration. Dr. [RS] will participate in monthly meeting and in the discussion of the results.

[GT], Ph.D., consultant. Dr. [GT] is an expert in biology of circulating endothelial colony forming cells. Our previous work was conducted in collaboration with Dr. [GT]. The proposed project is a logical extension of our collaboration. Dr. [GT] will participate in monthly meeting and in the discussion of the results.

[EH], PhD, consultant. Dr. [EH] is a highly reputed toxicologist. He is an expert in xenobiotic metabolism and particularly in human xenobiotic metabolism in human hepatocytes. We are collaborating with Dr. [EH] on metabolic and toxicological aspects of our model. Dr. [EH] will participate in monthly meeting and in the discussion of the results.

Consultant Costs

Name	Project Role	Rate/hr. (\$)	Hrs./ month	Number of months	Total hrs.	Total Cost (\$)
Dr. [DI]	Consultant	50	8	12	96	4,800
Dr. [SS]	Consultant	50	2	12	24	1,200
Dr. [RS]	Consultant	50	2	12	24	1,200
Dr. [EH]	Consultant	50	1	12	12	600
Dr. [GT]	Consultant	50	1	12	12	600
					Total	8,400

Equipment

xCELLigence RTCA-SP (ACEA Biosciences, Inc.) monthly lease including warranty \$1,500.00/months x 6 months = \$9,000.00

Infinite-M200-PRO (Tecan) monthly lease including warranty - \$1,000.00/months x 10 months = \$10,000.00

Total______\$19,000.00

Materials and Supplies:

The cost estimate of \$2,750.00 per month for supplies is derived from costs we currently experience in cell isolation, culture and performing cell based assays. The broad areas covered in this part of the budget are cell cultureware and other disposables, media and serum, growth factors and reagents, waste disposal, antibodies, and the purchase of cell lines and primary cells. The budget estimate for supplies is a conservative estimate and could be much more depending on a number of factors, including the number of compounds tested in the screening assays. The company is prepared for this eventuality and will pay any supply costs beyond those requested. Category cost estimates below are for the entire grant period of 12 months. Lab disposables – It is expected that the cost of these supplies will be approximately \$6,000.00. This category includes an extensive amount of serological pipets, gloves, gowns, tips, and other items necessary for the performance of the outlined work.

Cell isolation and culture reagents –These items such as culture ware, media and serum, enzymes, and biohazardous waste disposal are needed for the experiments conducted during the performance of the grant. The estimated cost for this is \$17,000.00

Antibodies, growth factors, cells and reagents – This category includes items such as assay reagents, phospho-specific antibodies, ELISAs, growth factors, and radiolabeled reagents (and their disposal). We anticipate that the cost of these items will be \$10,000.00

Tissue Procurement - These funds consist entirely of tissue procurement expenses. As with our established visceral adipose tissue procurement, we will utilize at least two medical institutions requiring approximately \$1,000 per location for IRB maintenance fees. We expect to procure up to 8 samples, at a cost of approximately \$400.00 per sample. This cost breaks down to \$50.00 in shipping costs and the remainder in compensation for nurse or physician time consenting the patient, physician time obtaining the sample during normal surgery, and nurse time involved in packaging and recording appropriate patient information. The total cost for these items is expected to be approximately \$4,200.00

Travel

Funds are requested to cover travel for the principal investigators to attend meetings with consultants and to major conference to present results. Funds for this purpose are to cover airfare, conference registration fees, room and board, and any taxi and parking costs.

Total

\$2,000.00

Indirect rate

[Company] is requesting a 40% indirect rate.

Fee

[Company] is requesting the standard 7% fee.

Special Instructions for Preparing Applications with a Subaward/ Consortium

In most circumstances, a minimum of two-thirds or 67% of the research or analytical effort must be carried out by the small business awarded a Phase I SBIR. That leaves a maximum of 33% of the total award (direct, F&A/indirect, and fee) which can go towards all third party consultant and contractual arrangements for portions of the scientific and technical effort.

According to NIH:

If the application is selected for an award, the Authorized Organization Representative (AOR) will need to certify that the applicant and all proposed consortium participants understand and agree to the following statement: 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.

What this means:

You, as the awardee organization, will make sure that 67% or more of the work will be performed by the award recipient, and no more than 33% will be performed by outside entities.



Complete subaward/consortium budget form (including the budget justification section) will need to be completed by each consortium grantee organization. Remember that separate budgets are required only for subawardee/consortium organizations that perform a substantive portion of the project.

As the awardee organization, 67% or more of the work must be performed by the award recipient, and no more than 33% can be performed by outside entities.

CONCLUSION

Although your budget is not one of the reviewer's five scored sections, what they think of your budget will influence their opinion of your proposal. Detailed budgets require careful planning and can take up a considerable amount of time to prepare. Whether you will have sufficient financial support to successfully achieve your project's research and development goals will depend on your budget.

Chapter 7: Application Submission

Now that you have come this far along in the process, take some time just prior to submission to review your finished product. Your proposal must read like a single, cohesive, flowing document as opposed to individual parts that were cobbled together. Make sure your message comes through loud and clear - that this research and development project deserves to be funded, you are the best person to do the work, and your company is the only place where this work can be successfully accomplished. Ensure all of the sections communicate this message. Here again, if you can have some of your colleagues also give it the once-over and provide their feedback, you will be ahead of the game. Don't discount the possibility of enlisting the services of a professional editor; they may be a nonexpert, but they can make sure the proposal reads as one integrated unit and that your message comes through.

You also need to compose a cover letter to introduce your proposal. This is part of the NIH's application upload process, and the agency encourages you to do so. If you are submitting a changed or corrected application, a cover letter is mandatory. Make sure to include all attachments and that the attachments comply with agency requirements. If you upload all of your materials at least two days prior to the deadline, the agency will allow you two days to make any changes. After the deadline, this 'grace period' is not available. The best advice is to have everything checked and get it uploaded right the first time.



Incomplete submissions will not be reviewed. Period.

Make Sure Everything is Attached and Submitted

Incomplete submissions will not be reviewed. "Incomplete" may include parts or attachments that are missing, or do not conform to the guidelines for submission. Certain components are mandatory for all SBIR applicants, and others are required only under certain circumstances.

Direct from NIH:

A completed application includes data in the following components:

Required Components

- SF424 (R&R) (Cover component)
- Research & Related Project/Performance Site Locations
- Research & Related Other Project Information
- Research & Related Senior/Key Person
- PHS398 Cover Page Supplement
- PHS398 Research Plan
- PHS398 Checklist
- PHS398 Research & Related Budget

Optional Components

- PHS398 Cover Letter File
- Research & Related Subaward Budget Attachment(s) Form
- Planned enrollment report
- PHS 398 Cumulative Inclusion Enrollment Report

Applications With More than One PI

An SBIR application may have more than one PD/PI, or multiple PDs/PIs, designated on the application for projects that require a "team science" approach that clearly does not fit the single-PD/PI model. To do so, each PD/PI must have a PD/PI role and a leadership plan must be included in the application package. The plan needs to explain your rationale for having multiple PIs in addition to the leadership team's organizational structure. Include communication plans, decision-making processes for scientific direction and conflict resolution procedures. If you have planned budget allocation, you should describe how resources will be distributed to the project's specific components or individual PIs. In addition, all PDs/PIs must be registered in the NIH eRA Commons prior to the submission of the application. The individual who serves as the contact PD/PI must be from the small business that was awarded the grant and he/she must meet the primary employment requirement. In contrast, other PDs/PIs need not meet this requirement.

The contact PD/PI is responsible for all communication, for assembling the application materials and for coordinating progress reports for the NIH. At the same time, this PI may not have other special roles or responsibilities within the project team. The contact's information should be entered on the SF424 (R&R) cover component. All other PIs should be listed in the research and related senior/ key person component as PIs. The commons login ID of each PI must be included in the credential field of the research and related senior/key person component. Failure to do so will result in your application being rejected.

References Cited

The agency does not require that you comply with a specific format. They do want you to make sure that your bibliography includes all references cited in the research plan, and that references are arranged in the same sequence as they appear in the document. Include the names of all authors, the article and journal title or the book title, the volume number, page numbers and year of publication.



For applications with more than one PI, all must be registered in the NIH eRA Commons prior to the submission of the application.

Facilities and Other Resources

Only describe those relevant to your work and identify them as laboratory, animal, computer, office, clinical and other. Where appropriate, indicate their capacities, applicable capabilities, proximity and availability to the project.

Consortium/Contractual Arrangements

Be sure to detail the programmatic, fiscal and administrative arrangements between the applicant organization and the consortium organization(s).

Letters of Support (e.g. Consultants)

Direct from NIH:

Attach all appropriate letters of support necessary to demonstrate the support of consortium participants and collaborators such as Senior/Key Personnel and Other Significant Contributors included in the grant application. Letters should state expectations for co-authorship, and whether cell lines, samples or other resources agreed to in the letter are also available to other investigators in the scientific community or will be provided to the particular investigators only.

For consultants, letters should include rate/charge for consulting services and level of effort/number of hours per year anticipated. Consultant biographical sketches should be in the Biographical Sketch section.

Involvement of consultants and collaborators in the planning and research stages of the project is permitted. Include with the application letters from each individual and/or collaborator confirming their role(s) in the project.

Following is guidance for such documentation:

- The letter(s) should be prepared on the consultant or collaborator's letterhead and addressed to the small business. A single page is recommended.
- Minimally, each consultant and collaborator letter should:
 - 1. verify their commitment to the project;
 - refer to the specific project by name, acknowledging the PD/PI as the lead on the project; and
 - specify what services /tasks the consultant or collaborator will contribute (e.g. expertise, number of hours/ percent of effort, summary of tasks to be completed).
- For consultants, the letter should also include the rate/charge for consulting services. Also include biographical sketches for each consultant.
- Letters of interest from potential commercial partners or investors and letters of commitment of funds or other resources that will enhance the likelihood of commercialization should be placed following the letters of support for consultants and collaborators.

What this means:

Letters of support are very important to include in your application. Be sure to attach letters from all consultants that corroborate their project roles. Letters from key opinion leaders (KOLs) are especially helpful. The letter should start with the title of the application and the submission date. The KOL should next describe their relevant background information, as a means to establish their credentials. Next, the KOL should state something to the effect that "This is a valuable and innovative product...(and explain why it is valuable and innovative)" The letter should conclude with a strong statement of desire to try the product once it becomes available.



Letters of support from big-names in your field can help your application a lot.

The Cover Letter

All SBIR grant applicants are encouraged to include a cover letter with their application. While the agency makes the final decision as to where your application is assigned, what you say in your cover letter may help the agency decide to assign it to where you feel it would be best.

Direct from NIH:

The cover letter is only for internal use and will not be shared with peer reviewers. The letter should contain any of the following information that applies to the application:

- 1. Application title.
- 2. Funding Opportunity (PA or RFA) title of the NIH initiative.
- 3. Request of an assignment (referral) to a particular awarding component(s) or Scientific Review Group (SRG). The PHS makes the final determination.
- 4. List of individuals (e.g., competitors) who should not review your application and why.
- 5. Disciplines involved, if multidisciplinary.
- 6. For late applications (see Late Application policy in Section 2.14) include specific information about the timing and nature of the cause of the delay.
- 7. When submitting a Changed/Corrected Application after the submission date, a cover letter is required explaining the reason for the Changed/ Corrected Application. If you already submitted a cover letter with a previous submission and are now submitting a Changed/Corrected Application, you must include all previous cover letter text in the revised cover letter attachment. The system does not retain any previously submitted cover letters until after an application is verified; therefore, you must repeat all information previously submitted in the cover letter as well as any additional information.
- 8. Explanation of any subaward budget forms that are not active for all periods of the proposed grant.

 Statement that you have attached any required agency approval documentation for the type of application submitted. This may include approval for applications \$500,000 or more, approval for Conference Grant or Cooperative Agreement (R13 or U13), etc.

There are study sections dedicated to reviewing SBIR and STTR applications. They can be found at <u>http://public.csr.nih.gov/StudySections/SmallBusinessTech-nologyTransfer/Pages/default.aspx</u>. These study sections have more representation from industry than standard study sections.

When requesting peer-review assignment, please adhere to the following format:

- A single request per line.
- The institute/center and SRG review requests need to be on separate lines.
- Positive and negative requests are placed on separate lines.
- Include the name of the institute/center or SRG, followed by a dash and the acronym. Do not use parentheses.
- Explain each request in a separate paragraph

Tips When Making Peer Review Suggestions

There are tips you should keep in mind when making your peer review sugges-

tions:

- It is never appropriate to request individual reviewers by name
- It is always appropriate to request reviewers having specific area(s) of expertise
- Make suggestions of study sections or funding agencies most applicable to your proposal
- Be sure to emphasize your application's disciplinary/multidisciplinary focus


Be mindful of the language you use when making peer review suggestions and for any individuals you would like to be excluded from reviewing your application. Think about including a list of disciplines important for understanding your proposal i.e. if it is as combination therapeutic product you are researching and developing, disciplines would include cell biology and biomaterials engineering.

Take advantage of the <u>http://era.nih.gov/roster/</u> website to read up on the reviewers who make up the various SRGs. It is inappropriate to correspond with them, and they will inform the SROs if you do try or succeed in communicating with them.

What About Conflict of Interest?

Suppose you request a specific study section in your cover letter, but there happens to be a direct competitor of your company who is a member of that study section? It is appropriate in this situation for you to request that this reviewer be excluded from evaluation of your proposal. To do so, you will need to:

- Name the individual in the cover letter.
- Explain why this person should be excluded from reviewing your application.

The following template is offered by the agency as a guide for crafting your cover letter.

Application title.

Funding Opportunity Announcement number:

Please assign this application to the following: Please note the outline of indentations.

Institutes/Centers

National Cancer Institute - NCI

National Institute for Dental and Craniofacial Research - NIDCR

Scientific Review Groups Molecular Oncogenesis Study Section - MONC Cancer Etiology Study Section - CE

Please do not assign this application to the following:

Scientific Review Groups Cancer Genetics Study Section - CG

The reasons for this request are [provide a narrative explanation for the request(s)]. List of individuals (e.g., competitors) who should not review the application and why.

Disciplines involved, if multidisciplinary.

Statement that required NIH approval documents are included. (e.g., budget over \$500K/year; approval for conference grant; cooperative agreement, etc.) For late applications, if applicable, include explanation of the delay as part of the letter.

Go Over Your Proposal One More Time for Content

You have now come to the point where all of the proposal components are assembled, required attachments are in place, and the cover letter is crafted. Now, it's time to review your entire proposal's content. To repeat what was stated in the respective previous chapters of this manual, make certain:

- that your abstract is convincing
- your budget is aligned with your research and development strategy

- your specific aims are clear and focused
- you've compellingly described your project's significance, innovation and approach

Common Problems with SBIR Applications

From a slide show presented by Rosemarie Hunziker, Program Director, National Institute of Biomedical Imaging and Bioengineering (NIBIB):

Common Problems with SBIR/STTR Applications

Low/No significance

- Unimportant problem
- Unconvincing case for commercial potential or societal impact
- Irrelevant, inconsistent, or insufficient reference to published work

Lack of innovation, evolutionary rather than revolutionary

Weak PD/PI/Research team

- Insufficient experience with essential methodologies
- Poor environment; weakly documented institutional support

Questionable reasoning in experimental approach

- Errors in design = FATAL FLAW
- Failure to consider potential pitfalls and alternatives

Diffuse, superficial, or unfocused research plan

- Lack of sufficient experimental detail
- Unrealistically large amount of work proposed

Inadequately defined Phase I feasibility test / milestones

Serious/unresolvable human or animal subjects concerns

While going over your proposal one more time for content, be sure to address any of these common problems.

Application Submission

The authorized organization representative (AOR) is usually the person who will submit all of you application materials. As the PI, you can submit materials with the approval of the AOR, but the agency will not accept any materials that have not been approved. To begin the process, go to the grants.gov login page and enter your username and password. Once logged in, the application package will be automatically uploaded to the website. A confirmation screen appears once the upload is complete, and a grants.gov tracking number is provided. Be sure and retain this number for your records.

If everything is in order and there are no glaring issues, no further action on your part is needed. From this point your application will automatically move to the Division of Receipt and Referral in the Center for Scientific Review for processing.

If for some reason there is an issue, for example there was a glitch in the document transfer process, the AOR can reject it and submit a changed/ corrected application. In this instance, you should contact the eRA help desk to ensure the issues are addressed and corrected. Once you have rejected the proposal, follow the instructions for correcting errors, including the requirement for cover letters on late applications.

You can also use the reject feature if you determine that the warnings you receive regarding your application are applicable and need to be handled now. Warnings alone will not stop the application process. If a submission receives warnings only, but no errors, it will automatically move forward after two weekdays. Work with your AOR to determine if or when the reject feature is appropriate.

TIP:

While some things may be out of your control, for those that you do control, make sure everything is in place to get your application uploaded correctly the first time. After the submission deadline, the SRO is under no obligation to accept corrective materials. Should you need to submit such materials, send them to the SRO in a PDF format via an e-mail, making sure that you have the consent of your AOR and that he/she is copied on any emails sent to the SRO.

Application Withdrawal

Direct from NIH:

There are two ways to stop the application from moving forward for peer review. You can withdraw it or you can simply reject the application image. Your application will undergo peer review as is unless your scientific review officer [SRO] allows you to send additional information or you have withdrawn it. You should consider withdrawing your application in the following circumstances:

- You feel the application is not up to snuff.
- You've run out of time for corrections and can't send additional data.

Remember that your goal is to impress your reviewers with the best possible application. Balance the severity of the problems with the amount of time you have left to correct them in the same review cycle. Compare that with the time lost if you wait for the next due date. To withdraw your application from consideration, ask your organization to fax a signed letter to the Center for Scientific Review's Division of Receipt and Referral at 301-480-1987. Provide your NIH accession number.

If you plan to withdraw the application and resubmit for the same deadline, be careful. Once you no longer have an active application in the system, you will have the same disadvantages as anyone else who applies at the last minute. Allow at least two days to get your corrected application into the system.

CONCLUSION

Congratulations on your submission. You made the application deadline and there were no errors that could sidetrack your proposal's advancement towards review. Since you planned and executed the writing of your proposal well in advance, and are comfortable and confident on its content, there should be no reason for you to withdraw your application.

Chapter 8: Application Review Process

Brief Overview

Once submitted, your SBIR undergoes a superficial review by the Center for Scientific Review to make sure there are no errors which will automatically disqualify your submission. Assuming there are no red-flags here, the proposal is then reviewed by the Integrated Review Groups (IRG). Each IRG represents a cluster of study sections around a general scientific area. From here, your submission goes to a Scientific Review Group (SRG), usually referred to as the study section. SRGs for SBIR and STTR applications have more representation from industry on them than standard study sections; however academicians still occupy the largest part of the panel positions. The SRG is composed of mostly a dozen or more non-federal scientists, who have expertise in relevant disciplines and current research areas. The scientific review officer (SRO) however is an NIH staff member. Their job is to lead the group and designate a few key reviewers to analyze your proposal in detail. The other members of the study section will skim over your application, reading only certain sections in any detail. The study section votes and scores your application on the five review criteria discussed previously:

- Significance
- Innovation
- Approach
- Investigator(s)
- Environment.

The group also evaluates your proposal's Overall Impact. Once completed, the SRO will compile a summary statement, including your application's scores as well as a more detailed critique. After assessment by the SRG, the application will go to the institute/center national advisory councils for review. Council recommendations are based on considerations of scientific merit (assessed by the SRGs) and relevance of the proposed study to an Institute/Center's mission, programs and priorities. Your application is only eligible for funding if both the study section and the institute/ center advisory council recommend it.

Reviewers also have another option they can use to streamline their review process and reduce the panel workload. If an application is unanimously judged by the peer review committee to be less competitive, it will not be discussed at the peer review meeting. These applications do not receive a numerical impact score, nor do they receive individual criterion scores. In short, these applications are not considered any further for funding.

What Does the CSR Look for During Their Check of Your Application?

The staff on the CSR makes sure that your application follows all administrative and formatting requirements. Failure to do so may result in the agency returning your application without further review. Common failures include:

- Late submission
- Improper format such as font size and margins
- Did not meet requirements of the agency announcement
- Company did not qualify as a small business

The take home message here is to follow the agency instructions to the letter.

Application Number Assignment

Your application will receive a unique identification number from the CSR. The format is as follows: 1 R43 ES023527-01.

What this means (from the NIH):

- The first number is the application type. A new application is Type 1. This indicates to the agency whether your application is a new, renewal, noncompeting or other type of application.
- The activity code comes next. This is the type of grant mechanism you have applied for. In the example above, an R43 designates an SBIR Phase I research grant.
- The two-letter abbreviation is the institute code. In this example, the National Institute of Environmental and Health Sciences code is ES.
- Next is the unique serial number the CSR assigns.
- The number after the hyphen shows the support year for the grant.



Make sure your submission is correctly formatted.



This unique identifying number is how you will track your application. When accessing the eRA Commons, the website where you submit your application (<u>https://commons.era.nih.gov/commons/</u>), you'll see this assignment number. Agency staff will typically refer to your application using this assignment number.

Assignment to an IRG, SRG, and Institute/Center

While you can request review assignments in your cover letter, it is up to the discretion of the CSR whether to honor your request or not. It may make different assignments based on NIH referral guidelines and workload factors.

Direct from NIH:

Your assignment should appear in the eRA Commons within 3 weeks after submission. Be sure to log into eCommons and verify. Call the NIH Referral Office at 301-435-0715 if you do not see it there.

Your requested study section may not be there yet, but the IRG should be. Updates will take place over the next several days, at which time your SRG will show up. What should you do if your application is assignment is not agreeable to you? You can request a change, and be prepared to justify why you are requesting the change. The CSR will try to accommodate your request, but remember that they are balancing referral guidelines and workloads, and that their decision is final. You may always withdraw the application from this round of review if you feel that this may be in the best interest of your application's chances for future success.

After the funding agency receives your application, it is assigned to a program division using internal referral guidelines. The program officer, grants management specialist and SRO fields will initially be blank in the eRA Commons.

Steps to Follow if You Want to Request a Reassignment

Direct from NIH:

- Inform your SRO of the problem well in advance of the initial peer review beginning. An appropriate justification for such a request would be a committee member having conflict of interest, working for a competitor's company, or, in your opinion, the panel doesn't have adequate expertise to review your research and development project.
- 2. Be sure to suggest an alternative, after checking the study section rosters.
- 3. Discuss the alternative you prefer with the chief of the IRG for your assigned study section. You can get his contact information from your SRO.
- 4. Fax a letter to the center at 301-480-1987 detailing your reasons for requesting a change. Here is an example of an acceptable request and an unacceptable one:
 - Acceptable: "Study section A seems to focus more on the contribution of the cells is the therapeutic function of regenerative medicine products. Since my application proposes to develop a combination product consisting of both cells and a biodegradable scaffold material, the bioengineering expertise of reviewers on study section B is critical to appreciate the approaches I have taken."
 - Not acceptable: "Study section A lacks the required expertise to evaluate my proposal, so please move my application to study section B".
- If your concerns are still not resolved, you may appeal to the Center for Scientific Review's director of receipt and referral by calling 301-435-0715.
- 6. Make sure to keep your program officer informed about your situation.

It may be better to withdraw you application and wait until the next receipt date rather than having it reviewed by an inappropriate study section. You also have grounds for an appeal if the group doesn't have the expertise required for an effective peer review and, as a result, the assessment turns out poorly.



TIP:

You will have an opportunity to submit additional information – use it wisely.

Submitting Additional Information

The agency will allow you to add certain types of information to your submitted application prior to review. However, there are restrictions on what can be added, how it needs to be added, and a deadline of up to 30 calendar days before the peer review meeting. Use this opportunity if you change companies and can take the funding with you, or if there was a catastrophic event such as the lab you were going to perform the work is for some reason inaccessible. Other good examples are; letters of support if you add a consultant or a biosketch if a key person leaves and is replaced by someone else. The SRO will determine whether your additional information will be included with your application. Postsubmission materials that the NIH will not accept include; changing specific aims or research approach, nor will they accept new data.

To Submit Additional Information

- Make sure to have the signature of the signing official at your company. The agency will not accept what you send them unless you have it.
- 2. Follow the guidelines for the pages you're submitting. If what you are sending has a form page (e.g. Biographical Sketch), be sure to use it. If a form page is not needed, such a letter of support from a new consultant, limit it to a single page. Remember to always follow NIH policies regarding margins, paper size and font size.
- 3. Describe the material you're submitting in a note.
- 4. Send the material to the SRO. Sending the information electronically as a PDF, in a single e-mail, is the preferred method. Be sure to include:
 - A brief note describing your attachment
 - Why you are submitting it (1-2 sentences at the most)
 - The grant application number and full title

If accepted, your additional material will be uploaded to eRA Commons, under the "Additions for Review" section of your application.

Peer Review

Direct from NIH:

Your application's most significant test is initial peer review. Your peers successful scientists in your field and related ones — use the information in your application to assess the merit of the science you've proposed and your ability to get the work done. Peer review results in a numerical value indicating the reviewers' judgment of the likelihood that your project will have a powerful impact on its area of science. That number is the most important factor in determining your application's success.

The agency goes on to say:

Your SRO does an initial check of your application to make sure the key parts are there. If you're responding to a request for applications, program staff will check to ensure it is responsive to the request for application.

Before sending your application to reviewers, SROs look at it more thoroughly to make sure it's complete, and they may contact you if anything is missing. If this happens, send in the information quickly so reviewers receive it well before the review.

At least three reviewers will be selected by the SRO to examine each proposal and report on it to the rest of the study section. They were selected based on their degree of familiarity with your area of research and development. Sometimes, if none of the members have the necessary expertise, the SRO will find at least one ad hoc reviewer with the appropriate credentials. How well these three individuals like your proposal will determine how well the SRG grades your application.



The fate of your proposal depends on how well three individual reviewers on the study section like your proposal.

SBIR/STTR Study Sections

These study sections are centered around general areas, such as orthopedic and skeletal biology, sensory technologies, and basic and integrative bioengineering, just to name a few. The reviewers are going to be experts in the discipline, but not all are going to be experts in your particular area. Each study section meeting may have 50-100 applications to review.

Successful SBIR grants generate enthusiasm for the project, even though they may be high-risk but the applicant makes it clear what the end-point measurements will be for success and failure. While it should go without saying that the best SBIR proposals have good science, they also have a defined product goal with scenarios for use.

The Review Process

Approximately 1-2 months before the study section meets, reviewers receive the grant application on a CD. Each reviewer receives 4-7 grants to review. This may not seem like much time to do a thorough review, and the reality is that 2-3 weeks before the study section meets is when your proposal may actually receive a fast read for the first time, focusing on the specific aims, biographical sketch, and the company. It is at this time in which a general impression is formed. The SRA will send each reviewer a reminder that written reviews are due in one week; this is when they generally go back and finish their review, scoring each section and giving their assessment of impact. Based on the preliminary scores an order of review is made. Best preliminary score to worst preliminary score. Only the top 40-60% are scheduled to be discussed by the group. The remainder are deemed noncompetitive and undergo what is called a ''streamlined review".



The reality is that 2-3 weeks before study section meets is when your proposal may actually receive a fast read for the first time, focusing on the specific aims, biographical sketch, and the company. It is at this time in which a general impression is formed.

Direct from NIH:

NIH uses a process called "streamlining" so reviewers can focus on applications that have a chance of being funded. Review committees don't review any application the group unanimously feels is roughly in the bottom half of applications being reviewed at the meeting. That percentage varies by grant type as well as by study section. Because no institute funds 50% of applications assigned to it, there's no need to review the bottom half. Here is how streamlining works:

- One week before the study section meets, SROs ask members for a list of applications they feel should not be reviewed and prepare a combined list.
- If any reviewer disagrees with a call, the group will review that application.

What this means:

Your application is not discussed during the study section meeting. As such they do not receive a numerical impact/priority score, but they do receive individual criterion scores. One of the more common reasons for this approach is that the application lacked significant and substantial merit.

For the competitive applications, the five criteria discussed in previous chapters (Significance, Investigator(s), Innovation, Approach, and Environment) determine the score. The reviewers will assign scores to these criteria based on their opinion of your proposal's scientific and technical merit. The scores are based on the 1-to-9 scale. Your application does not necessarily need to be strong in all categories to be judged likely to have major scientific impact. For instance, a project that is not necessarily innovative may be essential to advance a particular scientific field.

Impact	Score	Descriptor	Additional Guidance on Strengths/Weaknesses
High	1	Exceptional	Exceptionally strong with essentially no weaknesses
	2	Outstanding	Extremely strong with negligible weaknesses
	3	Excellent	Very strong with only some minor weaknesses
Medium	4	Very good	Strong but with numerous minor weaknesses
	5	Good	Strong but with at least one moderate weakness
	6	Satisfactory	Some strengths but also some moderate weaknesses
Low	7	Fair	Some strengths but at least one major weakness
	8	Marginal	A few strengths and a few major weaknesses
	9	Poor	Very few strengths and numerous major weaknesses
Minor weakness — An easily addressable weakness that does not substantially lessen impact			
Moderate weakness — A weakness that lessens impact			
Major weakness — A weakness that severely limits impact			

Direct from NIH:

As part of NIH's effort to enhance peer review a new scoring system took effect starting with Sept 2009 council (FY2010). Please refer to NOT-OD-09-024. This scoring system was designed to encourage more reliable scoring of applications. Highly rating all applications greatly diminishes the ability of a reviewer or study section to communicate the scientific impact of an application. Therefore, reviewers who carefully consider the rating guidance provided in determining their scores improve not only the reliability of their scores, but also improve their ability to communicate the scientific impact of the applications reviewed. The new scoring system uses a 9-point rating scale (1 = exceptional; 9 = poor). The overall impact score for each discussed application will be determined by calculating the mean score from all the eligible members' impact scores, and multiplying the average by 10; the overall impact score will range from 10 - 90. Overall impact scores will not be reported for applications that are not discussed.

Summary Statements

Direct from NIH:

Your summary statement is an official document with a short synopsis of peer reviewer critiques scores, codes indicating various concerns, and budget.

Summary Statements include:

- Resume and summary of the main points discussed during the review meeting and major strengths and weaknesses
- Reviewer critiques containing more information about the strengths and weaknesses detected by peer reviewers
- Codes and budget information
- Meeting Roster
- Contact information for the Program Official (PO) to whom the grant is assigned

Within approximately 30 days, your summary statement will be available via your NIH Commons account.

The information on your summary statement is not intended to be allinclusive; there may be additional concerns that are not reflected in the statement. Nonetheless, you should use this information if you decide to resubmit.

Institute/Council Review

Once the SRG has evaluated your application, the institute/center's advisory council or board will conduct a second review. These groups are comprised of scientists from the extramural research community and public representatives who are approved by the U.S. Department of Health and Human Services. During this review process, agency staff will examine applications, Overall Impact scores, and



View your Summary Statement like a report card.



You may still get awarded if there are funds remaining at the end of the funding cycle. summary statements. They provide the advisory council with a grant-funding plan. The council considers the institute/center's goals before advising the director, and the director makes the final funding decision.

In the event that your application did not make the payline, yet is still in line with the agency's priorities, you may be placed on the "select pay" list. What this means is, if there is money remaining at the end of the funding cycle, selected applications will be funded in the order they are listed.

If you are fortunate enough to win an award, you will be working closely with the institute/center program officer on scientific and programmatic matters and a grants management officer to make sure that all budgetary or administrative issues are addressed to the agency's satisfaction. Your scores will be available in the eRA Commons three business days after the review is complete. Your summary statement should appear there within three weeks.

Tracking Your Application

Direct from NIH:

The eRA Commons provides a valuable resource for applicants and PIs to track an application throughout various phases of the grants process. Within the eRA Commons , the Status tab is where most of the tracking information is found.

- 1) Use eRA Commons to track status. eRA Commons provides the status of your grant application and allows you to review detailed information associated with your applications/grants.
 - a) Log in to eRA Commons with your user name and password
 - b) Click the Status tab on the blue navigation bar across the top of the screen
 - c) Find the application/grant of interest
 - d) Click on the application ID.

The Status screen contains the most current status and relevant documents for that application/grant.

- 2) Watch for email notifications. Email notices are sent to notify the PI and/or signing official to check the eRA Commons for a change in status.
- 3) Tracking during Peer Review phase.
 - a) Score and percentile. Following the review group meeting, any available score and percentile information can be found in the application information section of the Status screen.
 - b) Summary statement. Approximately three weeks after the review meeting a full summary statement is available in the other relevant documents section.
- 4) Tracking during Pre-Award and Award phase.
 - a) Just-in-time (JIT). Some application information (other support, institutional review board and/or Institutional Animal Care and Use Committee approval dates and human subjects education information) is requested just prior to a final award decision. If needed, NIH will send a request for this information.
 - b) Notice of award (NoA). The NoA is the official grant award document notifying the grantee and others that an award has been made and stating the terms and conditions of the award. You will find a link to the NoA under the other relevant documents section of the Status screen. NoAs can also be automatically emailed to the grantee organization. Organizational officials can maintain an NoA email address in the eRA Commons institutional profile.
- 5) Tracking during Post-Award Management phase. Several post-award tasks can be managed through the eRA Commons..
 - a) Electronic Streamlined Non-Competing Award Process (eSNAP). eSNAP allows extramural grantee institutions to submit an electronic version

of a PHS 2590 progress report. This information is needed to receive a non-competing award. An eSNAP link is available under actions in your Status list of grants.

- b) Closeout. Electronically submit required closeout documents including Final Status Report (FSR), Final Progress Report and Final Invention Statement. At the appropriate time, a Requires Closeout link is available under actions in your Status list of grants.
- c) No-cost extension. You can extend the final budget period of the project one time for up to 12 months beyond the original expiration date on your NoA as long as no cost or scope change is involved. At the appropriate time, an Extension link is available under actions in your Status list of grants. This may be completed electronically up to one day prior to the end of the project period.

New Program Certifications Required for SBIR and STTR Awards-2013

Notice Number NOT-OD-13-116, released September 17, 2013 by the NIH, the purpose of which is to announce that the agency is implementing new SBIR/STTR program-specific certifications based on the SBIR/STTR Reauthorization Act of 2011 and the Small Business Administration's (SBA) SBIR and STTR Policy Directives. There has been a revision in the certifications required prior to award and there has been an added requirement that small businesses certify they are meeting the program's requirements during the life cycle of the funding agreement. The agency will replace the pre-award small business concern "Verification Statement" form with a revised "Funding Agreement Certification". The agency will also introduce a post-award "Life Cycle Certification" form consistent with the SBIR and STTR Policy Directives.

Direct from NIH:

Implementation

Revised Certification: Effective October 1, 2013, NIH will require completion of a SBIR Funding Agreement Certification by all SBIR applicants for new or renewal grants prior to award of a new award (grant or contract) or a competing renewal award (grant or contract). Likewise, a STTR Funding Agreement Certification will be required of applicants for all new and competing renewal STTR grants. Submission of these Funding Agreement Certifications for grants will be implemented using NIH's Just-in-Time pre-award procedures for SBIR/STTR grants. The SBIR and STTR Funding Agreement Certifications are revised and re-named versions of the Verification Statements formerly used at the pre-award stage. They are being implemented to mirror the content and format contained in the current SBIR and STTR Policy Directives. These certifications are necessary to assure that the applicant meets the SBA size criteria, and that the organization will comply with other program-specific requirements such as all work must be conducted in the United States and that a minimum amount of work be performed by its own employees within its own facilities, before NIH to can issue an award.

As done previously, if the funding agreement officer (for grants this is the Grants Management Officer) believes that the business may not meet certain eligibility requirements at the time of award, they may request a size determination from the SBA, who will determine eligibility. At that time, SBA will request further clarification and supporting documentation from the applicant small business concern in order to assist in the verification of any of the information provided as part of the determination request.

New Certification: Effective October 1, 2013, NIH also will require that all recipients of new or continuing SBIR and STTR awards complete a "Life Cycle Certification" once certain milestones are reached during the project period. Grant awardees are not required to submit this certification directly to NIH, but must instead complete a certification and maintain it on file in accordance with the

records retention policy in Section 8.4.2 of the NIH Grants Policy Statement. A certification is required at the following times:

- For SBIR and STTR Phase II Awardees: prior to receiving more than 50% of the total award amount and prior to final payment or disbursement from the Payment Management System (PMS).
- For SBIR and STTR Phase I Awardees: At the time of receiving final payment or disbursement from the Payment Management System

In addition, SBIR and STTR awardees indicate compliance with these certification requirements by drawing or requesting funds from PMS. The "Life Cycle Certification" is intended to ensure the ongoing compliance of the awardee with the assurances it provided in the Funding Agreement Certification prior to award.

If the Grants Management Officer believes, after award, that the business is not meeting certain funding agreement requirements, the agency may request further clarification and supporting documentation in order to assist in the verification of any of the information provided.

The Funding Agreement Certification and Life Cycle Certification forms are now available for SBIR and STTR applicants and awardees in fillable format at: <u>http://grants.nih.gov/grants/forms.htm#sbir</u>. Applicants and awardees are encouraged to carefully review each form prior to apply for or accepting an award.



Revised and New certifications are required for SBIR awardees beginning in 2013.

Just-in-Time Procedures

Just-in-Time means just that; the information requested will be just-in-time should the agency need it to make you an award.

Direct from NIH:

NIH uses Just-in-Time procedures for certain programs and award mechanisms (each FOA will include specific guidance on the use). These procedures allow certain elements of an application to be submitted later in the application process, after review when the application is under consideration for funding. The standard application elements include other support information (both active and pending) for senior/key personnel; certification of IRB approval of the project's proposed use of human subjects; verification of IACUC approval of the project's proposed use of live vertebrate animals; and evidence of compliance with the education in the protection of human research participants requirement. Other program-specific information may also be requested using this procedure. (Applications in response to RFAs also may be subject to these procedures. The RFA will specify the timing and nature of required submissions.)

Applicants will be notified (primarily by e-mail) when Just-in-Time information is needed. This notification is not a Notice of Award nor should it be construed to be an indicator of possible funding. Applicants should only submit this information when requested. Information must be submitted electronically using the Just-in-Time feature in the eRA Commons. In some circumstances the GMO may ask for information in addition to the descriptions below, e.g., if the application involves hESCs and the applicant did not identified a hESC from the NIH Registry in the application.

The requirement for applicants to verify the accuracy and validity of all administrative, fiscal, and programmatic information extends to information submitted through the Just-in-Time process. Applicants are responsible for promptly notifying NIH of any substantive changes to previously submitted Just-in-Time information up to the time of award. This includes items such as Other Support changes that could lead to budgetary overlap, scientific overlap, or commitment of effort greater than 12 person-months for the PD/PI(s) or any Senior/Key Personnel; or any changes in the use or approval of vertebrate animals or human subjects. Similar to the NIH public policy requirements, applicants are responsible for establishing and maintaining the necessary processes to monitor its compliance and informing NIH of any problems or concerns. Failure to address changes to Just-in-Time submissions prior to award does not diminish the applicant's responsibility to address changes post-award by submitting a prior approval request to NIH in accord with Administrative Requirements—Changes in Project and Budget—NIH Standard Terms of Award.

Other Support. Information on other active and pending support will be requested as part of the Just-in-Time procedures. Other support includes all financial resources, whether Federal, non-Federal, commercial or institutional, available in direct support of an individual's research endeavors, including but not limited to research grants, cooperative agreements, contracts, and/or institutional awards. Training awards, prizes or gifts are not included. Other support is requested for all individuals designated in an application as senior/key personnel—those devoting measurable effort to a project. Information on Other Support is not specifically requested for Program Directors, training faculty, and other individuals involved in the oversight of training grants since applicable information is collected in other sections of a training grant application. It is also not requested for individuals categorized as Other Significant Contributors.

IC scientific program and grants management staff will review this information before award to ensure the following:

- Sufficient levels of effort are committed to the project.
- There is no scientific, budgetary, or commitment overlap.
 - o Scientific overlap occurs when (1) substantially the same research is proposed in more than one application or is submitted to two or more funding sources for review and funding consideration or (2) a

specific research objective and the research design for accomplishing the objective are the same or closely related in two or more applications or awards, regardless of the funding source.

- Budgetary overlap occurs when duplicate or equivalent budgetary items (e.g., equipment, salaries) are requested in an application but already are provided by another source.
- Commitment overlap occurs when an individual's time commitment exceeds 100 percent (i.e., 12 person months), whether or not salary support is requested in the application.
- Overlap, whether scientific, budgetary, or commitment of an individual's effort greater than 100 percent, is not permitted. Any overlap will be resolved by the IC with the applicant and the PD/PI at the time of award.
- Only funds necessary to the approved project are included in the award.

Certification of IRB Approval. If the proposed project involves human subjects research, the certification date of IRB review and approval must be submitted. Pending or out-of-date approvals are not acceptable. See Public Policy Requirements/Human Subjects for additional information.

Verification of IACUC Approval. If the proposed project involves research with live vertebrate animals, verification of the date of IACUC approval of those sections of the application that involve use of vertebrate animals along with any IACUC-imposed changes must be submitted. Pending or out-of-date approvals are not acceptable. See Public Policy Requirements/Animal Welfare for additional information.

Human Subjects Education Requirement. If the proposed project involves human subjects research, certification that any person identified as senior/key personnel involved in human subjects research has completed an education program in the protection of human subjects must be submitted. See Public Policy Requirements/Human Subjects/Education in the Protection of Human Research Participants for additional information.

Human Embryonic Stem Cells (hESCs). If the proposed project involves hESCs and the applicant did not identify a hESC line from the NIH Human Embryonic Stem Cell Registry in the application, the line(s) should be included in the Just-in-Time submission.

Other Information Requested by the Awarding IC. NIH IC's may also request additional Just-in-Time information on a case-by-case basis, such as revised budgets or changes to the human subjects or vertebrate animal sections of the application.

Reasons for Rejection

"Multiple and varied" sums up the reasons for SBIR application rejection. Most of the time, however, the reasons focus on lack of enthusiasm for the research and development problem the proposal addresses, the investigator's ability to get the work done, the company setting, naive budget requests, and/or poor project presentation.

Reviewer Comments

Now, of what value are the reviewer's comments if the application is not funded? First off, addressing these comments in a resubmission (A1) of the same request is expected. Sufficiently putting to rest the reviewer's concerns are your best chance of having the proposal awarded the next time around. The one caveat here, however, is that if your resubmission doesn't have the same reviewers, you may still not be funded owing to different concerns by the different reviewers. The agency tries to avoid this inconsistency in reviewing, but it does still occur. While there are many reasons for not funding an application, including technical, not falling within the agency's mission, failure to write persuasively, and poor scientific design, it is important to discern between those that can be addressed and those that cannot.

Resubmission (A1) or New Application (A0)

Nearly every PI who submits a proposal to the NIH is denied the first time out. In fact, the estimated first-time rejection rate is 75 percent or more. Fortunately, the NIH does allow resubmissions for SBIR proposals.

From 2009 to 2014 the NIH only allowed one resubmission (A1) and if the resubmitted proposal was rejected your only choice was to develop an entirely new scope for your project or revised to be submitted through another mechanism or Institute/Center. Applicants now have another option of submitting the rejected proposal as a new application (A0).

Tips for Resubmitting

Provide sufficient evidence to justify your project. Include specific background data. Highlight compelling new data you gathered while waiting for the initial response, and cite newly published research papers. Ensure your outcomes/objectives are measurable, obtainable and specific. And create a clear budget narrative.

Focus on your writing. Create a strong introduction that keeps reviewers engaged and sets your proposal's tone. Be sure to label the progression of ideas, and keep your narrative concise by writing in short sentences and paragraphs.

Familiarize yourself with review process changes. Take note of new requirements like page limit reductions, and adhere to them.



If space permits, your resubmitted application should include a reply to each comment, and highlight your explanations and changes.



It is important to read the initial RFA or program announcement you applied under carefully to see if there are any special rules regarding A1 resubmissions.

NIH Policy Change on Resubmitting Applications

The NIH still allows only one resubmission of an unfunded application (see NOT-OD-09-016 at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-09-016.html), which must be submitted within 37 months of the new (A0) application (see NOT-OD-10-140 at http://grants.nih.gov/grants/guide/notice-files/ NOT-OD-10-140.html). If the resubmission is not funded, the previous policy stated that the application had to substantially differ in both content and scope in order to be eligible for submission as a new application. However, for all application due dates after April 16, 2014, if your resubmission application (A1) was unsuccessful at receiving funding, you may now submit the same idea as a new (A0) application for the next appropriate new application due date (see NOT-OD-14-074 at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-14-074. html). This change in resubmission policy applies to applications submitted to all grant and cooperative agreement funding opportunities that allow resubmissions, including all fellowship, training, and career development awards.

Direct from NIH: http://grants.nih.gov/grants/policy/amendedapps.htm

OD-14-074.html), for application due dates after April 16, 2014:

• following an unsuccessful resubmission (A1) application, applicants may submit the same idea as a new (A0) application for the next appropriate due date.

Per NOT-OD-14-074 (see http://grants.nih.gov/grants/guide/notice-files/NOT-

NIH will not assess the similarity of the science in the new (A0) application to any previously reviewed submission when accepting an application for review.

This policy applies to all NIH Funding Opportunity Announcements (FOAs) that allow resubmissions, including FOAs for research grants, the NIH Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs, Career Development Awards, Individual Fellowships, Institutional Training Grants, Resource Grants, Program Projects, and Center Grants.



TIP:

The revised proposal requires a one page introduction that explains how the investigator has revised the grant.

NIH's policy for accepting overlapping applications remains in effect (see NOT-OD-09-100 at <u>http://grants.nih.gov/grants/guide/notice-files/NOT-OD-09-100.html</u>). The NIH will not accept duplicate or highly overlapping applications under review at the same time. This means that the NIH will not review:

- a new (A0) application that is submitted before issuance of the summary statement from the review of an overlapping new (A0) or resubmission (A1) application.
- a resubmission (A1) application that is submitted before issuance of the summary statement from the review of the previous new (A0) application.
- an application that has substantial overlap with another application pending appeal of initial peer review (see NOT-OD-11-101 at <u>http://grants.nih.gov/</u> grants/guide/notice-files/NOT-OD-11-101.html).

NIH will not accept a resubmission (A1) application that is submitted later than 37 months after submission of the new (A0) application that it follows (see NOT-OD-12-128 at <u>http://grants.nih.gov/grants/guide/notice-files/NOT-OD-12-128</u>. <u>html</u> and NOT-OD-10-140 at <u>http://grants.nih.gov/grants/guide/notice-files/NOT-OD-10-140.html</u>).

Applicants should check the individual FOA to determine whether resubmission applications are allowed. Resubmissions normally are not permitted for applications received in response to a Request for Applications (RFA) unless it is specified in the FOA, in which case only one resubmission will be permitted. Since an RFA often has special considerations of eligibility, scientific scope, and review criteria, unfunded applications to an RFA must be submitted as new applications to another FOA, using that FOA's target due date for new applications.

Similarly, a change of grant activity code (e.g., from an R01 to an R21 or from an R03 to an R01) usually involves a change of eligibility criteria, application characteristics, dollar limits, time limits, or review criteria. These applications also MUST be prepared as new applications. More information on these policies can be found in the NOT-OD-03-019 (see <u>http://grants.nih.gov/grants/guide/notice-files/</u> <u>NOT-OD-03-019.html</u>).



Not counting the introduction, a revised proposal must keep to the same page limits as other proposals.

The Purpose of this Policy Change

The new policy allows for ideas that were unsuccessfully submitted as a resubmission to be presented in a new grant application without having to substantially redesign the content and scope of the project. This policy change from the requirement that previously reviewed applications be substantially redesigned in order to be accepted as a new application is in response to researcher's concerns that changing the scope to be accepted as new resulted in many meritorious research ideas being deemed ineligible for resubmission. It was argued that this previous policy was especially hard on new investigators, since finding new research directions can be quite difficult during this phase of their career. Likewise, established investigators expressed concern about the need to redirect the research focus of productive labs in order to submit future NIH applications.

Resubmission of an idea as new means that the application will be considered without a connection to a previous submission. As such, the applicant will not provide an introduction to describe how this application has changed or specifically respond to previous reviewer critiques. During review, the reviewers will be instructed to evaluate the submission as a new idea, even if they have seen this project in prior cycles. While there may not be major changes to the research direction of these previously reviewed ideas, the NIH does expect that applicants will still take advantage of previous comments to bolster the application for each submission. Also, if you had an unsuccessful resubmission before this new policy was issued, this previously rejected A1 is now eligible for submission as a new A0 application.

What Does This Mean in Practice?

- You may now submit a new A0 following an unsuccessful new A0
- Unless you would like the opportunity to address reviewer comments directly, you do not have to resubmit as an A1
- The new resubmission policy does not limit the number of times an application may be submitted as new



If you had an unsuccessful resubmission before this new policy was issued, this previously rejected A1 is now eligible for submission as a new A0 application.

- Following an unsuccessful A1, you can submit as an A0 having the same title if you wish; it is not a requirement that you change the title
- As a new submission, it will receive a new grant number
- You still need to have received your summary statement before you can submit an unsuccessful A1 as an A0

Keep in mind, these rules refer to grants submitted through a general program announcement, not necessarily requests for applications (RFA). Most RFAs, which are one time competitions to meet a specific need, do not allow resubmissions. If an investigator wants to resubmit an RFA with revisions under a regular program announcement, that would be considered a new proposal.

Direct from NIH: How does NIH's current resubmission policy affect SBIR/STTR Applicants?

Please review the four case studies for Phase I, Phase II/Phase IIB, Fast-Track, and Direct Phase II to understand how the current NIH resubmission policy relates to SBIR/STTR applicants.

Phase I

A Phase I application is a "Type 1" or "New" application. When the applicant submits a New Phase I application (A0) and it is not funded, the applicant can address reviewer comments and submit as a Resubmission A1 for the next appropriate application due date, or they can submit a New application (A0).

Fast-Track

A Fast-track application is also a "Type 1" or "New" application and follows the same rules as a Phase I. If a New Fast-track (A0) is not funded, the applicant can address reviewer comments and submit as a Resubmission Fast-track A1, or they can submit a New Fast-track (A0) for the next appropriate application due date.

If the Fast-track (A0 or A1) was not funded, the applicant can also revise down the scope of their application and submit as a New Phase I (A0).

Phase II/Phase IIB

A Phase II and Phase IIB are considered "Type 2" or "Renewal" applications. If an applicant does not get funded on the first submission (A0), they can re-submit an A1 for a Phase II/IIB.

If a Phase II or Phase II resubmission (Type 2, A1) is not funded, the applicant may submit a New Phase I, Fast-track, or SBIR Direct Phase II (Type 1, A0). However, the project will lose any association with the previously funded grant, and the New project must be substantially different than the previous project to avoid duplicative funding. If the applicant decides to submit a SBIR Direct Phase II, they must also have previously completed the Phase I equivalent work without any SBIR/STTR funds.

Direct Phase II

A Direct Phase II application is considered a "Type 1" or "New" application, but in order to be eligible for a Direct Phase II, the small business applicant must demonstrate the Phase I equivalence of their preliminary data in their Direct Phase II application. If a New SBIR Direct Phase II (A0) is not funded, the applicant can address reviewer comments and submit as a Resubmission SBIR Direct Phase II A1, or they can submit a SBIR New Direct Phase II (A0) for the next appropriate application due date. The small business applicant is not able to apply for a new Phase I or Fast-track (A0) unless they substantially change their project scope to prevent funding for a Phase I-like work already completed by the applicant.

For more information, please read the NIH Policy on Resubmission Applications (<u>http://grants.nih.gov/grants/policy/amendedapps.htm</u>) and check out the Resubmissions of NIH Applications FAQs (<u>http://grants.nih.gov/grants/policy/</u> <u>resubmission_q&a.htm</u>). General questions concerning this policy may be directed to the Division of Receipt and Referral at the Center for Scientific Review, 301-435-0715.

CONCLUSION

This final chapter describes the review process, from receipt of your application by the NIH to 'just in time' procedures in the event that an award may be made to you. The information that you can expect to receive, as well as the timing of when to anticipate this information becoming available, is also described. The NIH realizes that you spend a lot of time getting to this point and they strive to keep you up-to-date with you application's progress. Remember that the majority of applications received by the NIH are not awarded. So, if your application is not funded the first time around, shake off the initial disappointment, heed the reviewer comments, and submit again.

Appendix A: A Few Words Regarding Phase II SBIR Awards

Phase I awards cannot be renewed; applying for a Phase II is in effect asking for a renewal or a continuation of your research and development project, since you cannot apply for a Phase II unless you have been awarded a Phase I.

All of the information in the previous chapters of this manual is directly applicable to applying for a Phase II SBIR. The main things to keep in mind for Phase II are:

- Phase II is an extension of the Phase I.
- You must build the Phase II project from where the Phase I left off.
- If results for Phase I were insufficient, the Phase II application may not receive a score in the peer review process.
- Phase II must still demonstrate feasibility, scientific, technical merit, and commercial potential.
- You must include a commercialization plan in Phase II (12 page limit)
- Phase II applications may be submitted either before or after expiration of the Phase I budget period.
- Phase II grant applications should be submitted no later than the first six submission dates following expiration of the Phase I budget period.

Direct from NIH:

Funding shall be based on the results of Phase I and the scientific and technical merit and commercial potential of the Phase II application. Part I: Instructions for Preparing and Submitting an Application I-4 SBIR/STTR SF424 (R&R) Adobe Forms Version B Application Guide.
All Phase II applications must include a succinct Commercialization Plan. Specific details for preparing this section are described in Section 5.6 of this Application Guide.

SBIR Phase II awards normally may not exceed \$1,000,000 total (direct costs, F&A/indirect costs, and fee) for a period normally not to exceed 2 years. STTR Phase II awards normally may not exceed \$1,000,000 total (direct costs, F&A/indirect costs, and fee) for a period normally not to exceed 2 years.

According to statutory guidelines, total funding support (direct costs, indirect costs, and fee) normally may not exceed \$150,000 for Phase I awards and \$1,000,000 for Phase II awards. With appropriate justification from the applicant, Congress will allow awards to exceed these amounts by up to 50% (\$225,000 for Phase I and \$1,500,000 for Phase II, a hard cap). As written in the statute and under appropriate circumstances, NIH can apply for a waiver from SBA to issue an award exceeding \$225,000 for Phase I or \$1,500,000 for Phase II, if this hard cap will interfere with NIH's ability to meet its mission. Award waivers from the SBA are not guaranteed and may delay the release of funds. Applicants are strongly encouraged to contact NIH program officials prior to submitting any award in excess of the guidelines. In all cases, applicants should propose a budget that is reasonable and appropriate for completion of the research project.

Only Phase I awardees are eligible to apply for and obtain Phase II funding at this time. Awardees identified via a "successor-in-interest" or "novated" or similarly-revised funding agreement, or those that have reorganized with the same key staff, regardless of whether they have been assigned a different tax identification number, are eligible to apply for Phase II funding. Agencies may require the original awardee to relinquish its rights and interests in an SBIR/STTR project in favor of another applicant as a condition for that applicant's eligibility to participate in the SBIR/STTR program for that project. Only one new Phase II award may be made for a single SBIR/ STTR project.

You may submit a Phase II application either before or after expiration of the Phase I budget period, unless you elect to submit a Phase I and Phase II application concurrently under the Fast-Track procedure. To maintain eligibility to seek Phase II support, a Phase I grantee organization should submit a Phase II application within the first six receipt dates following the expiration of the Phase I budget.

Commercialization Plan

From the agency:

Commercialization Plan

(Applicable to all Phase II and Phase IIB Applications and Phase I/Phase II Fast-Track Applications.)

If you are submitting a Phase II, Phase IIB or Phase I/Phase II Fast-Track application, include a Commercialization Plan in accordance with the agency announcement and/or agency-specific instructions. To attach a Commercialization Plan file, click the Add Attachment button to the right of this field, browse to where you saved the file, select the file, and then click Open.

All Phase II, Phase IIB and Fast-Track applications must include a succinct Commercialization Plan. The Commercialization Plan is limited to 12 pages. Be succinct. There is no requirement for applicants to use the maximum allowable pages allotted to the Commercialization Plan.

Create a document entitled, "Commercialization Plan," and provide a description in each of the following areas:

a. Value of the SBIR/STTR Project, Expected Outcomes, and Impact. Describe, in layperson's terms, the proposed project and its key technology objectives. State the product, process, or service to be developed in Phase III. Clarify the need addressed, specifying weaknesses in the current approaches to meet this need. In addition, describe the commercial applications of the research and the innovation inherent in this application. Be sure to also specify the potential societal, educational, and scientific benefits of this work. Explain the noncommercial impacts to the overall significance of the project. Explain how the SBIR/STTR project integrates with the overall business plan of the company.

b. Company. Give a brief description of your company including corporate objectives, core competencies, present size (annual sales level and number and types of employees), history of previous Federal and non-Federal funding, regulatory experience, and subsequent commercialization, and any current products/services that have significant sales. Include a short description of the origins of the company. Indicate your vision for the future, how you will grow/ maintain a sustainable business entity, and how you will meet critical management functions as your company evolves from a small technology R&D business to a successful commercial entity.

<u>c. Market, Customer, and Competition.</u> Describe the market and/or market segments you are targeting and provide a brief profile of the potential customer. Tell what significant advantages your innovation will bring to the market, e.g., better performance, lower cost, faster, more efficient or effective, new capability. Explain the hurdles you will have to overcome in order to gain market/customer acceptance of your innovation.

Describe any strategic alliances, partnerships, or licensing agreements you have in place to get FDA approval (if required) and to market and sell your product.

Briefly describe your marketing and sales strategy. Give an overview of the current competitive landscape and any potential competitors over the next several years. (It is very important that you understand and know the competition.)

<u>d. Intellectual Property (IP) Protection.</u> Describe how you are going to protect the IP that results from your innovation. Also note other actions you may consider taking that will constitute at least a temporal barrier to others aiming to provide a solution similar to yours.

e. Finance Plan. Describe the necessary financing you will require to commercialize the product, process, or service, and when it will be required. Describe your plans to raise the requisite financing to launch your innovation into Phase III and begin the revenue stream. Plans for this financing stage may be demonstrated in one or more of the following ways:

Letter of commitment of funding.

- Letter of intent or evidence of negotiations to provide funding, should the Phase II project be successful and the market need still exist.
- Letter of support for the project and/or some in-kind commitment, e.g., to test or evaluate the innovation.
- Specific steps you are going to take to secure Phase III funding.

<u>*f. Production and Marketing Plan.*</u> Describe how the production of your product/process/service will occur (e.g., in-house manufacturing, contract manufacturing). Describe the steps you will take to market and sell your product/process/service. For example, explain plans for licensing, Internet sales, etc.

g. Revenue Stream. Explain how you plan to generate a revenue stream for your company should this project be a success. Examples of revenue stream generation include, but are not limited to, manufacture and direct sales, sales through value added resellers or other distributors, joint venture, licensing, service. Describe how your staffing will change to meet your revenue expectations.

Applicants are encouraged to seek commitment(s) of funds and/or resources from an investor or partner organization for commercialization of the product(s) or service(s) resulting from the SBIR/STTR grant. Place relevant letters following letters from consultants and collaborators in Item 14, Letters of Support in the PHS 398 Research Plan Form.

Your Phase III funding may be from any of a number of different sources including, but not limited to: SBIR/STTR firm itself; private investors or "angels"; venture capital firms; investment companies; joint ventures; R&D limited partnerships; strategic alliances; research contracts; sales of prototypes (built as part of this project); public offering; state finance programs; non SBIR-funded R&D or production commitments from a Federal agency with the intention that the results will be used by the United States government; or other industrial firms.

What this means:

- A. Value proposition of project
 - Define the opportunity. What need will you address addressed? Why are current solutions not sufficient?
 - State expected outcomes, impact. How will the success of your research and development project make a difference?
- B. Company
 - Overview: origins, number of employees, annual sales, previous or current SBIR support
 - Corporate objectives: vision, mission, plans for growth and expansion
 - Core competencies
 - Commercialization experience

C. Market

- Customer and competition/competitive landscape
- D. Intellectual Property (IP) Protection
 - Your patent position and plans moving forward
 - Freedom to operate

- E. Finance Plan
 - Milestone-based
 - Diversified
 - Documented
- F. Production and Marketing plan
 - Manufacturing in-house, contracted, or licensed?
 - Marketing out-sourced?
- G. Revenue Stream
 - Sales
 - Services
 - Royalties
 - Other

The Commercialization Plan is perhaps the most critical section of the Phase II proposal. It is your best opportunity to describe the strategy that your company will use to generate revenue from the proposed research and development innovation. The plan must clearly spell out the business opportunity enabled by the innovation. The plan also needs to communicate the current status of the innovation, as well as describing your company's strategy for advancement and how the innovation fits into the future market. Your Commercialization Plan should:

- Cover a specific product, service, or technology
- Define the route to market
- Identify milestones and risks related to the product, service, or technology commercialization
- Provide financial information (i.e. cost, price, sales projections, margin) related to the product, service, or technology.

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