Guidelines for Reviewers

Small Business Innovation Research (SBIR)
Small Business Technology Transfer Research (STTR)

The Center for Scientific Review
National Institutes of Health

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Important Features:

- Instructions and forms for SBIR and STTR applications appear in the Application for a Public Health Service Grant[1] (PHS 398; revised 05/2001), and instructions are in the Omnibus Solicitation for SBIR/STTR Grant Applications[2] (PHS 2004-2).
- Applications with direct costs greater than $500,000 in any single year must address data-sharing in the application. This is per NIH policy as stated in Notice NOT-OD-03-032.
- The evaluation of the applicant's plan for the protection of **human subjects** from research risks and the plans for the enrollment of **women**, **minorities**, and **children** in the proposed research is a critical portion of your review.
- Applicants must not, without a waiver from the Small Business Administration, subcontract any portion of their work back to the NIH, to any other Federal Government agency, or to other units of the Federal Government. Note any circumstances in any application which suggest this practice.
- Some NIH Institutes/Centers (ICs) now offer, through Program Announcement (PA), SBIR/STTR Phase II continuation awards. There are additional review criteria for these applications. The identification of this PA should be indicated on the face page and is on the CD which accompanies your applications.

[1] Reviewers may also refer to the Instructions and Application Forms for a Public Health Service Grant (PHS 398; http://grants.nih.gov/grants/funding/phs398/phs398.pdf and http://grants.nih.gov/grants/funding/phs398/phs398.html#forms) for additional information and formats.

[2] Reviewers may also refer to the Omnibus Solicitation of the National Institutes of Health, Centers for Disease Control and Prevention, and Food and Drug Administration for Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) Grant Applications (PHS 2003-2) (http://grants.nih.gov/grants/funding/sbirsttr1/index.pdf) for additional information.

I. General Program Description

The objectives of the SBIR/STTR programs include stimulating technological innovation in the private sector, strengthening the role of small business in meeting Federal Research/Research & Development needs, increasing private sector commercialization of innovations developed through Federal SBIR/STTR R&D, increasing small business participation in Federal R/R&D, and fostering and encouraging participation by socially and economically disadvantaged small business concerns and women-owned business concerns in the SBIR/STTR programs. The unique feature of the STTR program is the requirement for the applicant small business organization to formally collaborate with a research institution in both Phase I and Phase II.

The SBIR and STTR programs differ in significant ways. First, the STTR program requires the small business: (1) to have a formal collaboration with researchers at a university or other non-profit research institution, and (2) to play a significant intellectual role in the conduct of the STTR project. Second, only the SBIR program stipulates that the Principal Investigator must have their primary employment with the small business. Therefore, the Principal Investigator on an STTR may be from the small business or the research institution *as long as they have a formal appointment with or commitment to the applicant small business, which is characterized by an official relationship between the small business and the Research Institution.*

A. SBIR/STTR Programs: First Two Phases

Phase I: Feasibility (type 1R41 and type 1R43 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[3] 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[3] 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.
- 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 research institution.
- For STTR awards, the principal investigator must spend a minimum of ten percent effort on the research effort.

Phase II: Full Research/R&D Effort (type 2R42 and type 2R44 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.[4]

- SBIR Phase II awards normally may not exceed $750,000 in total costs[3] 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[3] for an entire period normally not to exceed 2 years.

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[3] Total costs are the sum of direct costs, facilities and administration costs, and a negotiated fixed fee.

[4] Reviewers should refer to the SBIR and STTR Phase II Grant Application Introduction and Instructions (http://grants.nih.gov/grants/funding/sbirsttr2/PhaseII_SBIRSTTR.pdf) for additional information.

- 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.
- 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.
- For STTR awards, the principal investigator must spend a minimum of ten percent effort on the grant.
- All Phase II SBIR/STTR applications must include a succinct Commercialization Plan (Section I.C., below) within the application.[5]

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

The NIH Fast-Track mechanism expedites the award of SBIR and STTR Phase II funding for scientifically meritorious applications that have a high potential for commercialization.[6] Fast Track incorporates a parallel review option, in which the Phase I and Phase II grant applications are submitted and reviewed together. Preliminary data are not required, but the Phase I of a Fast Track must specify clear, measurable milestones that should be achieved prior to initiating Phase II work.

C. Amended Applications

NIH policy limits the number of amended (revised) versions of an application to two. These are identified by the suffix A1 or A2 in the application number. The Summary Statement from the immediate previous version is included on the CD sent to you. While the score for the previous version is included on the Summary Statement, that score should not be considered in evaluating the current version. The current application should be considered in the context of the other applications being reviewed. The score for a revised application need not necessarily improve simply because the application has been revised.

D. Commercialization Plan

All Phase II and Fast-Track applications must include a succinct Commercialization Plan within the Phase II application.[5] 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.[6]
- 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.

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[5] Phase II SBIR/STTR applications are submitted on the PHS 398 forms; the Commercialization Plan should be included as Section j., and is excluded from the 25 page limit.

[6] Commercialization is defined in PHS 398 and PHS 2003-2 as "[t]he process of developing marketable products and/or services and producing and delivering products for sale (whether by the originating party or by others) to Government and/or commercial markets."

E. Budgets

For Phase I applications which request up to and including $100,000 in total costs, i.e., the sum of the direct costs, the indirect costs, and the negotiated Fixed Fee, the applicants may submit a non-modular, detailed budget or use features of the Modular Grant Application and Award procedures.

Non-modular budget format

Detailed budgets may be submitted for applications totaling less than $100,000 and must be submitted for applications totaling greater than $100,000. SBIR Phase I and Phase II applications must include Form Page 4 and Form Page 5. Costs should be justified on Form Page 5. STTR Phase I and Phase II applications must include Form Page 4, Form Page 5, and the "STTR Research Institution Budget Form Page." This latter page should include the signature of the duly authorized representative of the research institution affirming certifications made by the research institution upon signing the budget page. The total cost of the portion of the project to be performed by the Research Institution should be indicated on Form Page 4 as "Consortium/Contractual Costs." You should determine whether the percent effort listed for the Principal Investigator is appropriate for the work proposed. Is each budget category realistic and justified in terms of the aims and methods? Information for other items in a Phase I or Phase II application[7] may be requested by the awarding component if the likelihood exists for the application to be funded.

Modular budgets (requests up to $100,000 total costs[3])

The NIH is employing features of the Modular Grant Application and Award procedures under its SBIR/STTR programs for SBIR/STTR applications requesting up to $100,000 in total costs.[3] For modular SBIR applications, only the "Modular Budget Format Page" is required.[8] For modular STTR applications, the "Modular Budget Format Page" plus the "Research Institution Certification Format Page" are required. The latter page should note the Direct and the Facilities and Administrative Costs; these total costs should be included in the total costs on the "Modular Budget Page." Reviewers should evaluate these modular budgets on the basis of a general, expert estimate of the total costs and resources required to carry out the proposed research in the requested period, rather than on the basis of detailed categorical costs. You should determine whether the percent effort listed for the Principal Investigator is appropriate for the work proposed. Review panel recommendations for SBIR/STTR modular budgets need not conform to modules of $25,000.

Multi-year Phase I budgets

Multi-year Phase I budget requests that exceed the normal guidelines in terms of amount and duration are allowable for certain SBIR/STTR projects,[9] if the requests are well-justified or stipulated in a specific Program Announcement.

F. Just-in-Time Considerations

Certain items required for 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.

- Human Subjects Assurance (item 4b.) and Institutional Review Board (IRB) approval.

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[7] Information on institutional base salary for personnel, salaries requested, fringe benefits, total personnel costs requested, and Other Support is NOT required at the time an SBIR/STTR application is submitted.

[8] For modular SBIR budgets submitted on the PHS 398 forms, the "Modular Budget Format Page" is required, but the "Detailed Budget for Initial Budget Period" (Form Page 4) and the "Budget for Entire Proposed Project Period" (Form Page 5) are NOT required. For modular STTR budgets submitted on PHS 398 forms, the "Modular Budget Format Page" and the "STTR Research Institution Certification Format Page" are required, but the "STTR Research Institution Budget Form Page" and the "Budget for Entire Proposed Project Period" (Form Page 5) are NOT required.

[9] Instructions to applicants submitting multi-year Phase I budgets on PHS 398 forms are available on the Internet at http://grants.nih.gov/grants/funding/phs398/phs398.pdf.

- Institutional Animal Care and Use Committee (IACUC) approval (item 5a.) date. Animal welfare assurance numbers (item 5b.) are not required for the review of an application.
- Documentation to establish the "primary employment" of the Principal Investigator 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 Principal Investigator and the other "Key Personnel Engaged on the Project" named on Form Page 2, excluding consultants.

II. Review Procedures

Grant applications submitted to NIH are subjected to a peer review process involving two sequential steps that are required by law. The first step is performed by the Scientific Review Groups (SRGs), composed primarily of non-federal scientists, physicians, and engineers (from academia and industry) who are selected for their expertise and stature in particular scientific fields. The Scientific Review Administrator (SRA) is the designated government official responsible for ensuring that each application receives a fair review, according to NIH policy. The second step is performed by the National Advisory Council or Board of the potential awarding component to which the grant application is assigned.

The first task of the SRGs is to make a recommendation for each application on the basis of the SRG's evaluation of the application's scientific and technical merit, potential for commercialization and/or societal benefit.[10] The second task of the SRGs is to make budget recommendations concerning time and dollar amounts that are appropriate for the work proposed.[10]

A. Streamlining

NIH uses a numerical scoring range from 100 (most meritorious) to 500, and a streamlining procedure[11] to determine those applications that the SRG considers to be in the "upper" and "lower" halves. Applications in the "upper half" are discussed by the SRG and *generally* receive a score between 100 and 300; applications that generally would have received a score between 300 and 500 are not discussed and receive an "unscored" designation. At *any* time during the meeting, *any* SRG member may identify an application that they believe should be discussed and scored.

In accordance with federal regulations, the Principal Investigator clearly must be responsible for the scientific and technical direction of the project. When the Principal Investigator does not have sufficient qualifications to assume this role, the application should be streamlined.

B. Scoring

For applications that are not streamlined, each member records on a scoring sheet a numerical rating that reflects his/her opinion of the merit of each application. Numerical scores are assigned by reviewers in increments of 0.1. In special circumstances, a member may record a non-numerical rating such as NP (Not Present), AB (Abstention), or CF (Conflict of Interest), as appropriate.

Deferral

An application should be deferred if insufficient information exists to make a recommendation. This includes missing sections on human subjects and vertebrate animals. The applicant will be requested to submit the additional information prior to the next review, or in special cases a project site visit (applicable to Phase II applications only) may be recommended.

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[10] Reviewers may refer to the document "Review Procedures for Scientific Group Meetings" for additional information at http://www.csr.nih.gov/guidelines/proc.htm.

[11] The streamlining procedure for NIH is described in the document entitled "Streamlined Review Procedures Used in CSR" at http://www.csr.nih.gov/REVIEW/streamln.htm.

Not Recommending for Further Consideration

The SRG may recommend an application for "no further consideration" in rare cases where 1) the application lacks significant and substantial merit, or 2) the research risks to human subjects are sufficiently serious and protections against the risks are so inadequate as to consider the proposed research unacceptable on ethical grounds. The decision for "NRFC" must be made by majority vote of the SRG. An application designated as "NRFC" cannot be considered for funding because, by definition it has been assessed as lacking significant and substantial merit.

C. Fast Track Applications

In most cases, a single score should be assigned to a Fast Track application to reflect the reviewers' enthusiasm for the entire project. The SRG should 1) evaluate the goals that will be achieved during Phase I and the ability of the applicant to demonstrate their probable achievement in a convincing way, and 2) discuss their appropriateness for determining the feasibility of the Phase I. The SRG also may recommend additional milestones that should be achieved before progressing to the Phase II project. In some cases, the SRG may review and score only the Phase I portion of a Fast Track application, if:

- the application does not contain clear, measurable Phase I goals that are appropriate for demonstrating feasibility; or
- the Phase II project is significantly less meritorious than the Phase I project; or
- the application does not include a Commercialization Plan that includes the seven items listed in Section I.C.

If the SRG scores only the Phase I, then only material from the Phase I application may be used in determining the priority score.

III. Conflict of Interest

A conflict of interest in scientific peer review exists when a reviewer has an interest in an application that may bias or give the appearance of biasing his/her review of it on grounds other than those specified in the review criteria. All reviewers must read the "NIH Conflict of Interest, Confidentiality, and Non-Disclosure Rules and Information for Reviewers of Grant Applications and R&D Contract Proposals" and submit a completed, signed "NIH Pre-Review Certification Form Regarding Conflict of Interest, Confidentiality, and Non-Disclosure for Reviewers of Grant Applications and R&D Contract Proposals" before participating in peer review. A reviewer who has a conflict of interest with an application may not participate in its review, and the appearance of a conflict of interest should be avoided whenever possible.

An SRG must not review an application if:

- One of its members, or a member's close relative,[12] is the Principal Investigator or is listed on the budget page in any capacity; or
- One of its members is an owner, officer, or employee in the small business submitting the application; or
- A member's close professional associate[13] is the Principal Investigator or is responsible for conducting a significant portion of, or has significant intellectual input into, the planned research.

An SRG member must leave the room during the discussion of an application:

- Submitted by a small business from whom the member has received or could receive direct financial benefit —of any amount—that is related to the project under review, but is not derived from employment;

[12] A close relative is defined as a parent, spouse/domestic partner, son or daughter.

[13] A professional associate is defined as any colleague, scientific mentor, or student with whom the reviewer is currently conducting research or other professional activities or with whom the reviewer has personally worked within three years of the date of the review. The determination of a close professional association is a matter of judgment on the part of the SRA.

- Submitted by a small business from whom the member has received or could receive a financial benefit that has a value of $5,000 or more per year and is clearly unrelated to the project under review;
- Submitted by an applicant or small business with whom the member has longstanding scientific or personal differences that may be viewed as biasing the member's judgment;
- Submitted by a major competitor of the member; or
- If the member feels unable to provide objective evaluation.

The SRA is responsible for determining whether the participation of particular reviewers is appropriate, and for answering all questions about conflicts-of-interest.

IV. Confidentiality

All materials pertinent to the applications being reviewed are privileged communications prepared for use only by NIH consultants and NIH staff, and should not be shown to or discussed with other individuals. Reviewers' telephone inquiries, all correspondence, and requests for additional information regarding reviewed applications should be directed to the SRA. Reviewers are required to leave all review material with the SRA at the conclusion of the review meeting (except materials that are already in the public domain, e.g., reprints).

Respect for the privacy of the investigators' ideas is also important. Misappropriation of intellectual property, including the unauthorized use of ideas or unique methods obtained from a privileged communication, such as a grant application, is considered plagiarism and falls under the definition of scientific misconduct.

In accordance with NIH policy, all applications for NIH funding must be self-contained within specified page limitations. Unless otherwise specified in an NIH solicitation, internet addresses (URLs) should not be used to provide information necessary to the review because reviewers are under no obligation to view the internet sites.[14] Reviewers are cautioned that their anonymity may be compromised when they directly access an Internet site.

V. Communication

The member composition of each Scientific Review Group (SRG) is posted on the NIH web site prior to the SRG meeting and is public information. However, applicants should not contact reviewers in any SRG about their application, the review process, nor should they send any related information to reviewers. If contacted by an applicant, reviewers are to refer all questions to the SRA or to IC program staff and must report any such contact to the SRA.

VI. Scientific Misconduct

Scientific misconduct is defined by the NIH as "fabrication, falsification, plagiarism, or other practices that seriously deviate from those that are commonly accepted within the scientific community for proposing, conducting, or reporting research. It does not include honest error or honest differences in interpretations or judgments of data."[15] It also does not include unintentional failure to comply with federal requirements affecting specific aspects of the conduct of research, e.g., the protection of human subjects and the welfare of laboratory animals It is vital that reviewers do not make allegations of potential scientific misconduct at the study section meeting or in their written critiques. Such concerns must be brought to the attention of the SRA in a confidential manner, preferably before the study section meets.

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[14] The NIH Guide Notice OD-00-004, namely "URL's in Applications, Proposals, or Appendices," at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-004.html, presents the NIH policy on URL usage.

[15] PHS regulations, 42 CFR 50, Subpart A.

VII. Writing Your Review

"Formulae" do not exist for calculating an individual reviewer's score for an application. Rather, reviewers should balance the strengths and weaknesses of each application, using the criteria below.

A. All SBIR/STTR Applications (R41, R42, R43, and R44 designations)

Significance

- Does the proposed project have commercial potential to lead to a marketable product or process? Does this study address an important problem?
- What may be the anticipated commercial and societal benefits of the proposed activity?
- If the aims of the application are achieved, how will scientific knowledge be advanced?
- Does the application lead to enabling technologies (e.g., instrumentation, software) for further discoveries?
- Will the technology have a competitive advantage over existing/alternate technologies that can meet the market needs?

Approach

- Are the conceptual framework, design, methods, and analyses adequately developed, well-integrated, and appropriate to the aims of the project?
- Is the proposed plan a sound approach for establishing technical and commercial feasibility?
- Does the applicant acknowledge potential problem areas and consider alternative strategies?
- Are the milestones and evaluation procedures appropriate?

Innovation[16]

- Does the project challenge existing paradigms or employ novel technologies, approaches or methodologies?
- Are the aims original and innovative?

Investigators

- Is the Principal Investigator capable of coordinating and managing the proposed project?
- Is the work proposed appropriate to the experience level of the Principal Investigator and other researchers, including consultants and sub-awardees (if any)?
- Are the relationships of the key personnel to the small business and to other institutions appropriate for the work proposed?

Environment

- Is there sufficient access to resources (e.g., equipment, facilities, capabilities)?
- Does the scientific and technological environment in which the work will be done contribute to the probability of success?
- Do the proposed experiments take advantage of unique features of the scientific environment or employ useful collaborative arrangements?

B. Additional Criteria for Phase II Applications (Type 2R42 and Type 2R44 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?

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[16] Innovation is defined in PHS 2003-2 and PHS 398 as "Something new or improved, having marketable potential, including research for (1) development of new technologies, (2) refinement of existing technologies, or (3) development of new applications for existing technologies. For the purposes of PHS programs, an example of 'innovation' would be new medical or biological products, for improved value, efficiency, or costs."

- Did the applicant submit a concise Commercialization Plan that adequately addresses the seven areas described in Section I.C?
- Does the project carry a high degree of commercial potential, as described in the Commercialization Plan?

C. Additional Criteria for Fast Track Applications (Type 1R42 and Type 1R44 applications)

- Does the Phase I application specify clear, appropriate measurable goals (milestones) that should be achieved prior to initiating Phase II?
- Did the applicant submit a concise Commercialization Plan that adequately addresses the seven areas described in Section I.C?
- 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?

D. Additional Criteria for Amended Applications (applications with -A1 or -A2 suffixes)

- Are the responses to comments from the previous SRG review adequate?
- Do the changes improve the revised application?

E. Additional Criteria for Applications Involving Human Subjects Research

In accordance with NIH policy, the following five headings should be addressed in critiques of applications that propose the use of human subjects,[17] and consideration of these points should be reflected in the priority score.

Protection of Human Subjects[18] — *for all studies involving human subjects*

- If the application indicates that the proposed human subjects research is exempt from coverage by the regulations, determine if adequate justification is provided. If the claimed exemption is not justified, indicate "Unacceptable" and explain why you reached that conclusion.[17]
- What are the risks to human subjects recruited by the proposed study? Are the plans proposed for the protection of human subjects from research risks adequate, appropriate, and acceptable?
- When the proposed research includes vulnerable populations such as pregnant women, prisoners, and children, are additional requirements for protections, as described in 42 CFR 46, included?
- Are the risks reasonable in relation to the anticipated benefits to the subjects and others? Are the risks reasonable in relation to the importance of the knowledge that reasonably may be expected to be gained?
- If all 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 subject concerns.

Data and Safety Monitoring Plan[18] — *for clinical trials only*

- Does the applicant describe a Data and Safety Monitoring Plan that defines the general structure of the monitoring entity and mechanisms for the reporting of Adverse Events to the NIH, the IRB, and the FDA, as appropriate?
- Does the applicant describe the establishment of the data safety monitoring boards (DSMBs) for multi-site clinical trials involving interventions that entail potential risk to the participants?

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[17] Reviewers should refer to the document "NIH Instructions to Reviewers for Evaluating Research Involving Human Subjects in Grant and Cooperative Agreement Applications" at http://grants.nih.gov/grants/peer/hs_review_inst.pdf.

[18] Instructions to applicants concerning Human Subjects, the four required criteria, and the inclusion of women, minorities, and children are presented on pages 18-28, PHS 398 (ftp://grants.nih.gov/forms/phs398.pdf). Applicant organizations are NOT required to submit an Assurance or IRB approval at the time an application is submitted. An assurance number issued to a collaborator or contractor is not sufficient.

Inclusion of Women Plan[18] Public law requires that women must be included in all NIH-sponsored clinical research projects 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.[19]

- Does the applicant include subject selection criteria and rationale?
- Does the applicant include a rationale for any exclusions?
- Does the applicant detail the enrollment dates?
- Does the applicant detail outreach strategies for recruitment?
- Does the proposed plan use the new tables to present the proposed composition?

Inclusion of Minorities Plan[18] Public law requires that minorities must be included in all NIH-sponsored clinical research projects 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.[19]

- Does the applicant include subject selection criteria and rationale?
- Does the applicant include a rationale for any exclusions?
- Does the applicant detail the enrollment dates?
- Does the applicant detail outreach strategies for recruitment?
- Does the proposed plan use the new tables to present the proposed composition?

Inclusion of Children Plan[18] NIH requires that children (individuals under the age of 21 years) of all ages be involved in all NIH-sponsored human subjects research unless there are scientific or ethical reasons for excluding them.

- Does the applicant describe the rationale for selecting/excluding specific age ranges?
- What is the expertise of the investigative team?
- Are the facilities for recruiting children appropriate?
- Are sufficient numbers of children included?

F. Human Subjects Codes

Each project involving human subjects must be assigned a code using the categories "1" to "4" below. Examine whether the gender, minority and children 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 your overall score. Explain the reasons for the recommended codes; this is particularly critical for any item coded "U."[20] Category 5 for minority representation in the project means that only foreign subjects are in the study population, no United States subjects. If the study uses both, then use codes "1" through "4."

Category	Gender (G)	Minority (M)	Children (C)

[19] The 1997 Report of the NIH Director's Panel on Clinical Research (http://www.nih.gov/news/crp/97report/execsum.htm) adopted the following definition of Clinical Research: "(a) Patient-oriented research. Research conducted with human subjects (or on material of human origin such as tissues, specimens or cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. This area of research includes: mechanisms of human disease, therapeutic interventions, clinical trials, and development of new technologies, (b) Epidemiological and behavioral studies, and (c) Outcomes research and health services research. Excluded from this definition are *in vitro* studies that utilize human tissues but do not deal directly with patients."

[20] For example, proposed studies that involve men and women (over the age of 21), with only minority representation, would be designated "G1, M2, C3". If the reviewers found the representation of these groups to be scientifically acceptable, the studies would be designated "G1A, M2A, C3A". However, if the reviewers found the absence of non-minority subjects to be unacceptable in terms of the study design, the studies would be designated "G1A, M2U, C3A".

1	Both Genders	Minority & non-minority	Children & adults
2	Only Women	Only minority	Only children
3	Only Men	Only non-minority	No children included
4	Gender Unknown	Minority representation unknown	Representation of children unknown
5		Only foreign subjects	

G. Additional Criteria

Biohazards — *may impact the priority score*

- Is the use of materials or procedures that are potentially hazardous to research personnel and/or the environment proposed?
- Is the proposed protection adequate?

Animal Welfare[21] — *may impact the priority score*

- If vertebrate animals are involved, are adequate plans proposed for their care and use?
- Are the applicant's responses to the five required points[21] appropriate?
- Will the procedures be limited to those that are unavoidable in the conduct of scientifically sound research?

Data Sharing[22] — *should NOT impact the priority score*

- On applications requesting $500,000 or more in direct costs in any year of a project, have the applicants included a plan for data sharing or stated why data sharing is not possible?

Budget — *should NOT impact the priority score*

- For all applications, is the percent effort listed for the Principal Investigator appropriate for the work proposed?
- On applications requesting up to $100,000 total costs,[3] is the overall budget realistic and justified in terms of the aims and methods proposed?
- On applications requesting over $100,000 in total costs,[3] is each budget category realistic and justified in terms of the aims and methods? Reviewers should provide justification for any modification in time or amount that they recommend.

H. Guide for Preparing Critiques

Follow the outline below and use the review criteria (Sections VII.A.-G.) to provide a comprehensive evaluation of each application's strengths and weakness. The goals of NIH-sponsored research are to advance our understanding of biological systems, improve the control of disease, and enhance health. In your written review, you should comment on the following aspects of the application in order to judge the likelihood that the proposed research will have a substantial impact on the pursuit of these goals. Written comments are included virtually verbatim in the Summary Statements that are sent to the applicants and to NIH program staff. The use of personal identifiers or offensive comments must be avoided.

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[21] Instructions to applicants concerning Animal Welfare, including the five required points, are presented on page 28-29 of PHS 398 at http://grants.nih.gov/grants/funding/phs398/phs398.pdf. Applicant organizations that do not have an Animal Welfare Assurance on file with OLAW are NOT required to submit an Assurance Number or IACUC approval date at the time an application is submitted. An assurance number issued to a collaborator or contractor is neither acceptable nor sufficient.

[22] For the specifics of this requirement see http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-035.html and http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-032.html.

Reviewers Critique

Significance: all applications
Approach: all applications
Innovation: all applications
Investigators: all applications
Environment: all applications
Progress in Phase I: Phase II applications only
Response to Previous Review: amended applications only
Commercialization Plan: Phase II and Fast Track applications only
Protection of Human Subjects: all applications involving human subjects, to include

1) Risks to the Subjects;
2) Adequacy of Protection Against Risks;
3) Potential Benefits of the Proposed Research to the Subjects and Others; and
4) Importance of the Knowledge to be Gained.

Data and Safety Monitoring Plan: clinical trials only
Inclusion of Women Plan: all applications involving clinical research
Inclusion of Minorities Plan: all applications involving clinical research
Inclusion of Children Plan: all applications involving human subjects
Human Subjects Codes: all applications involving human subjects
Animal Welfare: all applications involving vertebrate animals
Biohazards: only if a comment is warranted
Overall Evaluation: for each application, provide an overall evaluation of its strengths and weaknesses and a preliminary recommendation of its overall scientific and/or technical merit
Dara Sharing: all applications requesting ≥$500,000 in direct costs in any year of the project
Budget: all applications