# Advice on NIH SBIR & STTR Grant Applications – Grantsmanship

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May 2007

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Hello, I am Gregory Milman. In this presentation I provide advice on grantsmanship to help you prepare an NIH SBIR or STTR grant application. This presentation was updated in May 2007. Send your comments, suggestions, and criticisms to gmilman@niaid.nih.gov.

## Know NIH Review Criteria

- **Significance**: Does the study address an important problem and have commercial potential? Will scientific knowledge be advanced and/or enabling technologies created?
- **Approach**: Are design and methods well-developed and appropriate? Are problem areas addressed?
- **Innovation**: Are there novel concepts or approaches? Are the aims original and innovative?
- **Investigator**: Is the investigator appropriately trained and capable of managing the project?
- **Environment**: Does the scientific environment contribute to the probability of success? Are there unique features of the scientific environment?

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Peer reviewers use five criteria to evaluate your application: significance, approach, innovation, investigator, and environment.

These are the same criteria used to judge all NIH applications. Although some are more important than others, none is unimportant. Prepare your application to address each area.

Organize your application to make it easy for reviewers to find information relating to each criteria.

You do not need to excel in all criteria because reviewers do not rate them separately. Instead, reviewers' priority score assignments are a gestalt reflecting your entire application, based on what they read and what they hear from other reviewers.

## Phase I Objective

- Establish the technical and scientific merit, and feasibility of proposed R/R&D efforts.
- Not “feasibility” of producing the product.
- Multiple “feasibility” studies may be necessary between the inception of an idea and the sale of a product.
  - The window is open for more than one Phase I and Phase II grant for any product.
  - You should carefully define and limit your proposals.

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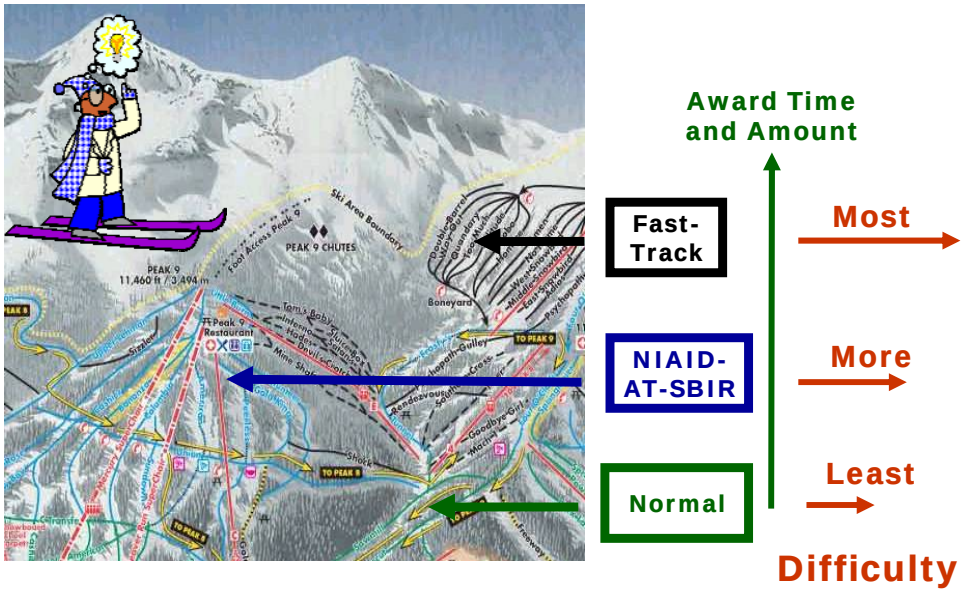
One of the most common mistakes made by applicants is lack of focus - thinking too big. It may not be likely or even desirable to go from concept to product in a single Phase I/Phase II application.

Your objective for Phase I is to establish the technical and scientific merit, and feasibility of Phase II, not of producing your product.

You may need to test feasibility at many steps along the path from concept to product.

If you are careful and limit the scope of your application, you may be able to have multiple Phase I and Phase II funding to support your voyage from concept to product.

## Master the Beginner Slopes First




Our advice skier may help you decide what type of NIAID application you should consider. Small business applications are like most NIH applications: the more time and money you request, the greater the difficulty of writing an application that gets funded.

The “normal” SBIR application, like the beginner green slopes, is the least difficult to master but comes with the least award of funds and time.

The NIAID-AT-SBIR, and similar multi-year, higher award applications are more difficult to master, like the intermediate blue slopes. Successful applications usually include more preliminary data and require better grant-writing proficiency. You are more likely to be successful on the blue slopes after you have received a Phase II award on the green ones.

The fast-track application, like the most difficult double diamond black slopes on the top of the mountain, should be attempted only by those who have mastered the art of SBIR grantsmanship, have compelling preliminary data, and propose a project with crystal clear go-no-go milestones.

Keep in mind that about half of Phase I awardees receive over $100,000 and thus appear to have mastered the intermediate slopes. Only you can determine on which slope you belong.


I use a balloon metaphor to illustrate why applications that exceed normal guidelines are less likely to be funded.

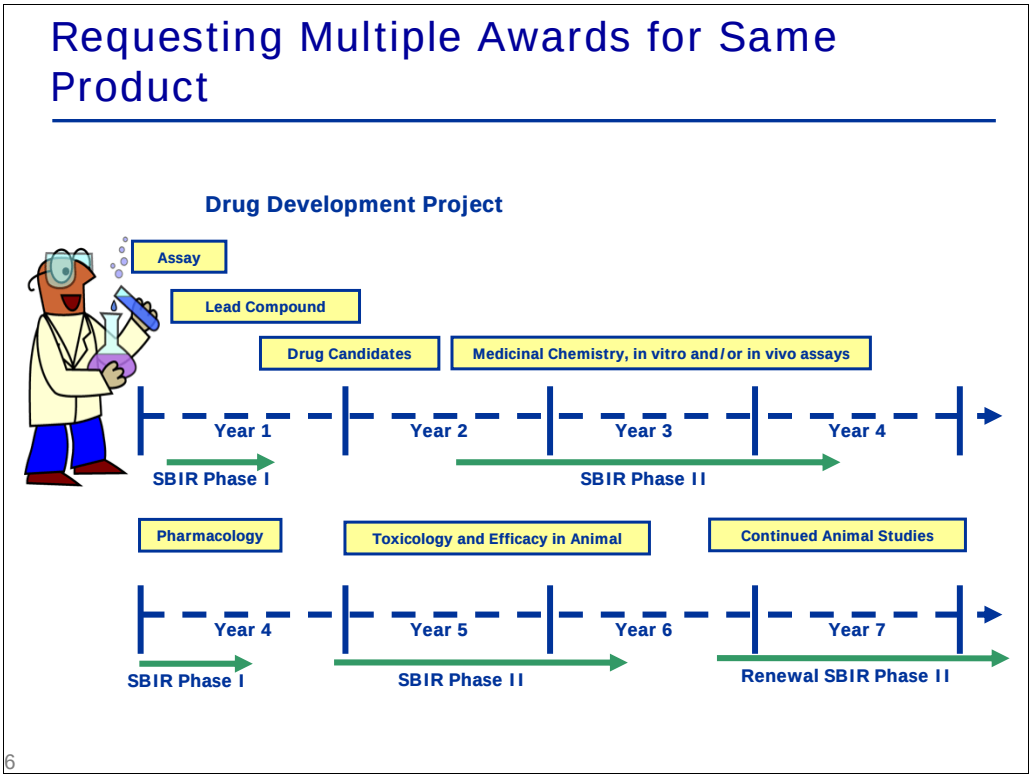
Review committees use a triage process to spend the most time on applications most likely to be funded. They search for any weakness in an application which may quickly eliminate it from further consideration.

Compared to normal applications, NIAID-AT-SBIR and fast-track applications are often larger in scope and more likely to have a discernable weakness that leads to their downfall. Like a balloon, the more you expand your application, the more likely it is to have weak spots.

The review committee's sharp criticism will be directed at the first weak spot they detect, and they will pop your balloon. Once the air is released, your application is no longer considered seriously.

As a result, the criticisms you receive may not fully describe all that is wrong with your application. If you patch only the identified holes and resubmit, you may miss other problems which may be uncovered at the next review.

Your best strategy is to keep your Phase I application as small and well-focused as possible, like the smallest balloon. Limit your Phase I goals to only those absolutely necessary to support your application for Phase II. Then, ask for no more and no less than the funds required to conduct your Phase I research.




Using a drug development project, I provide an example of how you might request multiple SBIR Phase I and Phase II grants for the studies leading to an investigational new drug FDA application, an IND.

The first Phase I takes the project from assay to lead compounds. This Phase I is the feasibility study for the first Phase II which conducts medicinal chemistry to move from lead compound to drug candidate using in vitro and/or cell culture assays.

The second Phase I begins the critical path to drug development following the selection of a drug candidate. Phase I studies could include formulation and animal model studies on pharmacology. A follow-on Phase II might continue with animal model studies of toxicology and efficacy. If additional pre-IND studies are required, you could apply for a competing renewal of your Phase II grant as I describe in the next slide.

## NIAID Phase II Competing Renewals

- Many ICs offer competing renewal Phase II grants for products that require approval of the FDA.
- NIAID accepts competing renewal Phase II grant applications for a project period up to three years and a budget not to exceed a total cost of $1 million per year.
- Competing renewal Phase II applications to NIAID may exceed 50% consultant and contractual costs when well justified and necessary to support well-justified studies and related expenses.
- NIAID supports SBIR/STTR clinical trials only through the NIAID R34 – U01 application process.

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A number of NIH ICs allow Phase II grantees to apply for Phase II renewal funding for projects whose products require FDA approval.

NIAID accepts Phase II renewal applications for grants up to three years and a budget not to exceed a total cost of $1 million per year.

Also, NIAID Phase II renewal applications may request in excess of 50% consultant and contractual costs when well justified and necessary to support studies and related expenses.

Note that NIAID supports SBIR and STTR clinical trials only through NIAID's R34 – U01 application process.

## Electronic Applications

- Bookmark and follow the NIH step by step Electronic Application Process.
- Print the Electronic Application Flow Chart to track your progress.
- Open and print the official "SBIR/STTR Application Guide SF424 (R&R)" from the link on the SF424 (R&R) Application and Electronic Submission Information page.
- Grants.gov may switch from Pure Edge to Adobe Forms by the August or December 2007 receipt dates.
- Register for application submission:
  - Company and company official must be registered in Grants.gov.
  - PI and company official must be registered in the eRA Commons.

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All NIH SBIR and STTR applications are submitted electronically. I suggest you bookmark and follow the NIH step by step Electronic Application Process. You can track your progress using the Electronic Application Flow Chart. Application instructions change frequently. Always print the most recent official "SBIR/STTR Application Guide SF424 (R&R)" from the link on the SF424 (R&R) Application and Electronic Submission Information page. Be aware that Grants.gov may switch from Pure Edge to Adobe Forms by the August or December 2007 receipt dates.

To submit an application, a company must be registered in both Grants.gov and the eRA Commons, and the PI must be registered and associated with the company in the Commons. Allow at least a month to complete these registrations. Also, I suggest you submit your application two or more weeks before an application receipt date to give you plenty of time to correct errors and resubmit.

## Budget and Fee


- Follow the budget instructions in the Application Guide.
- Complete budget sections A to K for the company.
- STTR applicants and SBIR applicants with partner institutions must follow the instructions for a subaward.
- Complete a detailed budget for each year of support requested. Round calculations down to nearest dollar.
- Use whole numbers: months for percent effort and dollars for cost.
- Do not exceed the salary cap.
- A fee up to 7% can be used for expenses that may not be charged to your grant.

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On this slide I highlight a few important items about budgets and fees. As always, carefully read and follow the official instructions.

Complete the detailed budget sections for the company for each year of requested support. You may need to complete the first year's budget before you can access the next year's budget. If your application includes a partner institution, your partner must complete a subaward budget.

Use only whole numbers: dollars for cost and personnel months for effort.

Do not request salaries that exceed the annual salary cap or NIH will decrease your award. The salary cap link provides information on the allowed amount.

A fee, if requested, can be used to pay for things related to your grant but not permitted as direct or indirect costs. For example, you could use the fee to pay for patent costs, for market research, or for expenses outside the U.S. Explain how you will use a fee in your justification. The fee is limited to 7% of the total cost.

## Specific Aims


- Your specific aims are the milestones of your research project, driven by your hypothesis or research objective.
- Do not confuse your specific aims with your long-term goals.
- Specific aims are the criteria by which success of Phase I will be judged.
- Choose specific aims that can be easily assessed by the review committee.
- Include concrete specific aims that reviewers will expect.

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Begin the Specific Aims section of your research plan with your hypothesis or research objective. Then describe your specific aims as the milestones for your Phase I research. Make your Specific Aims section about half a page in length and no more than one. Unless essential, I suggest you avoid citations in this section.

Do not confuse specific aims with your project's long-term goals. Specific aims are what you will accomplish before the end of the first funding period.

When your Phase II application is considered, reviewers will judge your Phase I accomplishments against the Phase I specific aims that you proposed. Thus, you want to select specific aims you are reasonably confident that you can accomplish. However, the review committee will doubt your judgment if you omit a milestone that they think is essential before Phase II funding.

To be easily assessed, a specific aim should be an "end point" as opposed to a "best effort."

For example, in a drug development project, instead of a specific aim "to evaluate a number of potential drug candidates," which would be a "best effort," make your specific aim "to select the best drug candidate for further study," which is an "end point." In the latter case, you will have reached a conclusion and will be ready to move on to the next phase of your project.

## Background and Significance

- Significant product potential
  - A product-focused application is more likely to have support of business reviewers.
  - A project with sound financial projections is more likely to attract a partner.
- Significant, innovative science
  - A scientifically focused application is more likely to have a knowledgeable reviewer.
- Significant to NIH institute or center
  - An application that addresses a program's need is more likely to have a champion.
  - Identify and speak with your potential champion.

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The Background and Significance section of your Research Plan may have different meanings for different reviewers. Aim for two pages and no more than three.

To be competitive, applications for NIH small business funds need to show a significant product, significant science, and significant public health need.

Business reviewers will judge your application on its likelihood to lead to a commercially successful product in a reasonable period of time. They are impressed by a project with sound financial projections and partners who will help get your product to the market.

Science reviewers will judge your application on its science innovation and its likelihood to increase knowledge. The more focused the application, the more likely it will be assigned to a knowledgeable reviewer.

Both the product and the science should be targeted to the needs (the mission) of an NIH IC and to a specific program area administered by a program officer (a champion) who will support funding your project over its competition. A supportive program officer may be particularly important in ICs that do not use paylines.

Innovation does not necessarily mean a new paradigm. Either the ends or the means should be innovative, but both do not have to be.

Thus, if the result of the research is critical, it may not be important that your means are not innovative and vice versa.

## Illustrate Background and Significance

- Describe the state of the art for your research area, the gaps and roadblocks, and the opportunity you have identified.
- Use citations to demonstrate the breadth of your knowledge of both published and unpublished work.
- Tell why your proposal will increase knowledge and improve public health.
- Identify how the proposed Phase I research milestones will justify Phase II.

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The following are my tips to make the Background and Significance section better.

Illustrate background by describing the state of art of your research area, the gaps as well as the roadblocks, and how your project addresses these.

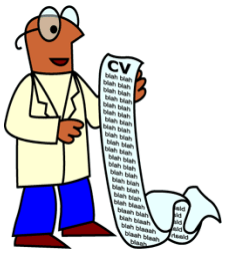
Show reviewers you know the field by the breadth of your knowledge of both published and unpublished work by others, some of whom could be your reviewers.

Illustrate significance by telling reviewers explicitly why your proposal is innovative, how it will increase scientific knowledge, and the way in which it could improve public health.

Show how the Phase I research milestones you outlined in your specific aims will justify your application for a Phase II award.

## Preliminary Studies

- Preliminary data
  - Solicitation states “Preliminary data are not required.”
  - Other applications present preliminary data.
  - Reviewers like to see preliminary data.
  - Preliminary data should support your proposal and the feasibility of the project.
  - Preliminary data may consist of your own publications and unpublished data from your laboratory.
  - Interpret results critically. Evaluate alternative meanings.
- Previous experience (publications, patents, similar products) basis for investigator evaluation criterion.

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The Preliminary Studies section of your Research Plan should convince reviewers that you can do what you propose.

Although the SBIR/STTR solicitation states that “Preliminary data are not required,” most applications present preliminary data. Review committees are likely to have greater enthusiasm for proposals with preliminary data.

Preliminary data support your proposal and the feasibility of the project. It may consist of your own publications and those of others, as well as unpublished data from your laboratory.

Interpret results critically and evaluate alternative meanings. You can be assured that critical members of the review committee will look for explanations other than the ones you propose.

Describe your relevant experience. Emphasize work you have accomplished that indicates you can direct the proposed research and achieve your project's aims.

Reviewers use this section and the biographical sketches section in their Investigator evaluation.

## Research Design and Methods

- Describe your research design and methods in parallel to your specific aims, including for each experiment:
  - Timelines.
  - Rationale, innovation, supporting data, and references.
  - Expected results, limitations, potential difficulties, and planned statistical analysis if relevant.
  - Criteria for evaluating success, failure, or other possible interpretations.
  - Hazards anticipated, precautions proposed.
  - Reagents, animals, human subjects, equipment, etc.
  - Collaborators: purpose and letters of agreement.

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The Research Design and Methods 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. I suggest you include a timeline to convey your entire project quickly to reviewers.

Give a rationale for your choice 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.

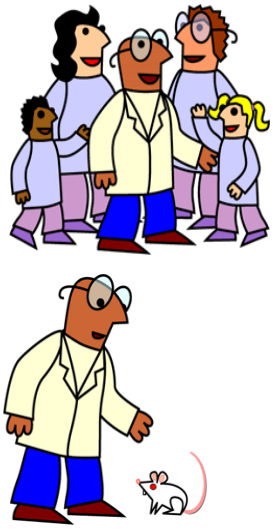
Describe the kinds of results expected and how they would support continuation of your project. Present other possible outcomes and contingency plans.

Define the criteria for evaluating the success or failure of each experiment. If possible, include statistical analysis as reviewers are often 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.

Explain how credible collaborators will participate in your proposed research. Include letters that describe collaborators agreements with you, including their role on the project and hours to be committed.

## Other Issues You Must Address



- Protection of Human Subjects.
- Inclusion of Women and Minorities.
- Targeted/Planned Enrollment Table.
- Inclusion of Children.
- Data and Safety Monitoring Plan.
- Vertebrate Animals.
- Consortium/Contractual Agreements
- Select Agent Information.
- Resource Sharing Plans.
- Letters of Support.

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Failure to adhere to regulations on human subjects can easily delay or abort funding for a research project. If your research requires only human samples, I suggest you try to design your experiments so that they are not considered human subjects research.

Failure to adhere to regulations on vertebrate animals can also sidetrack your award. Even if you plan to use animal facilities in a collaborating institution, the company must have an approved animal welfare assurance on file before an award. I suggest you design experiments that do not require vertebrate animals unless you really need them, and if you need them, get your assurance paper work done early.

Although absence of some details on Consortium and Contractual Arrangements and Resource Sharing may not affect your priority score, they can delay or even sidetrack your award.

Required information on select agents must be included if you will work with them.

The letters of support can affect your score, so follow directions to attach letters from all people who have significant roles on your project.

## Just-in-Time – Our Time, Not Yours

- Other support data for PI and all key personnel.
- Lease agreement.
- PI and applicant institution eligibility verification.
- Human subjects Federalwide Assurance (FWA) number.
- Institutional review board (IRB) approval certification date.
- Human subjects education certification.
- Institutional animal care and use committee (IACUC) assurance number and approval date.

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Some application information is required just-in-time, meaning at the time NIH wants to award you a grant.

At that time you will:

- Provide NIH a list of other research support for the PI and all key personnel.
- Provide a lease agreement or other documentation showing you control your research space.
- Verify that an SBIR PI works over half-time for the company and that the company is eligible for SBIR or STTR funding.
- If you are conducting human research, provide an FWA number, IRB approval information, and human subjects education certification.
- If your research uses vertebrate animals, provide an IACUC assurance number and protocol approval date.

If any of this information is not available when NIH is ready to fund your application, your award will be delayed. If you do not provide the information within a time specified by the funding IC, your application may be inactivated.

## Key to Avoiding Human Subjects Regulations

- Research involving samples from dead people is not considered human subjects research.
- Research involving only coded private information or human biological specimens is not considered to be human subjects research if:
  - Specimens or data are not obtained specifically for your research.
  - Subject's identity is coded.
  - The providers do not collaborate on the research.
- If you will use non-identifiable human samples,
  - Select “no” for the Human Subjects’ field on the Research and Related Other Project Information form.
  - Attach PDF document titled, “No Human Subjects Research in this application” describing your justifications to the Protection of Human Subjects field of the PHS 398 Research Plan form.
- If your research requires human subjects, view our tutorial, How to Write a Human Subjects Application and refer to Supplemental Instructions for Preparing the Human Subjects Section of the Research Plan for detailed information.

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Federal human subjects regulations only apply to living individuals and not to samples from the dead.

Research using human samples is not considered human subjects research if:

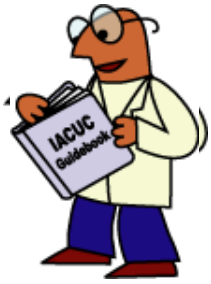
- The samples are obtained for reasons other than your proposed research, for example as a biopsy for other health reasons.
- You sign a written agreement with the provider of the samples that specifies that coded private information will not be released to you.
- The provider of the samples is not a collaborator on your research.

If you will use non-identifiable human samples:

- Select “no” for the Human Subjects field on the Research and Related Other Project Information form.
- Create a PDF document titled, “No Human Subjects Research in this Application” describing your justifications.
- Attach this document to the Protection of Human Subjects field of the PHS 398 Research Plan form.

If your proposed project is subject to federal human subjects regulations, view our human subjects tutorial and refer to the official application instructions. Be sure to allow plenty of time to complete all requirements.

## Using Vertebrate Animals




- Consider alternatives to using vertebrate animals.
- If using vertebrate animals, check yes in the Vertebrate Animals field of the Research and Related Other Project Information and review the NIH Office of Laboratory Animal Welfare (OLAW) PHS Policy on Humane Care and Use of Laboratory Animals Tutorial.
- Your animal protocols must be approved by an Institutional Animal Care and Use Committee (IACUC) before award.
- Start the IACUC approval process early because it can take considerable time.
- You can designate a partner institution's IACUC as yours if it has an animal welfare assurance on file with the NIH OLAW.
- You must still apply for and receive an inter-institutional assurance and obtain an animal welfare assurance number before award.

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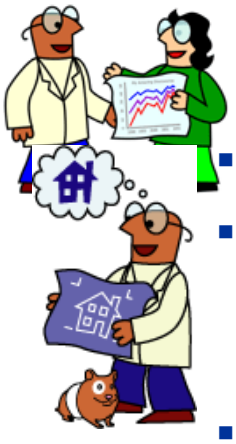
Consider alternatives to using vertebrate animals. If your research requires vertebrate animals, check “yes” in the Vertebrate Animals field of the Research and Related Other Project Information. Also review the Office of Laboratory Animal Welfare, abbreviated as OLAW, tutorial on animals in research.

Your animal protocols must be approved by an Institutional Animal Care and Use Committee, abbreviated as IACUC. Though you submit IACUC approval as just-in-time information before an award, you should start the IACUC process early because it can take considerable time.

You can designate a partner institution's IACUC as yours if it has an animal welfare assurance on file with OLAW. You must still apply for and receive an inter-institutional assurance and obtain an animal welfare assurance number before award.

## Resource Sharing Plans



- Data sharing – Investigators seeking $500,000 or more in direct costs in any year should include a one paragraph description of how final research data will be shared, or explain why data sharing is not possible.
- See NIAID data sharing example and NIAID Data Sharing Policy for guidance.
- Model organisms – All applications where the development of model organisms is anticipated must describe a plan for sharing and distributing unique model organism research resources, or state appropriate reasons why such sharing should be restricted or is not possible.
- See NIAID Sharing Model Organisms for guidance.

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Investigators seeking $500,000 or more in direct costs in any year should include a one-paragraph description of how final research data will be shared, or explain why data sharing is not possible. Although you should describe data sharing plans, they are not considered in determining your priority score. Follow the links to view an NIAID data sharing example and the NIAID Data Sharing policy.

If your application includes the development of a model organism for research, you should include a description of a plan for sharing it, or state appropriate reasons why such sharing is restricted or not possible. This NIH policy covers all funded research that could produce model organisms, regardless of the amount of the budget. Follow the link to view the NIAID Sharing Model Organisms policy.

## SBIR/STTR Information Commercialization Plan

- Value of the SBIR/STTR Project, Expected Outcomes, and Impact.
- Company.
- Market, Customer, and Competition.
- Intellectual Property Protection.
- Finance Plan.

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A commercialization plan is required only for Phase II and Phase I/II fast-track applications and should not be attached to a Phase I application. However, I suggest you include one or two paragraphs on commercialization in the significance section of your Phase I application. This will both provide a framework for reviewers and start you thinking about a detailed commercialization plan for your Phase II application. Briefly include a sentence each on the value of your project, how it affects your company, the market for your product, your customers and competition, how you protect your intellectual property, and the financial resources necessary to commercialize your product.

## Research and Related Other Project Information

- Project Summary/Abstract.
- Project Narrative.
- Bibliography and References Cited.
- Facilities and Other Resources.
- Equipment.
- Other Attachments.

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Think of your Project Summary as an advertisement for your proposal. It should give readers a complete description of what you intend to accomplish, and engender enthusiasm for accomplishing it. You have limited space, so take time to hone your language to convey your message. Do not exceed 30 lines of text, and do not include confidential information.

Think of your Project Narrative as a description in three sentences or less of the relevance of your proposal to public health.

I suggest you sequentially number references in the PHS 398 sections and include the complete citations in your bibliography.

Describe the company-controlled facilities for your project, the company equipment, and that of collaborators that will be available for your project.

Do not include any other attachments for Phase I applications.

## More Presentations

TOPICS

- Basics
- Choices and FY2006 Data
- Grantsmanship
- Electronic Application
- NIH Timeline

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Thank you for watching this presentation. Close this window to select another topic.