R41, R42, R43, R44 GUIDE FOR REVIEWERS

Small Business Innovation Research (SBIR) Awards

Small Business Technology Transfer (STTR) Awards

EXECUTIVE SUMMARY

Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) Awards (R41), (R42), (R43), and (R44)

Objectives of SBIR/STTR programs:

- Stimulate technological innovation in the private sector
- Strengthen role of small business in meeting Federal Research/Research & Development needs
- Increase private sector commercialization of innovations developed through Federal SBIR/STTR R&D
- Increase small business participation in Federal Research/R&D
- Foster and encourage socially and economically disadvantaged small business and women-owned business concerns in the areas of technological innovation

The SBIR and STTR programs differ in significant ways:

Project Director/Principal Investigator (PD/PI):

- The SBIR program stipulates that the PD/PI must have his/her primary employment with the small business. Note: Agencies are permitted to grant waivers to PD/PIs who are not primarily employed by the small business. These however, are given infrequently for extraordinary circumstances.
- The PD/PI on an STTR may be from the small business or the research institution, provided an official relationship exists between the small business and the research institution.
- Both programs may have multiple PD/PIs on individual applications/grants. If an SBIR application has more than one PD/PIPI, only one of the PD/PIs must be primarily employed by the small business.

Research Collaborator:

- STTR requires the applicant small business organization to formally collaborate with a U.S. research institution in both Phase I and Phase II.
- For STTR:
    - The small business must perform at least 40% of the work/R&D.

- The single partnering U.S. research institution must perform at least 30% of the work/R&D.
- These percentages are in statute and deviations are not allowed.

- SBIR grants are not required to have research collaborators, but they may; collaborators may perform up to 33% of the work/R&D for Phase 1 and up to 50% for Phase 2.

Visit the PHS 2009-02 Omnibus Solicitation and special SBIR/STTR funding opportunity announcements at http://grants.nih.gov/grants/funding/sbir.htm.

SBIR/STTR PROGRAMS

Phase I: Feasibility [type 1 R41 (STTR) and type 1 R43 (SBIR) applications]

The objective of Phase I is to establish the technical/scientific merit and feasibility of the proposed R/R&D efforts and to determine the quality of performance of the small business grantee organization prior to providing further Federal support in Phase II.

- Preliminary data are not required.
- SBIR Phase I awards normally may not exceed $100,000 total costs for a period normally not to exceed 6 months. The total amount of all contractual costs and consultant fees normally may not exceed 33% of the total costs requested.
- STTR Phase I awards normally may not exceed $100,000 total costs for a period of 1 year.
- These award levels for duration and total costs are statutory guidelines, not ceilings. Deviations from the guidelines are acceptable, but must be justified in the application.
- Note: The mean Phase I award (FY 2006 – 2008) for SBIR and STTR projects is $170,000.
- For STTR awards, at least 40% of the work must be performed by the small business and 30% of the work must be performed by the single partnering U.S. research institution.
- For STTR awards, the principal investigator must spend a minimum of 10% effort on the research effort.

Phase II: Full Research/R&D Effort [type 2 R42 (STTR) and type 2 R44 (SBIR) applications]

The objective of the Phase II is to continue the research or R&D efforts initiated in Phase I. Evaluation is based on the results of Phase I, scientific and technical merit, and commercial potential and societal impact of the Phase II application. Reviewers may access additional information on Phase II applications.

- SBIR Phase II awards normally may not exceed $750,000 in total costs for an entire period normally not to exceed 2 years. The sum of the consultant costs and contractual costs normally may not exceed 50% of the total costs requested.
- STTR Phase II awards normally may not exceed $750,000 in total costs for an entire period normally not to exceed 2 years.
- These award levels for duration and total costs are statutory guidelines, not ceilings. Deviations from the guidelines are acceptable, but must be justified in the application.
- Note: The mean Phase II award (FY 2006 – 2008) for SBIR and STTR projects is $850,000.
- For an STTR award, at least 40% of the work **must** be performed by the small business and 30% of the work **must** be performed by the research institution.
- These percentages **are** in statute and deviations are not allowable.
- For STTR awards, the principal investigator must spend a minimum of 10% effort on the grant.
- All Phase II SBIR/STTR applications must include a succinct Commercialization Plan (Section I.D., below) within the application.

Phase II Competing Renewal Applications

- Some NIH Institutes/Centers (ICs) offer Phase II SBIR/STTR awardees the opportunity to apply for Phase II Competing Renewal awards.
- These are available for those projects that require extraordinary time and effort in the R&D phase and may or may not require FDA approval for the development of such projects, including drugs, devices, vaccines, therapeutics, and medical implants related to the mission of the IC. In addition, some ICs will accept competing renewal Phase II SBIR grant applications to continue the development of technologies that do not require FDA approval, but are intended to continue the process of developing complex instrumentation, clinical research tools, or behavioral interventions and treatments.
- Some ICs have used targeted announcements in the NIH Guide for Grants and Contracts and some are using the Omnibus SBIR/STTR Grant Solicitation, a.k.a. parent announcements. (All FOAs are available from http://grants1.nih.gov/grants/funding/sbir.htm)
- Only those small business concerns who have been awarded a Phase II are eligible to apply for a Phase II Competing Renewal award. Prospective applicants are strongly encouraged to contact NIH staff prior to submission.
- Additional requirements and instructions (e.g., submission of a letter of intent) are available in the specific IC research topics section and in the specific IC Program Funding Opportunity Announcements; http://grants.nih.gov/grants/funding/sbir_announcements.htm.
- The following NIH ICs will accept applications for Phase II Competing Renewal awards: **NCRR** (SBIR only), **NIA, NIAAA, NIAID, NICHD** (SBIR only)**, NIDA, NIDCD,**

NIDDK, NIGMS (SBIR only), **NEI** (SBIR only and only Competing Renewals of NEI-supported Phase II awards), **NHLBI** (SBIR only and only Competing Renewals of NHLBI-supported Phase II awards), **NIMH** (SBIR only), and **NINDS.**

Fast-Track Applications (type 1R42 and type 1R44 applications)

- Expedite the award of SBIR and STTR Phase II funding for scientifically meritorious applications that have a high potential for commercialization. (Closes the funding gap between phases.)
- Incorporate a parallel review option, in which the Phase I and Phase II grant applications are submitted and reviewed together.
- The Phase I of a Fast Track must specify clear, measurable criteria for success (milestones) that should be achieved prior to initiating Phase II work. It is expected that the Phase I portion of a Fast-Track will include preliminary data.

Commercialization Plan

Phase II and Fast-Track and Phase II Competing Renewal applications must include a succinct Commercialization Plan within the application. The Commercialization Plan (limited to fifteen pages) should address:

- The value of the SBIR/STTR project, expected outcomes, and societal and educational benefits including: a description of key technology objectives, the commercial applications of the research, and the advantages compared to competing products or services.
- Company information including: corporate objectives, core competencies, present size, products/services with significant sales, history of previous Federal and non-Federal funding, regulatory experience, and how the company plans to develop from a small technology R&D business to a successful commercial entity.
- Market, customer, and competition including: the market/market segments being targeted, plans to gain customer acceptance of the product/service, and analysis of potential competition.
- Intellectual property protections: patent or provisional patent status.
- Finance plan including: letters of commitment or intent of funding, letters of support, and specific steps being taken to secure Phase III funding.
- Production and marketing plan including: manufacturing, marketing, licensing, and internet sales.
- Revenue stream generation including: manufacture and direct sales, distributors, joint ventures, licensing, and staffing expectations.
- Reviewers should use the commercialization plan when evaluating the “significance” core review criteria and comment on the plan’s strengths and weaknesses in this section.

Just-in-Time Considerations

Certain items required for funding a grant application are termed "Just-in-time." These items are not required prior to the review of the application, but will be routinely requested by the awarding component prior to making the grant award.

- Eligibility for an SBIR or STTR is considered at the time of award, not at the time of application. Small Business Concerns must complete a Verification Statement to verify they meet the SBA's eligibility criteria as a small business concern for an award.
- Human Subjects Assurance and Institutional Review Board (IRB) approval.
- Institutional Animal Care and Use Committee (IACUC) approval date. Animal welfare assurance numbers are not required for the review of an application.
- Documentation to establish the "primary employment" of the PD/PI with the applicant small business concern (SBIR only).
- Documentation regarding the performance site(s) of the applicant small business concern as shown on the Face Page of the application, if that site(s) is not owned by the applicant organization.
- "Other support" for the PD/PI and the other Senior Key Personnel, excluding consultants, named in the Senior/Key Person profile.

INSTRUCTIONS FOR WRITTEN CRITIQUE AND PRELIMINARY SCORES

Please use the following guidelines when preparing written comments on SBIR/STTR applications assigned to you for review.

Written Critiques

- The format of the critiques should follow the structured template provided for each mechanism, which can be downloaded from the Internet Assisted Review (IAR) site and found on the CD.
- Each core criterion and additional review criteria are represented in the reviewer template and should be commented on, listing the strengths and weaknesses of each in a bulleted form.
- The goal is to provide the maximum and most pertinent information in a concise manner.
- After considering all of the review criteria, briefly summarize the strengths and weaknesses of the application in the Overall Impact section of the template.
- Assigned reviewers must upload critiques before entering an overall impact/priority score.
- Criterion scores should be entered in IAR before the review meeting.
- Assigned reviewers may submit criterion scores only after their critiques have been uploaded. At the SRO's discretion, discussants who are assigned to the

application and SRG members who are not assigned to the application may submit criterion scores without critiques.

- The criterion scores may be changed during FINAL SCORING on your electronic or paper Voter/Scoring Sheet, or following the review meeting during the EDIT phase.
- Please do not write your criterion scores on the critique template.

Preliminary Scores

- Each core review criterion should be given a score using the nine-point rating scale in accordance with the new Enhanced Peer Review Criteria.
- The criterion scores for the applications should be entered in the meeting Internet Assisted Review (IAR) site in NIH Commons before the review meeting using the same page that is used for submitting the preliminary impact/priority score and critique.
- The criterion scores may be changed following the review meeting during the EDIT phase.
- In the READ phase of the meeting reviewers may submit their scores and critiques, but may not edit them. Core criterion scores can be submitted only after your critique had been uploaded into IAR.
- The criterion scores will appear in the summary statement as part of your critique.

Core Review Criteria

Reviewers are asked to consider each of the five review criteria below in the determination of scientific and technical merit, and give a separate score for each. These individual criterion scores are considered part of your critique and will not be discussed at the review meeting. They may be changed in the EDIT phase in Commons. An application does not need to be strong in all categories to be judged likely to have major scientific impact. For example, a project that by its nature is not innovative may be essential to advance a field.

Significance

Does the proposed project have commercial potential to lead to a marketable product, process or service? Does the project address an important problem or a 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?

Investigator(s)

Are the program directors/principal investigators (PD/PIs), collaborators, and other researchers well suited to the project? If Early Stage Investigators or New Investigators, do they have appropriate experience and training? If established, have they demonstrated an ongoing record of accomplishments that have advanced their field(s)? If the project is collaborative or multi-PD/PI, do the investigators have complementary and integrated expertise; are their leadership approach, governance and organizational structure appropriate for the project?

Innovation

Does the application challenge and seek to shift current research or clinical practice paradigms by utilizing novel theoretical concepts, approaches or methodologies, instrumentation, or interventions? Are the concepts, approaches or methodologies, instrumentation, or interventions novel to one field of research or novel in a broad sense? Is a refinement, improvement, or new application of theoretical concepts, approaches or methodologies, instrumentation, or interventions proposed?

Approach

Are the overall strategy, methodology, and analyses well-reasoned and appropriate to accomplish the specific aims of the project? Are potential problems, alternative strategies, and benchmarks for success presented? If the project is in the early stages of development, will the strategy establish feasibility and will particularly risky aspects be managed? If the project involves clinical research, are the plans for 1) protection of human subjects from research risks, and 2) inclusion of minorities and members of both sexes/genders, as well as the inclusion of children, justified in terms of the scientific goals and research strategy proposed?

Environment

Will the scientific environment in which the work will be done contribute to the probability of success? Are the institutional support, equipment and other physical resources available to the investigators adequate for the project proposed? Will the project benefit from unique features of the scientific environment, subject populations, or collaborative arrangements?

Additional Review Criteria

As applicable for the project proposed, reviewers are asked to consider the following additional items in the determination of scientific and technical merit. These may affect the reviewers' scores of the individual core criteria, but separate scores for each additional criterion are not to be given.

Phase II Criteria (Type 2 R42 and Type 2 R44 applications)

- How well did the applicant demonstrate progress toward meeting the Phase I objectives, demonstrating feasibility, and providing a solid foundation for the proposed Phase II activity?
- Did the applicant submit a concise Commercialization Plan that adequately addresses the areas described on pages 2 and 3 of this document?
- To what extent was the applicant able to obtain letters of interest, additional funding commitments, and/or resources from the private sector or non-SBIR/STTR funding sources that would enhance the likelihood for commercialization?
- Does the project carry a high degree of commercial potential, as described in the Commercialization Plan?

Phase II Competing Renewal Criteria

- Did the applicant submit a concise Commercialization Plan that adequately addresses the areas described on page 3 of this document?

- To what extent was the applicant able to obtain letters of interest, additional funding commitments, and/or resources from the private sector or non-SBIR/STTR funding sources that would enhance the likelihood for commercialization?

- Does the project carry a high degree of commercial potential as described in the Commercialization Plan?

Fast Track Criteria (Type 1 R42 and Type 1 R44 applications)

- Does the Phase I application specify clear, appropriate measurable goals (criteria for success, milestones) that should be achieved prior to initiating Phase II? Are there clear criteria by which success will be evaluated?

- Did the applicant submit a concise Commercialization Plan that adequately addresses the areas described on page 4 of this document?

- To what extent was the applicant able to obtain letters of interest, additional funding commitments, and/or resources from the private sector or non-SBIR/STTR funding sources that would enhance the likelihood for commercialization?

- Does the project carry a high degree of commercial potential, as described in the Commercialization Plan?

Protections for Human Subjects

For research that involves human subjects but does not involve one of the six categories of research that are exempt under 45 CFR Part 46 (as described in Human Subjects Protection and Inclusion), reviewers are asked to evaluate the justification for involvement of human subjects and the proposed protections from research risk relating to their participation according to the following five review criteria: 1) risk to subjects, 2) adequacy of protection against risks, 3) potential benefits to the subjects and others, 4) importance of the knowledge to be gained, and 5) data and safety monitoring for clinical trials. If all of the criteria are adequately addressed, and there are no concerns, write "Acceptable Risks and/or Adequate Protections." A brief explanation is advisable. If one or more criteria are inadequately addressed, write, "Unacceptable Risks and/or Inadequate Protections" and document the actual or potential issues that create the human subjects concern. Also, if a clinical trial is proposed, evaluate the Data and Safety Monitoring Plan. (If the plan is absent, notify the SRO immediately to determine if the application should be withdrawn.) Indicate if the plan is "Acceptable" or "Unacceptable", and, if unacceptable, explain why it is unacceptable.

For research that involves human subjects and meets the criteria for one or more of the six categories of research that are exempt, evaluate: 1) the justification for the exemption, 2) human subjects involvement and characteristics, and 3) sources of materials. If the claimed exemption is not justified, indicate “Unacceptable”, and, if unacceptable, explain why it is unacceptable.

For additional information to assist you in making these determinations, please refer to http://grants.nih.gov/grants/peer/guidelines_general/Human_Subjects_Protection_and_Inclusion.pdf and http://grants.nih.gov/grants/peer/guidelines_general/Human_Subjects_Worksheet.pdf.

Inclusion of Women, Minorities and Children

When the proposed project involves clinical research, reviewers are asked to evaluate the proposed plans for inclusion of minorities and members of both genders, as well as the inclusion of children.

Public Law 103-43 requires that women and minorities must be included in all NIH-supported clinical research projects involving human subjects unless a clear and compelling rationale establishes that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. NIH requires that children (individuals under the age of 21) of all ages be involved in all human subjects research supported by the NIH unless there are scientific or ethical reasons for excluding them. Each project involving human subjects must be assigned a code using the categories "1" to "5" below. Category 5 for minority representation in the project means that only foreign subjects are in the study population (no U.S. subjects). If the study uses both then use codes 1 thru 4. Examine whether the minority and gender characteristics of the sample are scientifically acceptable, consistent with the aims of the project, and comply with NIH policy. For each category, determine if the proposed subject recruitment targets are "A" (acceptable) or "U" (unacceptable). If you rate the sample as "U", consider this feature a weakness in the research design and reflect it in the overall score. Explain the reasons for the recommended codes; this is particularly critical for any item coded "U".

NOTE: To the degree that acceptability or unacceptability affects the investigator's approach to the proposed research, such comments should appear under "Approach" in the five major review criteria above, and should be factored into the score as appropriate.

For additional information to assist you in making these determinations, please refer to http://grants.nih.gov/grants/peer/guidelines_general/Human_Subjects_Protection_and_Inclusion.pdf and http://grants.nih.gov/grants/peer/guidelines_general/Human_Subjects_Worksheet.pdf.

Gender Inclusion Code

G1 = Both genders

G2 = Only women

G3 = Only men

G4 = Gender composition unknown

Minority Inclusion Code

M1 = Minority and nonminority

M2 = Only minority

M3 = Only nonminority

M4 = Minority composition unknown

M5 = Only foreign subjects

Children Inclusion Code

C1 = Children and adults

C2 = Only children

C3 = No children included

C4 = Representation of children unknown

Vertebrate Animals

Reviewers are asked to evaluate the involvement of live vertebrate animals as part of the scientific assessment according to the following five points: 1) proposed use of the animals, and species, strains, ages, sex, and numbers to be used; 2) justifications for the use of animals and for the appropriateness of the species and numbers proposed; 3) adequacy of veterinary care; 4) procedures for limiting discomfort, distress, pain and injury to that which is unavoidable in the conduct of scientifically sound research including the use of analgesic, anesthetic, and tranquilizing drugs and/or comfortable restraining devices; and 5) methods of euthanasia and reason for selection if not consistent with the AVMA Guidelines on Euthanasia.

For additional information to assist you in determining if the Vertebrate Animals section is "Acceptable" or "Unacceptable", please refer to: http://grants.nih.gov/grants/olaw/VAChecklist.pdf.

Resubmission Applications

When reviewing a Resubmission application (formerly called an amended application), evaluate the application as now presented, taking into consideration the responses to comments from the previous scientific review group and changes made to the project.

Revision Applications

When reviewing a Revision application (formerly called a competing supplement application), the committee will consider the appropriateness of the proposed expansion of the scope of the project. If the Revision application relates to a specific line of investigation presented in the original application that was not recommended for approval by the committee, then the committee will consider whether the responses to comments from the previous scientific review group are adequate and whether substantial changes are clearly evident.

Biohazards

Reviewers will assess whether materials or procedures proposed are potentially hazardous to research personnel and/or the environment, and if needed, determine whether adequate protection is proposed.

Overall Impact/Priority

NIH peer reviewers are asked to 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 the additional review criteria (as applicable for the project proposed).

Additional Review Considerations

As applicable for the project proposed, reviewers will address each of the following items, but will not give scores for these items and should not consider them in providing an overall impact/priority score.

Budget and Period Support

The budget guidelines for those applications submitted in response to the omnibus solicitation as well as some of the targeted FOAs is $100,000 *total costs* for Phase I and $750,000 *total costs* for Phase II. Refer to the specific FOA as some may stipulate a cap/ceiling. In either case, modular budgets are not permitted for SBIR or STTR applications. Detailed budgets must be submitted for all applications.

For those applications received in response to the omnibus solicitation and those targeted FOAs for which it is stipulated, multi-year budget requests (including Phase I) that exceed the normal guidelines in terms of amount and duration may be allowable if the requests are well-justified in Section K of the application. Reviewers will consider whether the budget and the requested period of support are fully justified and reasonable in relation to the proposed research. Reviewers should also comment on whether the percent effort listed for the

Principal Investigator is appropriate for the work proposed and if each budget category is realistic and justified in terms of the aims and methods.

Select Agents

Reviewers will assess the information provided in this section of the application, including 1) the Select Agent(s) to be used in the proposed research, 2) the registration status of all entities where Select Agent(s) will be used, 3) the procedures that will be used to monitor possession use and transfer of Select Agent(s), and 4) plans for appropriate biosafety, biocontainment, and security of the Select Agent(s). Select agent information is available via http://grants.nih.gov/grants/policy/select_agent/.

Resource Sharing Plans

Reviewers will comment on whether the following Resource Sharing Plans, or the rationale for not sharing the following types of resources, are reasonable. The Small Business Act protects SBIR and STTR final reports for a period of four years upon completion of the project, so it would not be unusual for an SBIR/STTR applicant to cite this reference when discussing their sharing plans.

1) Data Sharing Plan

(http://grants.nih.gov/grants/policy/data_sharing/data_sharing_guidance.htm) Applications requesting more than $500,000 direct costs in any year of the proposed research are expected to include a data sharing plan in their application. Certain Program Announcements may request a data sharing plan for all applications regardless of the amount of direct costs. Assess the reasonableness of the data sharing plan or the rationale for not sharing research data.

2) Sharing Model Organisms

(http://grants.nih.gov/grants/guide/ntice-files/NOT-OD-04-042.html). All NIH grant applications are expected to include a description of a specific plan for sharing and distributing unique model organism research resources generated using NIH funding or state why such sharing is restricted or not possible. Unlike the NIH Data Sharing Policy, the submission of a model organism sharing plan is NOT subject to a cost threshold of $500,000 or more in direct costs in any one year, and is expected to be included in all applications where the development of model organisms is anticipated.

3) Genome Wide Association Studies

(http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-013.html). Applications and proposals that include GWAS, regardless of the requested costs, are expected to include as part of the Research Plan either a plan for submission of GWAS data to the NIH designated data repository or an appropriate explanation for why submission to the repository will not be possible.