



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

**SOLICITATION OF THE NATIONAL HEART, LUNG, AND
BLOOD INSTITUTE**

**SMALL
BUSINESS INNOVATION
RESEARCH
CONTRACT PROPOSALS**

NHLBI SOLICITATION NUMBER:

NHLBI-HL-SBIR-13-15

PROPOSAL RECEIPT DATE

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THE FOLLOWING APPENDICES ARE ATTACHED TO THIS SOLICITATION:

APPENDIX A — PROPOSAL COVER SHEET - USE FOR PHASE I AND FAST-TRACK PROPOSALS

[HTTP://GRANTS.NIH.GOV/GRANTS/FUNDING/SBIRCONTRACT/CONTRACTAPPENDIXA.DOC](http://grants.nih.gov/grants/funding/sbircontract/contractappendixa.doc)

APPENDIX B — ABSTRACT OF RESEARCH PLAN - USE FOR PHASE I, PHASE II, AND FAST-TRACK PROPOSALS

[HTTP://GRANTS.NIH.GOV/GRANTS/FUNDING/SBIRCONTRACT/CONTRACTAPPENDIXB.PDF](http://grants.nih.gov/grants/funding/sbircontract/contractappendixb.pdf)

APPENDIX C — PRICING PROPOSAL - USE FOR PHASE I, PHASE II AND FAST-TRACK PROPOSALS

[HTTP://GRANTS.NIH.GOV/GRANTS/FUNDING/SBIRCONTRACT/CONTRACTAPPENDIXC.PDF](http://grants.nih.gov/grants/funding/sbircontract/contractappendixc.pdf)

APPENDIX D — PHASE II TECHNICAL PROPOSAL COVER SHEET - USE FOR PHASE II AND FAST-TRACK PROPOSALS

[HTTP://GRANTS.NIH.GOV/GRANTS/FUNDING/SBIRCONTRACT/CONTRACTAPPENDIXD.DOC](http://grants.nih.gov/grants/funding/sbircontract/contractappendixd.doc)

APPENDIX E — STATEMENT OF WORK SAMPLE FORMAT - USE FOR PHASE II AND FAST-TRACK PROPOSALS

[HTTP://GRANTS.NIH.GOV/GRANTS/FUNDING/SBIRCONTRACT/CONTRACTAPPENDIXE.DOC](http://grants.nih.gov/grants/funding/sbircontract/contractappendixe.doc)

APPENDIX F — SUMMARY OF RELATED ACTIVITIES - USE FOR PHASE II AND FAST- TRACK PROPOSALS

[HTTP://GRANTS.NIH.GOV/GRANTS/FUNDING/SBIRCONTRACT/CONTRACTAPPENDIXF.DOC](http://grants.nih.gov/grants/funding/sbircontract/contractappendixf.doc)

APPENDIX G — PROPOSAL SUMMARY AND DATA RECORD - USE FOR PHASE II AND FAST-TRACK PROPOSALS

[HTTP://GRANTS.NIH.GOV/GRANTS/FUNDING/SBIRCONTRACT/CONTRACTAPPENDIXG.PDF](http://grants.nih.gov/grants/funding/sbircontract/contractappendixg.pdf)

The Appendices noted above are in Microsoft Word or Adobe Acrobat Reader fillable format.

NOTE: Other software packages for completing these proposals may be available from other sources; however, it is essential that the type size and format specifications are met or the proposal may be returned without review.

DISCLAIMER: Reference to these software packages neither constitutes nor should be inferred to be an endorsement or recommendation of any product, service, or enterprise by the National Institutes of Health, any other agency of the United States Government, or any employee of the United States Government. No warranties are stated or implied.

U. S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

SOLICITATION OF THE NATIONAL HEART, LUNG, AND BLOOD INSTITUTE
FOR
SMALL BUSINESS INNOVATION RESEARCH
CONTRACT PROPOSALS

PART I INSTRUCTIONS FOR PREPARING AND SUBMITTING A PROPOSAL

1. PROGRAM DESCRIPTION

1.1 PURPOSE OF SOLICITATION

The National Heart, Lung, and Blood Institute (NHLBI) invites small business concerns to submit research proposals under this Small Business Innovation Research (SBIR) Contract Solicitation. Firms with the capability to conduct research and development (R&D) and to commercialize the results of that R&D, are encouraged to participate.

This solicitation is for Phase I contract proposals and also for Phase I/Phase II Fast-Track contract proposals.

Included are instructions for offerors to prepare contract proposals, a description of the proposal review process, and some conditions of a contract award. **Contract proposals will be accepted only if they respond specifically to the research topic within this solicitation (see Section 12 "Research Topic").** Otherwise, proposals will be returned to the offeror(s) without evaluation.

The objectives of the SBIR program include stimulating technological innovation in the private sector, strengthening the role of small business in meeting Federal R/R&D needs, increasing private sector commercialization of innovations developed through Federal SBIR R&D, increasing small business participation in Federal R&D, and fostering and encouraging participation by socially and economically disadvantaged small business concerns and women-owned small business concerns in the SBIR program.

The Federal SBIR program is authorized under Public Laws 97-219, 99-443, 102-564, 106-554, and 112-81. The basic design of the NIH SBIR program is in accordance with the Small Business Administration (SBA) SBIR Program Policy Directive, 2002. This SBIR Contract solicitation strives to encourage scientific and technical innovation. The guidelines presented in this solicitation reflect the flexibility provided in the Policy Directive to encourage proposals based on scientific and technical approaches most likely to yield results important to the NHLBI and to the private sector.

1.2 THREE PHASE PROGRAM

The SBIR program consists of three separate phases:

Phase I: Feasibility

The objective of Phase I is to determine the scientific or technical feasibility and commercial merit of the proposed research or R&D efforts and the quality of performance of the small business concern, prior to providing further Federal support in Phase II.

Phase II: Full R/R&D Effort

The objective of Phase II is to continue the research or R&D efforts initiated in Phase I. Funding shall be based on the results of Phase I and the scientific and technical merit and commercial potential of the Phase II proposal.

Phase II proposals may only be submitted upon the request of the Contracting Officer, if not submitted concurrently with the initial Phase I proposal under the Fast-Track procedure (described in Section 5). Only one Phase II award may result from a single Phase I SBIR contract.

Phase III: Commercialization stage without SBIR funds

The objective of Phase III, where appropriate, is for the small business concern to pursue with non-SBIR funds the commercialization objectives resulting from the outcomes of the research or R&D funded in Phases I and II. Phase III may involve follow-on, non-SBIR funded R&D or production contracts for products or processes intended for use by the U.S. Government.

The competition for SBIR Phase I and Phase II awards satisfies any competition requirement of the Armed Services Procurement Act, the Federal Property and Administrative Services Act, and the competition in Contracting Act. Therefore, an agency that wishes to fund an SBIR Phase III project is not required to conduct another competition in order to satisfy those statutory provisions. As a result, in conducting actions relative to a Phase III SBIR award, it is sufficient to state for purposes of a Justification and Approval pursuant to FAR 6.302-5 that the project is a SBIR Phase III award that is derived from, extends, or logically concludes efforts performed under prior SBIR funding agreements and is authorized under 10 U.S.C. 2304(b)(2) or 41 U.S.C. 253(b)(2).

The NHLBI is interested in developing products and services via the SBIR program that improve the health of the American people. In its commitment to also support former President Bush's [Executive Order 13329](#), encouraging innovation in manufacturing-related research and development, NHLBI seeks, through the SBIR program, biomedical research related to advanced processing, manufacturing processes, equipment and systems; or manufacturing workforce skills and protection. This solicitation includes a topic area that is considered relevant to manufacturing-related R&D. Small businesses may be interested in reading a U.S. Department of Commerce 2004 report, "[Manufacturing in America: A Comprehensive Strategy to Address the Challenges to U.S. Manufacturers](#)".

1.3 SBIR PROGRAM ELIGIBILITY

Organizational Criteria: Each organization submitting a proposal under the SBIR program must qualify as a small business concern as defined in [Section 3](#). In determining whether an offeror is a small business concern, an assessment will be made of several factors, including whether or not it is independently owned and operated and whether or not it is an affiliate of a larger organization whose employees, when added to those of the offeror organization, exceed 500. In conducting this assessment, all appropriate factors will be considered, including common ownership, common management, and contractual relationships.

In accordance with 13 CFR 121.103, affiliation exists when "... one concern controls or has the power to control the other ... control may be affirmative or negative, ...it does not matter whether control is exercised, so long as the power to control exists." One of the circumstances that would lead to a finding that an organization is controlling or has the power to control another organization involves sharing common office space and/or employees and/or other facilities (e.g., laboratory space). 13 CFR 121.103 also states that control or the power to control exists when "... key employees of one concern organize a new concern ... and serve as its officers, directors, principal stockholders, and/or key employees; and one concern is furnishing or will furnish the other concern with subcontracts, financial or technical assistance, and/or other facilities, whether for a fee or otherwise." Where there is indication of sharing of common employees, a determination will be made on a case-by-case basis of whether or not such sharing constitutes control or the power to control.

Joint ventures and limited partnerships are eligible provided the entity created qualifies as a small business concern as defined in [Section 3](#) of this solicitation.

If it appears that an offeror does not meet eligibility requirements, the NHLBI will request an eligibility determination of the organization from the cognizant SBA Government Contracting Area Office. The evaluation of the proposal for scientific merit will be deferred until the SBA provides a determination.

Project Director/Principal Investigator Criteria. The primary employment of the Project Director/Principal Investigator (PD/PI) must be with the offeror at the time of contract award and during the conduct of the proposed

project. The PD/PI is the single individual designated in the proposal with responsibility for the scientific and technical direction of the project. Primary employment means that *more than one half of the PD/PI's time* is spent in the employ of the small business concern. *Primary employment with a small business concern precludes full-time employment at another organization.*

In the event that the PD/PI: (1) is a less-than-full-time employee of the small business, (2) is concurrently employed by another organization, or (3) gives the appearance of being concurrently employed by another organization, whether for a paid or unpaid position, at the time of submission of the proposal, *it is essential that documentation be submitted with the proposal to verify his/her eligibility.* If the PD/PI also is employed or appears to be employed by an organization other than the offeror (e.g., a university, a nonprofit research institute, or another company), a letter must be provided by the *non-offeror organization* confirming that the PD/PI will, if awarded an SBIR contract, become a less-than-half-time employee of such organization and will remain so for the duration of the SBIR project. If the PD/PI is employed by a university, the Dean's Office must provide such a letter. If the PD/PI is employed by another for-profit organization, the corporate official must sign the letter. This documentation is required for every proposal that is submitted, even one that is a revision of a previously submitted proposal.

Multiple Principal Investigators. Offerors may propose a multiple Project Director/Principal Investigator (PD/PI) model to direct the project or program to be supported by the contract. The multiple PD/PI model is intended to supplement, and not replace, the traditional single PI model. Ultimately, the decision to submit a proposal using the multiple PD/PI versus single PD/PI is the decision of the investigators and their organizations. The decision whether to employ multiple PDs/PIs should be consistent with and justified by the scientific goals of the project.

The offeror organization may designate multiple individuals as principal investigators (PD/PIs) who share the authority and responsibility for leading and directing the project, intellectually and logistically. When multiple principal investigators are named, each is responsible and accountable to the offeror organization, or as appropriate, to a collaborating organization for the proper conduct of the project or program including the submission of all required reports. The presence of more than one PD/PI on a proposal or award diminishes neither the responsibility nor the accountability of any individual PD/PI.

For Multiple PD/PI proposals: The first PI listed must be affiliated with the small business concern organization submitting the proposal and will serve as the **Contact PD/PI**. For both SBIR Phase I and SBIR Phase II, the *primary employment of the "Contact PD/PI" must be with the small business concern at the time of award and during the conduct of the proposed project.*

Performance Site Criteria. For both Phase I and Phase II, the research or R&D project activity *must be performed in its entirety in the United States* (see [Part I, Section 3. Definitions](#)).

Access to special facilities or equipment in another organization is permitted (as in cases where the SBIR awardee has entered into a subcontractual agreement with another institution for a specific, limited portion of the research project). However, research space occupied by an SBIR contractor organization must be space that is available to and under the control of the SBIR contractor for the conduct of its portion of the project.

Whenever a proposed SBIR project is to be conducted in facilities other than those of the offeror, a letter must be submitted *with* the proposal stating that leasing/rental arrangements have been negotiated for appropriate research space (i.e., space that will be available to and under the control of the SBIR contractor organization).

This letter must be signed by an *authorized official of the organization whose facilities are to be used for the SBIR project*. It also must include a description of the facilities and, if appropriate, equipment that will be leased/rented to the offeror organization.

Market Research. *The NHLBI will not support any market research under the SBIR program.* Neither will it support studies of the literature that will lead to a new or expanded statement of work. Literature searches where the commercial product is a database are acceptable.

For purposes of the SBIR program, "market research" is the systematic gathering, recording, computing, and analyzing of data about problems relating to the sale and distribution of the subject of the research project. It

includes various types of research, such as the size of potential market and potential sales volume, the identification of consumers most apt to purchase the products, and the advertising media most likely to stimulate their purchases. However, "market research" does not include activities under a research plan or protocol that require a survey of the public as part of the objective of the project to determine the impact of the subject of the research on the behavior of individuals.

2. AGENCY CONTACT FOR INFORMATION

Web Site. The NIH SBIR/STTR Web site at <http://grants.nih.gov/grants/funding/sbir.htm> offers electronic access to NIH SBIR solicitations, abstracts of ongoing NIH SBIR projects, the latest updates on the NIH SBIR program, hyperlinks to sources of business assistance, and other useful information.

General Questions about the NIH SBIR Program

Matthew E. Portnoy, Ph.D.
NIH SBIR/STTR Program Coordinator
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Rockledge I, Room 3540
Bethesda, MD 20892-7963
Phone: 301-435-2688 Fax: 301-480-0146
E-mail: sbir@od.nih.gov

Technical Questions about this NHLBI SBIR Solicitation or Contract Administration. Technical questions about the contract topic and general questions on the administration of an SBIR contract should be directed to the Contracting Officer listed below.

Scott Bredow
Contracting Officer
NHLBI Extramural Contracts Branch
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Listserv. The NIH maintains a ListServ e-mail broadcast service. To stay in touch with SBIR opportunities and receive notices about upcoming conferences and solicitations, subscribe by sending an e-mail to LISTSERV@LIST.NIH.GOV with the following text in the message body: subscribe lastname your name, where lastname is the name of the list you wish to subscribe to, and your name is your name. (LISTSERV will get your e-mail address from the "From:" address of your e-mail message.)

3. DEFINITIONS

Affiliate. This term has the same meaning as set forth in 13 CFR part 121 – Small Business Size Regulations, §121.103, "What is affiliation?"

Autopsy Materials. The use of autopsy materials is governed by applicable Federal, state and local law and is not directly regulated by 45 CFR part 46.

Child. The NIH Policy on Inclusion of Children defines a child as an individual under the age of 21 years. The intent of the NIH policy is to provide the opportunity for children to participate in research studies when there is a sound scientific rationale for including them, and their participation benefits children and is appropriate under existing Federal guidelines. Thus, children must be included in NIH conducted or supported clinical research unless there are scientific or ethical reasons not to include them.

DHHS Regulations (45 CFR part 46, Subpart D, Sec.401-409 (<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subpartd>)) provide additional protections for children involved as subjects in research, based on this definition: "Children are persons who have not attained the legal age for consent to treatments or procedures involved in research, under the applicable law of the jurisdiction in which the research will be conducted." Generally, state laws define what constitutes a "child." Consequently, the age at which a child's own consent is required and sufficient to participate in research will vary according to state law. For example, some states consider a person age 18 to be an adult and therefore one who can provide consent without parental permission.

Clinical Research. NIH defines human clinical research as research with human subjects that is:

(1) Patient-Oriented Research.

Research conducted with human subjects (or on material of human origin such as tissues, specimens, and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. Excluded from this definition are *in vitro* studies that utilize human tissues that cannot be linked to a living individual. Patient-oriented research includes: (a) mechanisms of human disease, (b) therapeutic interventions, (c) clinical studies, or (d) development of new technologies.

(2) Epidemiologic and Behavioral Studies.

(3) Outcomes Research and Health Services Research.

Studies falling under Exemption 4 for human subjects research are not considered clinical research by this definition.

Clinical Trial. The NIH defines a clinical trial as a prospective biomedical or behavioral research study of human subjects that is designed to answer specific questions about biomedical or behavioral interventions (drugs, treatments, devices, or new ways of using known drugs, treatments, or devices).

Clinical trials are used to determine whether new biomedical or behavioral interventions are safe, efficacious, and effective.

Behavioral human subjects research involving an intervention to modify behavior (diet, physical activity, cognitive therapy, etc.) fits this definition of a clinical trial.

Human subjects research to develop or evaluate clinical laboratory tests (e.g. imaging or molecular diagnostic tests) might be considered to be a clinical trial if the test will be used for medical decision making for the subject or the test itself imposes more than minimal risk for subjects.

Biomedical clinical trials of experimental drug, treatment, device or behavioral intervention may proceed through four phases:

- *Phase I* clinical trials test a new biomedical intervention in a small group of people (e.g., 20-80) for the first time to evaluate safety (e.g., to determine a safe dosage range and to identify side effects).
- *Phase II* clinical trials study the biomedical or behavioral intervention in a larger group of people (several hundred) to determine efficacy and to further evaluate its safety.
- *Phase III* studies investigate the efficacy of the biomedical or behavioral intervention in large groups of human subjects (from several hundred to several thousand) by comparing the intervention to other standard or experimental interventions as well as to monitor adverse effects, and to collect information that will allow the intervention to be used safely.

- *Phase IV* studies are conducted after the intervention has been marketed. These studies are designed to monitor effectiveness of the approved intervention in the general population and to collect information about any adverse effects associated with widespread use.
- *NIH-Defined Phase III Clinical Trial.* For the purpose of the Guidelines an NIH-defined Phase III clinical trial is a broadly based prospective Phase III clinical investigation, usually involving several hundred or more human subjects, for the purpose of evaluating an experimental intervention in comparison with a standard or controlled intervention or comparing two or more existing treatments. Often the aim of such investigation is to provide evidence leading to a scientific basis for consideration of a change in health policy or standard of care. The definition includes pharmacologic, non-pharmacologic, and behavioral interventions given for disease prevention, prophylaxis, diagnosis, or therapy. Community trials and other population-based intervention trials are also included.

Coded. With respect to private information or human biological specimens, *coded* means that:

- (1) identifying information (such as name or social security number) that would enable the investigator to readily ascertain the identity of the individual to whom the private information or specimens pertain has been replaced with a number, letter, symbol or combination thereof (i.e., the code); and
- (2) a key to decipher the code exists, enabling linkage of the identifying information with the private information or specimens.

Research that involves only coded private information/data or coded human biological specimens may not constitute human subjects research under the DHHS human subjects regulations (45 CFR 46) if:

- the specimens and/or information/data are not obtained from an interaction/intervention with the subject specifically for the research; and
- the investigator(s) cannot readily ascertain the identity of the individual(s) to whom the coded private information or specimens pertain (e.g., the researcher's access to subject identities is prohibited).

Individuals who provide coded information or specimens for proposed research and who also collaborate on the research involving such information or specimens are considered to be involved in the conduct of human subjects research.

(See the following guidance from the Office for Human Research Protections (OHRP) for additional information and examples: <http://www.hhs.gov/ohrp/policy/cdebiol.html>.)

Commercialization. The process of developing markets and producing and delivering products for profit (whether by the originating party or by others). As used here, commercialization includes both government and private sector markets.

Consultant. An individual who provides professional advice or services for a fee, but normally not as an employee of the engaging party. In unusual situations, an individual may be both a consultant and an employee of the same party, receiving compensation for some services as a consultant and for other work as a salaried employee. To prevent apparent or actual conflicts of interest, offerors and consultants must establish written guidelines indicating the conditions of payment of consulting fees. Consultants may also include firms that provide paid professional advice or services.

Contract. An award instrument establishing a binding legal procurement relationship between a funding agency and the recipient, obligating the latter to furnish an end product or service and binding the agency to provide payment therefore.

Data and Safety Monitoring Plan. For each clinical trial, NIH requires a data and safety monitoring plan that will provide oversight and monitoring to ensure the safety of participants and the validity and integrity of the data. The level of monitoring should be commensurate with the risks and the size and complexity of the clinical trial. A detailed data and safety monitoring plan must be submitted to the contractor's IRB and subsequently to the funding IC for approval prior to the accrual of human subjects. The reporting of Adverse Events must be reported to the IRB, the NIH funding Institute or Center, and other required entities. This policy requirement is in addition to

any monitoring requirements imposed by 45 CFR part 46 (<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html>).

Data and Safety Monitoring Board (DSMB). NIH requires the establishment of a Data and Safety Monitoring Board (DSMB) for multi-site clinical trials involving interventions that entail potential risk to the participants, *and generally for Phase III clinical trials.*

Essentially Equivalent Work. This term is meant to identify “scientific overlap,” which occurs when: (1) substantially the same research is proposed for funding in more than one contract proposal or grant application submitted to the same Federal agency; OR (2) substantially the same research is submitted to two or more different Federal agencies for review and funding consideration; OR (3) a specific research objective and the research design for accomplishing that objective are the same or closely related in two or more proposals or awards, regardless of the funding source.

Exemptions. The six categories of research exempt from the DHHS human subject regulations are:

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

Exemption 2: Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior, unless:

(i) information obtained is recorded in such a manner that human subjects can be identified directly or through identifiers linked to the subjects and (ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

Exemption 2 for research involving survey or interview procedures or observation of public behavior, does not apply to research with children (see 45 CFR part 46, Subpart D (<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subpartd>)), except for research involving observations of public behavior when the investigator(s) do not participate in the activities being observed.

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

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

The human subjects regulations decision charts (<http://www.hhs.gov/ohrp/policy/checklists/decisioncharts.html>) of the Office for Human Research Protection (OHRP) will determine whether the research falls under the human subjects regulations and if so, whether it meets the criteria for Exemption 4. The NIH Office of Extramural Research Web site also contains information that is helpful for determining whether human subjects research meets the criteria for Exemption 4. See <http://grants.nih.gov/grants/policy/hs/index.htm>.

Research that meets the criteria for Exemption 4 is not considered “clinical research” as defined by NIH. Therefore the NIH policies for inclusion of women, minorities and children in clinical research, and targeted/planned enrollment tables, do not apply to research projects covered by Exemption 4.

Exemption 5: Research and demonstration projects that are conducted by or subject to the approval of Department or Agency heads and that are designed to study, evaluate, or otherwise examine: (i) public benefit or service programs (ii) procedures for obtaining benefits or services under those programs (iii) possible changes in or alternatives to those programs or procedures or (iv) possible changes in methods or levels of payment for benefits or services under those programs.

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

Feasibility. The extent to which a study or project may be done practically and successfully.

Funding Agreement. Any grant, contract, or cooperative agreement entered into between any Federal agency and any small business concern for the performance of experimental, developmental, or research work, including products or services, funded in whole or in part by the Federal Government.

Gender. Refers to the classification of research subjects into either or both of two categories: male and female. In some cases, representation is unknown, because gender composition cannot be accurately determined (e.g., pooled blood samples or stored specimens without gender designation).

Human Subjects. The DHHS regulations “Protection of Human Subjects” ([45 CFR part 46](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html) (<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html>), administered by OHRP) define a human subject as a living individual about whom an investigator conducting research obtains:

- data through *intervention* or *interaction* with the individual or
- identifiable *private information*

Individually Identifiable Private Information. According to its guidance for use of coded specimens, OHRP generally considers private information or specimens to be *individually identifiable* as defined at 45 CFR 46.102(f) when they can be linked to specific individuals by the investigator(s) either directly or indirectly through *coding* systems. Conversely, OHRP considers private information or specimens not to be individually identifiable when they cannot be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems.

Innovation. Something new or improved, 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.

Intellectual Property. The separate and distinct types of intangible property that are referred to collectively as “intellectual property,” including but not limited to: patents, trademarks, copyrights, trade secrets, SBIR technical data (as defined in this section), ideas, designs, know-how, business, technical and research methods, and other types of intangible business assets, and including all types of intangible assets either proposed or generated by an SBC as a result of its participation in the SBIR program.

Intervention includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. (45 CFR 46.102(f)).

Interaction includes communication or interpersonal contact between investigator and subject. (45 CFR 46.102(f)).

Investigator. The OHRP considers the term investigator to include anyone involved in conducting the research. OHRP does not consider the act of solely providing coded private information or specimens (for example, by a tissue repository) to constitute involvement in the conduct of the research. However, if the individuals who provide

coded information or specimens also collaborate on other activities related to the conduct of the research with the investigators who receive such information or specimens, they will be considered to be involved in the conduct of the research. (See OHRP's Guidance on Research Involving Coded Private Information on Biological Specimens: <http://www.hhs.gov/ohrp/policy/cdebiol.html>.)

Joint Venture. An association of concerns with interests in any degree or proportion by way of contract, express or implied, consorting to engage in and carry out a single specific business venture for joint profit, for which purpose they combine their efforts, property, money, skill, or knowledge, but not on a continuing or permanent basis for conducting business generally. A joint venture is viewed as a business entity in determining power to control its management.

Manufacturing-related R&D as a result of Executive Order 13329. Encompasses improvements in existing methods or processes, or wholly new processes, machines or systems. Four main areas include:

1. *Unit process level technologies* that create or improve manufacturing processes including:
 - fundamental improvements in existing manufacturing processes that deliver substantial productivity, quality, or environmental benefits.
 - development of new manufacturing processes, including new materials, coatings, methods, and associated practices.
2. *Machine level technologies* that create or improve manufacturing equipment, including:
 - improvements in capital equipment that create increased capability (such as accuracy or repeatability), increased capacity (through productivity improvements or cost reduction), or increased environmental efficiency (safety, energy efficiency, environmental impact).
 - new apparatus and equipment for manufacturing, including additive and subtractive manufacturing, deformation and molding, assembly and test, semiconductor fabrication, and nanotechnology.
3. *Systems level technologies* for innovation in the manufacturing enterprise, including:
 - advances in controls, sensors, networks, and other information technologies that improve the quality and productivity of manufacturing cells, lines, systems, and facilities.
 - innovation in extended enterprise functions critical to manufacturing, such as quality systems, resource management, supply change integration, and distribution, scheduling and tracking.
 - technologies that enable integrated and collaborative product and process development, including computer-aided and expert systems for design, tolerancing, process and materials selection, life-cycle cost estimation, rapid prototyping, and tooling.
4. *Environment or societal level technologies* that improve workforce abilities, productivity, and manufacturing competitiveness, including:
 - technologies for improved workforce health and safety, such as human factors and ergonomics.
 - technologies that aid and improve workforce manufacturing skill and technical excellence, such as educational systems incorporating improved manufacturing knowledge and instructional methods.

Obtains. In general, obtaining identifiable private information or identifiable specimens includes, but is not limited to:

- (a) observing or recording private behavior;
- (b) using studying, or analyzing for research purposes identifiable private information or identifiable specimens provided to investigators from any source; and

- (c) using, studying, or analyzing for research purposes identifiable private information or identifiable specimens already in the possession of the investigators.

Principal Investigator, Program Director, or Project Director (PD/PI). The individual(s) designated by the applicant organization to have the appropriate level of authority and responsibility to direct the project or program to be supported by the award. The applicant organization may designate multiple individuals as principal investigators (PDs/PIs) who share the authority and responsibility for leading and directing the project, intellectually and logistically. When multiple principal investigators are named, each is responsible and accountable to the applicant organization, or as appropriate, to a collaborating organization for the proper conduct of the project or program including the submission of all required reports. The presence of more than one PD/PI on an application or award diminishes neither the responsibility nor the accountability of any individual PD/PI.

Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (for example, a medical record). Private information must be *individually identifiable* (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects. (45 CFR 46.102(f))

Prototype. A model of something that is to be further developed and includes designs, protocols, questionnaires, software, and devices.

Research or Research and Development (R/R&D). Any activity that is:

- A systematic, intensive study directed toward greater knowledge or understanding of the subject studied; or
- A systematic study directed specifically toward applying new knowledge to meet a recognized need; or
- A systematic application of knowledge toward the production of useful materials, devices, and systems or methods, including design, development, and improvement of prototypes and new processes to meet specific requirements.

SBIR Technical Data. All data generated during the performance of an SBIR award.

SBIR Technical Data Rights. The rights a small business concern obtains in data generated during the performance of any SBIR Phase I, Phase II, or Phase III award that an awardee delivers to the Government during or upon completion of a Federally-funded project, and to which the Government receives a license.

Senior/Key Personnel. The PD/PI and other individuals who contribute to the scientific development or execution of the project in a substantive, measurable way, whether or not salaries or compensation are requested under the contract.

Typically these individuals have doctoral or other professional degrees, although individuals at the masters or baccalaureate level should be included if their involvement meets the definition of senior/key personnel. Consultants and those with a postdoctoral role should also be included if they meet the definition of senior/key personnel. Senior/key personnel must devote measurable effort to the project whether or not salaries or compensation are requested--"zero percent" effort or "as needed" are not acceptable levels for those designated as senior/key personnel.

Significant Difference. For purposes of NIH policy, a "significant difference" is a difference that is of clinical or public health importance, based on substantial scientific data. This definition differs from the commonly used "statistically significant difference," which refers to the event that, for a given set of data, the statistical test for a difference between the effects in two groups achieves statistical significance. Statistical significance depends upon the amount of information in the data set. With a very large amount of information, one could find a statistically significant, but clinically small difference that is of very little clinical importance. Conversely, with less information one could find a large difference of potential importance that is not statistically significant.

Small Business Concern. A concern that, on the date of award for both Phase I and Phase II funding agreements:

1. is organized for profit, with a place of business located in the United States, which operates primarily within the United States or which makes a significant contribution to the United States economy through payment of taxes or use of American products, materials or labor;
2. is in the legal form of an individual proprietorship, partnership, limited liability company, corporation, joint venture, association, trust or cooperative, except that where the form is a joint venture, there can be no more than 49 percent participation by foreign business entities in the joint venture;
3. is at least 51 percent owned and controlled by one or more individuals who are citizens of, or permanent resident aliens in, the United States, except in the case of a joint venture, where each entity to the venture must be 51 percent owned and controlled by one or more individuals who are citizens of, or permanent resident aliens in, the United States; and
4. has, including its affiliates, not more than 500 employees.

Control can be exercised through common ownership, common management, and contractual relationships. The term "affiliates" is defined in greater detail in 13 CFR 121, as is the process for calculating "number of employees."

Business concerns include, but are not limited to, any individual (sole proprietorship), partnership, corporation, joint venture, association, or cooperative. Further information may be obtained by contacting the Small Business Administration Size District Office at <http://sba.gov/size>.

Socially and Economically Disadvantaged Individual. A member of any of the following groups: Black Americans; Hispanic Americans; Native Americans; Asian-Pacific Americans; Subcontinent Asian Americans; other groups designated from time to time by the Small Business Administration (SBA) to be socially disadvantaged; or any other individual found to be socially and economically disadvantaged by SBA pursuant to Section 8(a) of the Small Business Act, 15 U.S.C. 637(a).

Socially and Economically Disadvantaged Small Business Concern. A socially and economically disadvantaged small business concern is one that is at least 51% owned by (a) an Indian tribe or a native Hawaiian organization, or (b) one or more socially and economically disadvantaged individuals; **and** whose management and daily business operations are controlled by one or more socially and economically disadvantaged individuals.

Subcontract. Any agreement, other than one involving an employer-employee relationship, entered into by a Federal Government prime contractor calling for supplies or services required solely for the performance of the prime contractor another subcontract.

United States. The 50 states, territories and possessions of the U.S., Commonwealth of Puerto Rico, Trust Territory of the Pacific Islands, and District of Columbia.

Women-Owned Small Business Concern. A small business concern that is at least 51% owned by a woman or women who also control and operate it. "Control" in this context means exercising the power to make policy decisions. "Operate" in this context means being actively involved in the day-to-day management.

4. PHASE I PROPOSAL PREPARATION INSTRUCTIONS AND REQUIREMENTS

4.1 LIMITATIONS ON LENGTH OF PROPOSAL

SBIR Phase I proposals shall not exceed 50 single-sided, single-spaced pages for the entire proposal, all inclusive [including all pages, cover sheet(s), tables, CVs, resumes, references, pictures/graphics, and all enclosures, appendices or attachments, etc.]. Proposal pages shall be numbered "Page 1 of 50," "Page 2 of 50," and so on. Pages shall be of standard size (8.5" X 11") with a font size of 11 points (or larger). Two sided pages count as two pages. There are NO exclusions to the page limit – the complete proposal shall not exceed 50

pages. Pages in excess of the page limitation will be removed from the proposal and will not be read, considered, or evaluated.

4.2 TECHNICAL PROPOSAL FORMAT AND CONTENT REQUIREMENTS

4.2.1 Technical Proposal Cover Sheet - Complete the form identified as Appendix A (Proposed Cover Sheet) ([MS Word \(http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixA.doc\)](http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixA.doc) | [PDF \(http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixA.pdf\)](http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixA.pdf)), and use it as the first page of the proposal. *No other cover sheet should be used.*

If submitting a proposal reflecting Multiple Project Directors/Principal Investigators (PDs/PIs), the individual designated as the Contact PI should be entered here.

- **Project Title.** Select a title that reflects the substance of the project. Do not use the title of the topic that appears in the solicitation.

4.2.2 Abstract of Research Plan - Complete the form identified as Appendix B (Abstract of Research Plan)

([MS Word \(http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixB.doc\)](http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixB.doc) | [PDF \(http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixB.pdf\)](http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixB.pdf)), and insert it as the second page of each proposal. Do not include any proprietary information as abstracts of successful proposals will be published by NIH. The abstract should include a brief description of the problem or opportunity, specific aims, and a description of the effort. Summarize anticipated results and potential commercial applications of the proposed research.

Include at the end of the Abstract a brief description (two or three sentences) of the relevance of this research to **public** health. In this description, be succinct and use plain language that can be understood by a general, lay audience.

4.2.3 Research Plan

Beginning on page three of the proposal, discuss in the order indicated the following elements:

- a. **Identification and Significance of the Problem or Opportunity.** Provide a clear statement of the specific technical problem or opportunity addressed.
- b. **Technical Objectives.** State the specific objectives of the Phase I effort, including the technical questions it will try to answer to determine the feasibility of the proposed approach.
- c. **Work Plan.** Provide an explicit, detailed plan for the Phase I R&D to be carried out, including the experimental design, procedures, and protocols to be used. Address how the objectives will be met and the questions stated in Item b above. Discuss in detail the methods to be used to achieve each objective or task. The plan should indicate what is planned, how, when, and where the work will be carried out, a schedule of major events, the final product to be delivered, and the completion date of the effort. The Phase I effort should determine the technical feasibility of the proposed concept. For specific guidance and instructions related to Human Subjects research, please see the section entitled, "[Human Subjects Research and Protection from Risk](#)" and the "[Human Subjects Research Guidance and Information Supplement](#)."
- d. **Related Research or R&D.** Describe significant research activities directly related to the proposed effort, including any conducted by the Project Director/Principal Investigator (PD/PI), the proposing firm, consultants, or others. Describe how these activities interface with the proposed project and discuss any planned coordination with outside sources. *The PD/PI must persuade reviewers of his or her awareness of recent significant research or R&D conducted by others in the same scientific field.*
- e. **Relationship with Future R&D.**
 1. State the anticipated results of the proposed approach, assuming project success.
 2. Discuss the significance of the Phase I effort in providing a foundation for the Phase II R/R&D effort.

- f. **Potential Commercial Applications.** Describe why the proposed project is deemed to have potential commercial applications (for use by the Federal Government and/or private sector markets.) Describe the market as it currently exists and how your product may enter and compete in this market. Include the potential barriers to market entry and how you expect to overcome them.
- g. **Senior/Key Personnel and Bibliography of Directly Related Work.** Identify senior/key personnel, including their directly related education, experience, and bibliographic information. Where resumes are extensive, focus on summaries of the most relevant experience or publications. *Provide dates and places of employment* and some information about the nature of each position or professional experience. Resumes must identify the current or most recent position.

Multiple PD/PI Leadership Plan. For proposals designating multiple PDs/PIs, a leadership plan must be included. A rationale for choosing a multiple PD/PI approach should be described. The governance and organizational structure of the leadership team and the research project should be described, including communication plans, process for making decisions on scientific direction, and procedures for resolving conflicts. The roles and administrative, technical, and scientific responsibilities for the project or program should be delineated for the PDs/PIs and other collaborators.

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

- h. **Subcontractors/Consultants.** Involvement of a university or other subcontractors or consultants in the project may be appropriate and is permitted. If such involvement is intended, it should be described in detail and identified in the cost proposal. In addition, supported by appropriate letters from each individual confirming his/her role in the project must be included. Small business concerns must perform a minimum of two-thirds for Phase I of the research and/or analytical effort (i.e., total contract price less profit/fee) conducted under the resulting contract. The Contracting Officer must approve deviations from this requirement in writing after consultation with the SBIR Program Coordinator.
- i. **Facilities and Equipment.** Indicate where the proposed research will be conducted. *One of the performance sites must be the offeror organization.* Describe the facilities to be used; identify the location; and briefly indicate their capacities, pertinent capabilities, relative proximity, and extent of availability to the project. Include clinical, computer, and office facilities of the offeror and those of any other performance sites to be used in the project.

Whenever a proposed SBIR project is to be conducted in facilities other than those of the offeror, a letter must be submitted *with* the proposal stating that leasing/rental arrangements have been negotiated for appropriate research space (i.e., space that will be available to and under the control of the SBIR contractor organization).

This letter must be signed by an *authorized official of the organization whose facilities are to be used for the SBIR project.* It also must include a description of the facilities and, if appropriate, equipment that will be leased/rented to the offeror organization.

List the most important equipment items already available for this project, noting location and pertinent capabilities of each.

Any equipment and products purchased with Government funds shall be American-made, to the extent possible.

Title to Equipment. Title to equipment purchased with Government funding by the SBIR awardee in relation to project performance vests upon acquisition in the Federal Government. However, the Government may transfer such title to an SBIR awardee upon expiration of the project where the transfer would be more cost-effective than recovery of the property.

Any research proposal involving the collection of information, such as surveys or interviews, of 10 or more public respondents will require clearance by the U.S. Office of Management and Budget. Therefore, it is not practical to propose such an activity for Phase I, which normally has only a six-month duration.

4.2.4 Current Awards and Pending Proposals/Applications

A small business concern may not submit both a contract proposal and a grant application for essentially the same project to the same or different agencies of the NIH. The only exception would be the submission of a grant application after a contract proposal has been evaluated and is no longer being considered for award. A firm that receives a Phase I SBIR contract may submit a Phase II grant application and vice versa.

A Phase I contractor will have the opportunity to submit a Phase II contract proposal, if a Phase II fast-track proposal has not been submitted by the contractor.

While it is permissible, with proposal notification, to submit identical proposals or proposals containing a significant amount of essentially equivalent work (as defined in this solicitation) for consideration under numerous Federal program solicitations, it is unlawful to enter into contracts or grants requiring essentially equivalent effort.

If there is any question concerning this, it must be disclosed to the soliciting agency or agencies before award.

If a firm elects to submit identical proposals or proposals containing a significant amount of essentially equivalent work under other Federal program solicitations, include a statement in each such proposal indicating the information requested in items a-j set forth below.

In addition, provide the information requested in items a-j on (1) active funding through contracts, grants, and cooperative agreements from public or private sponsors; (2) contract proposals and grant and cooperative agreement applications pending review or funding; and (3) contract proposals and grant and cooperative agreement applications about to be submitted.

- a. Name and address of the funding source.
- b. Type of award (contract, grant, cooperative agreement) and identifying number.
- c. Title of research project.
- d. Name and title of Principal Investigator(s) or Project Manager(s).
- e. Hours per week on the project by the Principal Investigator(s) or Project Manager(s).
- f. Annual costs proposed or awarded.
- g. Entire period of support.
- h. Date of proposal/application submission or date of award.
- i. Title, number, and date of solicitations under which proposals or applications were submitted or awards received.
- j. The specific applicable research topic for each SBIR proposal or application submitted or award received.
Specifically identify those projects that are SBIR.

4.2.5 Prior SBIR Phase II Awards

If the small business concern has received more than 15 Phase II awards in the prior 5 fiscal years, submit name of awarding agency, date of award, funding agreement number, amount, topic or subtopic title, follow-on agreement amount, source, and date of commitment and current commercialization status for each Phase II.

This information must be submitted with the proposal.

4.2.6 Proposed Cost Breakdown

Complete the form identified as Appendix C (Contract Pricing Proposal) ([MS Word \(http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixC.doc\)](http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixC.doc) | [PDF \(http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixC.pdf\)](http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixC.pdf)). The cost breakdown should appear

as the last section of the proposal. *If some items on this form do not apply to the proposed project, they need not be completed.*

- Under “Government Solicitation No.,” NHLBI-HL-13-15.”
- If supplies are proposed, provide the quantities and the price per unit.
- Under “Direct Labor,” *list all senior/key personnel by name*. Support personnel may be consolidated into categories or labor classes, e.g., research assistants or data processing clerks.
- Cost for travel funds must be justified and related to the needs of the project. If travel is proposed, provide the following details on “Exhibit A – Supporting Schedule”: destination(s); duration of trip(s); number of travelers; and cost per trip, broken down by cost elements, e.g., airfare, lodging, and meals.
- If consultants are proposed, provide name(s), rate(s), and number of hours/days.
- If a subcontract is proposed, provide the same type of detailed cost breakdown as required for Appendix C. *Also provide a copy of the subcontractual agreement.*
- Use “Exhibit A – Supporting Schedule” to itemize and justify all major cost elements. If more space is needed, use Page 3 of Appendix C.
- Small business concerns must perform a minimum of two-thirds of the research and/or analytical effort (i.e., total contract price less profit/fee) conducted under the resulting contract. The Contracting Officer must approve deviations from this requirement in writing after consultation with the NIH SBIR Program Coordinator.

4.2.7 Streamlining the Contracting Process

The NIH uses special “*Just-in-Time*” procedures that are designed to reduce the administrative burden on offerors without compromising the information needed during the initial evaluation of proposals. Certain documents that would previously have been required for submission with the Phase II proposal will be requested by the NHLBI Contracting Officer at a later stage in the evaluation process. The following documentation is part of the “Just-in-Time” procedures and offerors who elect to submit proposals under the “*Fast-Track*” initiative below are not required to submit this documentation with their initial Phase II business proposal:

- **Travel Policy.** The offeror's written travel policy.
- **Annual Financial Report.** The offeror's most recent annual financial report.
- **Total Compensation Plan.** Salary and fringe benefits of professional employees under service contracts.
- **Data Substantiating the Costs and Prices Proposed.** That is, payroll documentation, vendor quotes, invoice prices, etc.

4.2.8 Requirement for Adequate Assurance of Protection of Human Subjects

The DHHS regulations for the Protection of Human Subjects, 45 CFR 46 (as amended), provide a systematic means, based on established ethical principles, to safeguard the rights and welfare of individuals who participate as subjects in research activities supported or conducted by the DHHS. *The requirement is that an approved assurance of compliance with the regulations must be on file with the Office for Human Research Protections (OHRP), DHHS (<http://www.hhs.gov/ohrp>) before a DHHS award can be made.*

Neither an Institutional Review Board (IRB) review nor an OHRP-approved Assurance is required at the time the proposal is submitted or at the time that the proposals are peer reviewed.

Human Subjects Research and Protection from Risk

Instructions and Required Information

This information must be submitted with the proposal.

Create a section heading entitled **“Human Subjects Research.”** Place it immediately following the “Research Plan” section of the proposal.

In the Human Subjects Research section, you must provide sufficient information for reviewers to determine that the proposed research meets (1) the requirements of the DHHS regulations to protect human subjects from research risks ([45 CFR part 46 \(http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html\)](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html)), (2) the requirements of NIH policies for data and safety monitoring of clinical trials, and (3) the requirements of NIH policies on inclusion of women, minorities, and children.

Provided in the [Human Subjects Research Guidance and Information Supplement](#) are six possible research scenarios, and links to the instructions for providing information on human subjects protection information and the inclusion of women, minorities, and children specific to each scenario. All research will fall into one of these six scenarios. Determine which scenario the proposed research falls into, then go to the specific instructions applicable to that scenario in Section 3 of the Supplement. Where appropriate, Section 3 provides instructions on addressing the Inclusion of Women and Minorities, the Targeted/Planned Enrollment Table, and the Inclusion of Children. All definitions related to human subjects research are linked to text found in Part I, Section 3, Definitions. Section 5 of this Part includes descriptions of and links to the DHHS Human Subjects Protections regulations and NIH policies that apply to clinical research.

Much of the information on the protection of human subjects that you are required to provide in this section is identical to information that will be required for IRB review.

4.2.9 Requirement for Adequate Assurance of Compliance with the PHS Policy on Humane Care and Use of Laboratory Animals

Instructions and Required Information

This information must be submitted with the proposal.

Create a section heading entitled **“Vertebrate Animals.”** Place it immediately following the “Research Plan” section of the proposal (or after Human Subjects Research section, if applicable).

Under the Vertebrate Animals heading, address the following five points. In addition, when research involving vertebrate animals will take place at collaborating site(s) or other performance site(s), provide this information before discussing the five points. Although no specific page limitation applies to this section of the proposal, be succinct.

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

Guidance and Additional Instructions

NIH no longer requires Institutional Animal Care and Use Committee approval of the proposed research before NIH peer review of a proposal (<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-064.html>).

In August, 2002 NIH announced an IACUC “Just-in-Time” process for applications submitted for the October 1, 2002 deadline or other deadlines where the applications had a May/June 2003 Council review. The PHS policy requirement that no award may be made without an approved Assurance and without verification of IACUC approval remains in effect. The new policy gave institutions flexibility in the timing of IACUC review relative to the submission of a proposal and the verification of IACUC review. The policy does not require that IACUC approval be deferred. Institutional officials retain the discretion to require IACUC approval prior to NIH peer review in circumstances of their choosing if deemed necessary. As part of the NIH peer review process, the scientific review group will continue to address the adequacy of animal usage and protections in the review of a proposal and will continue to raise any concerns about animal welfare issues. Verification of IACUC approval will be required in a “Just-in-Time” fashion prior to award.

The *PHS Policy on Humane Care and Use of Laboratory Animals* requires that offeror organizations proposing to use vertebrate animals file a written Animal Welfare Assurance with the Office of Laboratory Animal Welfare (OLAW), establishing appropriate policies and procedures to ensure the humane care and use of live vertebrate animals involved in research activities supported by the PHS. The PHS policy stipulates that an offeror organization, whether domestic or foreign, bears responsibility for the humane care and use of animals in PHS-supported research activities. This policy implements and supplements the *U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training* and requires that institutions use the *Guide for the Care and Use of Laboratory Animals* as a basis for developing and implementing an institutional animal care and use program. This policy does not affect applicable state or local laws or regulations that impose more stringent standards for the care and use of laboratory animals. All institutions are required to comply, as applicable, with the Animal Welfare Act as amended (7 U.S.C. 2131 et seq.) and other Federal statutes and regulations relating to animals. These documents are available from the Office of Laboratory Animal Welfare, National Institutes of Health, Bethesda, MD 20892, (301) 496-7163.

The PHS Policy defines “animal” as “any live, vertebrate animal used or intended for use in research, research training, experimentation or biological testing or for related purposes.”

No PHS award for research involving vertebrate animals will be made to an offeror organization unless that organization is operating in accordance with an approved Animal Welfare Assurance and provides verification that the IACUC has reviewed and approved the proposed activity in accordance with the PHS policy. Proposals may be referred by the PHS back to the IACUC for further review in the case of apparent or potential violations of the PHS policy. No award to an individual will be made unless that individual is affiliated with an assured organization that accepts responsibility for compliance with the PHS policy. Foreign offeror organizations applying for PHS awards for activities involving vertebrate animals are required to comply with PHS policy or provide evidence that acceptable standards for the humane care and use of animals will be met.

4.3 LIMITATIONS ON USE OF APPROPRIATED FUNDS

The Department of Health and Human Services Appropriation Act for Fiscal Year 2010 (Public Law 111-117), limits the use of appropriated funds on NIH grant, cooperative agreement, and contract awards for Fiscal Year 2010, as specified below. It is anticipated that these statutory provisions will continue in subsequent fiscal years.

Salary Rate Limitation

For FY 2012 the *Consolidated Appropriations Act, 2012* (Public Law 112-74) signed into law on December 23, 2011, restricts the amount of direct salary to **Executive Level II of the Federal Executive Pay scale**. The Executive Level II salary is \$179,700.

Anti-Lobbying

“(a) No part of any appropriation contained in this Act shall be used, other than for normal and recognized executive-legislative relationships, for publicity or propaganda purposes, for the preparation, distribution, or use of any kit, pamphlet, booklet, publication, radio, television, or video presentation designed to support or defeat legislation pending before the Congress or any State legislature, except in presentation to the Congress or any State legislature itself. (b) No part of any appropriation contained in this Act shall be used to pay the salary or

expenses of any grant or contract recipient, or agent acting for such recipient, related to any activity designed to influence legislation or appropriations pending before the Congress or any State legislature."

Restriction on Distribution of Sterile Needles

"None of the funds contained in this Act may be used to distribute any needle or syringe for the purpose of preventing the spread of blood borne pathogens in any location that has been determined by the local public health or local law enforcement authorities to be inappropriate for such distribution."

Acknowledgment of Federal Funding

"When issuing statements, press releases, requests for proposals, bid solicitations and other documents describing projects or programs funded in whole or in part with Federal money, all awardees receiving Federal funds included in this Act, including but not limited to State and local governments and recipients of Federal research grants, shall clearly state: (1) the percentage of the total costs of the program or project which will be financed with Federal money; (2) the dollar amount of Federal funds for the project or program; and (3) percentage and dollar amount of the total costs of the project or program that will be financed by non-governmental sources."

Restriction on Abortions

"(a) None of the funds appropriated under this Act, and none of the funds in any trust fund to which funds are appropriated in this Act, shall be expended for any abortion. (b) None of the funds appropriated in this Act, and none of the funds in any trust to which funds are appropriated in this Act, shall be expended for health benefits coverage that includes coverage of abortions. (c) The term "health benefits coverage" means the package of services covered by a managed care provider or organization pursuant to a contract or other arrangement."

Ban on Funding of Human Embryo Research

"(a) None of the funds made available in this Act may be used for: (1) the creation of a human embryo or embryos for research purposes; or (2) research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses in utero under 45 CFR 46.204(b) and section 498(b) of the Public Health Service Act (42 U.S.C. 289g(b)). (b) For purposes of this section, the term "human embryo or embryos" includes any organism, not protected as a human subject under 45 CFR 46 as of the date of the enactment of this Act, that is derived by fertilization, parthenogenesis, cloning, or any other means from one or more human gametes or human diploid cells."

Limitation on Use of Funds for Promotion of Legalization of Controlled Substances

"(a) None of the funds made available in this Act may be used for any activity that promotes the legalization of any drug or other substance included in schedule I of the schedules of controlled substances established by section 202 of the Controlled Substances Act except for normal and recognized executive-congressional communications. (b) The limitation in subsection (a) shall not apply when there is significant medical evidence of a therapeutic advantage to the use of such drug or other substance or that federally sponsored clinical trials are being conducted to determine therapeutic advantage."

NIH Public Access Requirement

"The Director of the National Institutes of Health shall require that all investigators funded by the NIH submit or have submitted for them to the National Library of Medicine's PubMed Central an electronic version of their final, peer-reviewed manuscripts upon acceptance for publication, to be made publicly available no later than 12 months after the official date of publication: *Provided*, that the NIH shall implement the policy in a manner consistent with copyright law."

Further information on the implementation of NIH's Public Access Requirement is available in NIH Guide Notice [NOT-OD-08-033](http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-033.html) (<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-033.html>) published on January 11, 2008.

Dissemination of False or Deliberately Misleading Scientific Information

“None of the funds made available in this Act may be used to disseminate scientific information that is deliberately false or misleading.”

While this mandate has not been included in past appropriations acts, it is similar to existing requirements concerning research integrity, fraud, and false claims, and as such, NIH does not expect this new requirement to impact significantly the business practices at most institutions. Offerors and contractors are advised to review their implementation of the PHS Policies on Research Misconduct contained in 42 CFR Part 93 and the Civil False Claims Act (31 U.S.C. 3729(a)), Criminal False Claims Act (18 U.S.C. 287 and 1001), and Program Fraud and Civil Remedies Act (31 U.S.C. 3801 et seq.).

Restriction on Employment of Unauthorized Alien Workers

“None of the funds in this Act may be used to employ workers described in section 274A(h)(3) of the Immigration and Nationality Act.”

While this mandate has not been included in past appropriations acts, it is similar to existing requirements contained in the Immigration and Nationality Act (18 U.S.C. 1324a), and as such, NIH does not expect this new requirement to impact significantly the business practices at most institutions. Grantees and contractors are advised to review their current hiring and employment practices to ensure compliance.

5. “FAST-TRACK” INITIATIVE

The “Fast-Track” initiative is a parallel review option available to those small business concerns (offeror organizations) whose proposals satisfy additional criteria that enhance the probability of the project's commercial success. This initiative is applicable only to NIH and only if an awarding component indicates it is accepting Fast-Track proposals for a particular topic. (Refer to [Section 12. “Research Topics,”](#) for notation.)

The Fast-Track initiative is an opportunity for small business concerns to submit both a Phase I and Phase II proposal for concurrent peer review. This initiative also has the potential to minimize any funding gap between Phase I and Phase II.

Phase I and Phase II are considered separate funding agreements under the Fast-Track Initiative. Therefore, Phase I Fast-Track awardees must recertify that they meet all of the eligibility criteria for an SBIR award prior to issuance of the Phase II award.

Fast-Track Proposal Process

To identify the proposals as Fast-Track, check the box marked “Yes” next to the words “Fast-Track Proposal” shown on the Phase I Proposal Cover Sheet, Appendix A ([MS Word \(http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixA.doc\)](http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixA.doc) | [PDF \(http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixA.pdf\)](http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixA.pdf)).

The small business concern must submit both a Phase I and a Phase II proposal for concurrent initial peer review and evaluation. The Fast-Track proposal must consist of the following parts:

1. **Phase I Proposal.** Prepared in accordance with Section 4, Phase I Proposal Preparation Instructions and Requirements, and addressing all factors stated in the evaluation criteria (Section 7) for Phase I proposals.
2. **Phase II Proposal.** Prepared in accordance with Section 6, Fast-Track Phase II Proposal Preparation Instructions and Requirements and addressing all factors stated in the evaluation criteria (Section 7) for Phase II proposals.
3. **Commercialization Plan.** Prepared in accordance with instructions in Section 6.2.

The Phase I and Phase II proposals are separate proposals and will be scored individually.

Fast-Track Phase II proposals may be funded following submission of the Phase I final report, and a determination that the Phase I objectives were met, feasibility was demonstrated, and funds are available.

6. FAST-TRACK PHASE II PROPOSAL PREPARATION INSTRUCTIONS AND REQUIREMENTS

6.1 LIMITATIONS ON LENGTH OF PROPOSAL

SBIR Phase II proposals shall not exceed a total of 150 single-spaced pages, including all enclosures and attachments. Pages should be of standard size (8.5" x 11") with a font size of 11 points (or larger). Excluded from the page limitation are cover letters and letters from collaborators and consultants. Pages in excess of the page limitation will be removed from the proposal, and will not be read, considered, or evaluated.

6.2 TECHNICAL PROPOSAL FORMAT AND CONTENT REQUIREMENTS

1. **Phase II Technical Proposal Cover Sheet** - Use Appendix D (Phase II Technical Proposal Cover Sheet) ([MS Word \(http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixD.doc\)](http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixD.doc) | [PDF \(http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixD.pdf\)](http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixD.pdf)).
2. **Table of Contents**
3. **Abstract of the Research Plan** - Use Appendix B (Abstract of Research Plan) ([MS Word \(http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixB.doc\)](http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixB.doc) | [PDF \(http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixB.pdf\)](http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixB.pdf)). State the broad, long-term objectives and specific aims. Do not include any proprietary information. Briefly and concisely describe the research design and methods for achieving these goals.
4. **Anticipated Results of Phase I Effort** - Briefly discuss and summarize the objectives of your Phase I effort, the research activities to be carried out, and the anticipated results.
5. **Research Plan**
 - a. *Detailed Approach and Methodology* - provide an explicit detailed description of the Phase II approach. This section should be the major portion of the proposal and must clearly show advancement in the project appropriate for Phase II. Indicate not only what is planned, but also how and where the work will be carried out. List all tasks in a logical sequence to precisely describe what is expected of the contractor in performance of the work. Tasks should contain detail to (1) establish parameters for the project; (2) keep the effort focused on meeting the objectives; (3) describe end products and deliverables; and (4) describe periodic/final reports required to monitor work progress under the contract. Offerors using [Human Subjects](#) or [Vertebrate Animals](#) in their research should refer to the specific instructions provided in this solicitation.
 - b. *Personnel* - List by name, title, department and organization, the extent of commitment to this Phase II effort, and detail each person's qualifications and role in the project. *Provide resumes for all key staff members*, describing directly related education, experience, and relevant publications. Describe in detail any involvement of subcontractors or consultants, and *provide resumes for all key subcontractor staff*. *Also, include letters of commitment with proposed consultants confirming the extent of involvement and hourly/daily rate.*
 - c. *Resources* - List/describe all equipment, facilities and other resources available for this project, including the offeror's clinical, computer and office facilities/equipment at any other performance site that will be involved in this project. Briefly state their capacities, relative proximity and extent of availability to this effort. *(Any equipment specifically proposed as a cost to the contract must be justified in this section as well as detailed in the budget. Equipment and products purchased with Government funds shall be American-made, to the extent possible. Title to the equipment will vest in the Government.)*
 - d. *Other considerations* - Provide a brief narrative of any unique arrangements, safety procedures in place, animal welfare issues, human subjects, etc. Note: If the research plan includes the use of human subjects or animals, refer to paragraphs [Sections 4.2.8 and 4.2.9](#) of this solicitation for further guidance.

Multiple PD/PI Leadership Plan. For proposals designating multiple PDs/PIs, a leadership plan must be included. A rationale for choosing a multiple PD/PI approach should be described. The governance and organizational structure of the leadership team and the research project should be described, including communication plans, process for making decisions on scientific direction, and procedures for resolving conflicts. The roles and administrative, technical, and scientific responsibilities for the project or program should be delineated for the PDs/PIs and other collaborators.

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

Resource Sharing Plan(s). NIH considers the sharing of unique research resources developed through NIH-sponsored research an important means to enhance the value and further the advancement of the research. When resources have been developed with NIH funds and the associated research findings published or provided to NIH, it is important that they be made readily available for research purposes to qualified individuals within the scientific community. If the final data/resources are not amenable to sharing (for example, human subject concerns, the Small Business Act provisions, etc.), this must be explained in the proposal. See http://grants.nih.gov/grants/policy/data_sharing/data_sharing_faqs.htm.

1. *Data Sharing Plan.* Offerors seeking \$500,000 or more in direct costs in any year are expected to include a brief 1-paragraph description of how final research data will be shared, or explain why data-sharing is not possible (for example human subject concerns, the Small Business Innovation Development Act provisions, etc.). See [Data-Sharing Policy \(http://grants.nih.gov/grants/policy/data_sharing/\)](http://grants.nih.gov/grants/policy/data_sharing/) or <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-032.html>.

2. *Sharing Model Organisms.* Regardless of the amount requested, all proposals where the development of model organisms is anticipated are expected to include a description of a specific plan for sharing and distributing unique model organisms or state appropriate reasons why such sharing is restricted or not possible. See [Sharing Model Organisms Policy \(http://grants.nih.gov/grants/policy/model_organism/index.htm\)](http://grants.nih.gov/grants/policy/model_organism/index.htm), and [NIH Guide NOT-OD-04-042 \(http://grants.nih.gov/grants/guide/notice-files/NOT-OD-04-042.html\)](http://grants.nih.gov/grants/guide/notice-files/NOT-OD-04-042.html).

3. *Genome Wide Association Studies (GWAS).* Regardless of the amount requested, offerors seeking funding for a genome-wide association study are expected to provide a plan for submission of GWAS data to the NIH-designated GWAS data repository, or an appropriate explanation why submission to the repository is not possible. GWAS is defined as any study of genetic variation across the entire genome that is designed to identify genetic associations with observable traits (such as blood pressure or weight) or the presence or absence of a disease or condition. For further information see Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-Wide Association Studies, [NIH Guide NOT-OD-07-088 \(http://www.nih.gov/grants/guide/notice-files/NOT-OD-07-088.html\)](http://www.nih.gov/grants/guide/notice-files/NOT-OD-07-088.html), and <http://gwas.nih.gov/>.

e. *Appendices*

(1) **Work Statement** – Offerors shall develop a Statement of Work similar in format to the sample in Appendix E (Statement of Work Sample Format) ([MS Word \(http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixE.doc\)](http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixE.doc) | [PDF \(http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixE.pdf\)](http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixE.pdf)). Create this from your detailed approach and methodology. It will be incorporated into the final contract document. Do not include proprietary information.

(2) **Commercialization Plan** – Required for the Phase II portion of ALL Fast-Track proposals.

The Phase II portion of Fast-Track proposals must include a succinct Commercialization Plan. The Commercialization Plan is limited to 12 pages. Be succinct. There is no requirement for offerors to use the maximum allowable pages allotted to the Commercialization Plan.

Create a section entitled, “Commercialization Plan,” and provide a description in each of the following areas:

- a. **Value of the SBIR Project, Expected Outcomes, and Impact.** Describe, in layperson's terms, the proposed project and its key technology objectives. Clarify the need addressed, specifying weaknesses in

the current approaches to meet this need. In addition, describe the commercial applications of the research and the innovation inherent in this proposal. Be sure to also specify the potential societal, educational, and scientific benefits of this work. Explain the non-commercial impacts to the overall significance of the project. Explain how the SBIR project integrates with the overall business plan of the company.

- b. **Company.** Give a brief description of your company including corporate objectives, core competencies, present size (annual sales level and number and types of employees), history of previous Federal and non-Federal funding, regulatory experience, and subsequent commercialization, and any current products/services that have significant sales. Include a short description of the origins of the company. Indicate your vision for the future, how you will grow/maintain a sustainable business entity, and how you will meet critical management functions as your company evolves from a small technology R&D business to a successful commercial entity.
- c. **Market, Customer, and Competition.** Describe the market and/or market segments you are targeting and provide a brief profile of the potential customer. Tell what significant advantages your innovation will bring to the market, e.g., better performance, lower cost, faster, more efficient or effective, new capability. Explain the hurdles you will have to overcome in order to gain market/customer acceptance of your innovation.
- Describe any strategic alliances, partnerships, or licensing agreements you have in place to get FDA approval (if required) and to market and sell your product.
- Briefly describe your marketing and sales strategy. Give an overview of the current competitive landscape and any potential competitors over the next several years. (*It is very important that you understand and know the competition.*)
- d. **Intellectual Property (IP) Protection.** Describe how you are going to protect the IP that results from your innovation. Also note other actions you may consider taking that will constitute at least a temporal barrier to others aiming to provide a solution similar to yours.
- e. **Finance Plan.** Describe the necessary financing you will require, and when it will be required, as well as your plans to raise the requisite financing to launch your innovation into Phase III and begin the revenue stream. Plans for this financing stage may be demonstrated in one or more of the following ways:
- Letter of commitment of funding.
 - Letter of intent or evidence of negotiations to provide funding, should the Phase II project be successful and the market need still exist.
 - Letter of support for the project and/or some in-kind commitment, e.g., to test or evaluate the innovation.
 - Specific steps you are going to take to secure Phase III funding.
- f. **Production and Marketing Plan.** Describe how the production of your product/service will occur (e.g., in-house manufacturing, contract manufacturing). Describe the steps you will take to market and sell your product/service. For example, explain plans for licensing, internet sales, etc.
- g. **Revenue Stream.** Explain how you plan to generate a revenue stream for your company should this project be a success. Examples of revenue stream generation include, but are not limited to, manufacture and direct sales, sales through value added resellers or other distributors, joint venture, licensing, service. Describe how your staffing will change to meet your revenue expectations.

Offerors are *encouraged to seek commitment(s) of funds and/or resources from an investor or partner organization for commercialization* of the product(s) or service(s) resulting from the SBIR contract.

Your Phase III funding may be from any of a number of different sources including, but not limited to: SBIR firm itself; private investors or “angels”; venture capital firms; investment companies; joint ventures; R&D limited partnerships; strategic alliances; research contracts; sales of prototypes (built as part of this project); public offering; state finance programs; non SBIR-funded R&D or production commitments from a Federal agency with the intention that the results will be used by the United States government; or other industrial firms.

Fast-Track proposals that do not contain all parts described above will be redirected for Phase I consideration only.

6. **Summary of Related Activities** – Use Appendix F (Summary of Related Activities [MS Word \(http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixF.doc\)](http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixF.doc) | [PDF \(http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixF.pdf\)](http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixF.pdf)).
7. **Number of Copies** - Submit one (1) original and nine (9) copies.

6.3 BUSINESS PROPOSAL FORMAT AND CONTENT REQUIREMENTS

1. **Cover Page** - Use NIH Form 2043, Proposal Summary and Data Record, Appendix G (Pricing Proposal [MS Word \(http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixG.doc\)](http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixG.doc) | [PDF \(http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixG.pdf\)](http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixG.pdf)).
2. **Proposed Cost Breakdown – For Phase I**, use Appendix C ([MS Word \(http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixC.doc\)](http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixC.doc) | [PDF \(http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixC.pdf\)](http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixC.pdf)). Explain the basis for all costs and submit documentation to support all proposed costs. Prepare a separate Appendix C for each year of the contract and a summary of the entire project. **For Phase II Fast-Track**, use Appendix C (Pricing Proposal). Prepare a separate Appendix C for each year of the contract and a summary of the entire project.
3. **NIH Policy on Threshold for Negotiation of Facilities and Administrative (F&A)/Indirect Costs (IDC) Rates for SBIR proposals** - SBIR offerors who propose in the contract an F&A/IDC rate of 40 percent of total direct costs or less will not be required to provide further justification at the time of award, and F&A/ID costs will be awarded at the requested rate. However, the Division of Financial Advisory Services (DFAS) will retain the authority to require well-documented proposals for F&A/IDC rates on an *ad hoc* basis. If the SBC has a currently effective negotiated indirect cost rate(s) with a Federal agency, such rate(s) should be used when calculating proposed F&A/ID costs for an NIH proposal. (However, the rate(s) must be adjusted for IR&D expenses, which are not allowable under HHS awards.)

SBCs are reminded that only actual F&A/ID costs may be charged to projects. If awarded at a rate of 40 percent or less of total direct costs, the rate used to charge actual F&A/ID costs to projects cannot exceed the awarded rate unless the SBC negotiates an indirect cost rate(s) with DFAS. DFAS will negotiate F&A/IDC rates for SBCs receiving awards if the requested rate is greater than 40 percent of total direct costs.
4. **Number of Copies** - Submit one (1) original and five (5) copies.

7. METHOD OF SELECTION AND EVALUATION CRITERIA

All Phase I and Fast-Track proposals will be evaluated and judged on a competitive basis. Using the technical evaluation criteria in Section 7.2, a panel of scientists, consisting primarily of nongovernment experts knowledgeable in the disciplines or fields under review, will evaluate proposals to determine the most promising technical and scientific approaches. Each proposal will be judged on its own merit. The NHLBI is under no obligation to fund any proposal or any specific number of proposals in response to this solicitation. The NHLBI may elect to fund several or none of the proposed approaches to the same topic or subtopic.

7.1 EVALUATION PROCESS

Your proposal will be peer reviewed by a panel of scientists selected for their competence in relevant scientific and technical fields. Each peer review panel will be responsible for evaluating proposals for scientific and technical merit. When relevant, reviewers will be instructed to comment on the reasonableness of the following Resource Sharing Plans, or the rationale for not sharing the following types of resources. However, reviewers will not factor the proposed resource sharing plan(s) into the determination of scientific merit or priority score. The NHLBI Program staff will be responsible for monitoring the data sharing policy

- Data Sharing Plan [http://grants.nih.gov/grants/policy/data_sharing/data_sharing_guidance.htm]
- Sharing Model Organisms [<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-04-042.html>]
- Genome Wide Association Studies (GWAS) [<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-07-088.html>].

The peer review panel provides a rating, makes specific recommendations related to the scope, direction and/or conduct of the proposed research, and for those proposals recommended for award, may provide a commentary about the funding level, labor mix, duration of the proposed contract project, vertebrate animal and human subject research issues. The NHLBI program staff of the awarding component will conduct a second level of review. Recommendations of the peer review panel and program staff are based on judgments about not only the technical merit of the proposed research but also its relevance and potential contributions to the mission and programs of the awarding component and commercial potential. A Phase I or Fast-Track contract may be awarded only if the corresponding proposal has been recommended as technically acceptable by the peer review panel. *Funding for any/all acceptable proposals is not guaranteed.*

7.2 TECHNICAL EVALUATION CRITERIA

In considering the technical merit of each proposal, the following factors will be assessed:

FACTORS FOR PHASE I PROPOSALS	WEIGHT
1. The soundness and technical merit of the proposed approach and identification of clear measurable goals (milestones) to be achieved during Phase I. (Preliminary data are not required for Phase I proposals.)	40%
2. The qualifications of the proposed PDs/PIs, supporting staff, and consultants. For proposals designating multiple PDs/PIs, is the leadership approach, including the designated roles and responsibilities, governance, and organizational structure, consistent with and justified by the aims of the project and the expertise of each of the PDs/PIs?	20%
3. The potential of the proposed research for technological innovation.	15%
4. The potential of the proposed research for commercial application. The commercial potential of a proposal will be assessed using the following criteria: a. Whether the outcome of the proposed research activity will likely lead to a marketable product or process. b. The offeror's discussion of the potential barriers to entry and the competitive market landscape.	15%
5. The adequacy and suitability of the facilities and research environment.	10%

FACTORS FOR PHASE II PROPOSALS (FOR FAST-TRACK ONLY)	WEIGHT
1. The scientific/technical merit of the proposed research, including adequacy of the approach and methodology, and identification of clear, measurable goals to be achieved during Phase II.	30%

FACTORS FOR PHASE II PROPOSALS (FOR FAST-TRACK ONLY)	WEIGHT
2. The potential of the proposed research for commercialization, as documented in the offeror's Commercialization Plan and evidenced by (a) the offeror's record of successfully commercializing its prior SBIR/STTR or other research projects, (b) commitments of additional investment during Phase II and Phase III from private sector or other non-SBIR funding sources, and (c) any other indicators of commercial potential for the proposed research.	30%
3. The qualifications of the proposed PDs/PIs, supporting staff and consultants. For proposals designating multiple PDs/PIs, is the leadership approach, including the designated roles and responsibilities, governance, and organizational structure, consistent with and justified by the aims of the project and the expertise of each of the PDs/PIs?	25%
4. The adequacy and suitability of the facilities and research environment.	15%

7.3 PROPOSAL DEBRIEFING

Offerors will be notified promptly in writing if their proposals are no longer being considered for award. Offerors may request a debriefing by submitting a written request to the Contracting Officer within three days of receipt of the notification. Untimely requests may be accommodated at the Government's discretion.

7.4 AWARD DECISIONS

For proposals recommended for award, the NHLBI will consider the following:

1. Ratings resulting from the scientific/technical evaluation process;
2. Areas of high program relevance;
3. Program balance (i.e., balance among areas of research); and
4. Availability of funds.

The NHLBI is not under any obligation to fund any proposal or make any specific number of contract awards in response to this solicitation. The NHLBI may also elect to fund several or none of the proposals received within a given topic area. The SBIR contract projects do not require establishing a competitive range or requesting final proposal revisions before reaching source selection decisions.

8. CONSIDERATIONS

8.1 AWARDS

1. The award instrument will be a contract.
2. A profit or fixed fee may be included in the proposal, as specified in Federal Acquisition Regulation (FAR) Part 15.404-4. The fee will be negotiated as an element of the potential total contract amount over and above allowable costs.
3. Phase I awards will be firm fixed price contracts. Normally, Phase II awards will be cost-plus-fixed-fee contracts.
4. Phase I contracts shall not exceed \$200,000 including direct costs, indirect costs, and negotiated fixed fee. The NHLBI will support Phase II budgets appropriate to the complexity and scope of this solicitation and within the guidelines of the SBIR program. These budget guidelines normally do not exceed \$1,500,000.

Offerors proposing budgets in excess of this amount should contact the NHLBI Contracting Officer listed in this solicitation. The \$1,500,000 amount includes direct costs, indirect costs, and negotiated fixed fee.

5. Cost-sharing is permitted for proposals under this solicitation; however, cost sharing is not required nor will it be an evaluation factor in the consideration of your proposal. Cost-sharing is an explicit arrangement under which the contractor bears some of the burden of reasonable, allocable, and allowable contract cost. If cost-sharing is proposed, it should be reflected in your budget summary.
6. Approximate number of Phase I contract awards: one (1) Award
7. Scientific and Technical Merit Review: November 7, 2012
8. Estimated Time of Award: April 29, 2013
9. North American Industry Classification System (NAICS) Code: 541712

8.2 MONTHLY PROGRESS REPORT

Contractors will be required to submit monthly progress reports during Phase I along with their invoices. Phase II reports will be required at intervals stipulated in the terms and conditions of award.

8.3 FINAL REPORT

A final report is required of all Phase I and Phase II contractors. It should include a detailed description of the project objectives, the activities that were carried out, and the results obtained. **An original and two copies** of this report must be submitted as directed by the Contracting Officer not later than the expiration date of the Phase I contract.

Each Phase II "Fast-Track" contractor must submit semi-annual progress reports. A final report is required no later than the expiration date of the Phase II contract. *All reports must be submitted as specified in the contract or as directed by the Contracting Officer.*

8.4 PAYMENT

The Government shall make payments, including invoice and contract financing payments, by electronic funds transfer (EFT). As a condition to any payment, the contractor is required to register in the Central Contractor Registration (CCR) database before the award of a contract. The registration site for the CCR is <http://www.ccr.gov>.

Payments on Phase I contracts may be made on a monthly advance basis. Invoices/financing requests submitted for costs incurred under Phase II cost reimbursement contracts will be on a monthly basis unless otherwise authorized by the contracting officer.

8.5 LIMITED RIGHTS INFORMATION AND DATA

Proprietary Information. Information contained in unsuccessful proposals will remain the property of the offeror. The Government, however, may retain copies of all proposals. Public release of information in any proposal will be subject to existing statutory and regulatory requirements.

The Department of Health and Human Services (DHHS) recognizes that, in responding to this solicitation, offerors may submit information that they do not want used or disclosed for any purpose other than for evaluation. Such data might include trade secrets, technical data, and business data (such as commercial information, financial information, and cost and pricing data). The use or disclosure of such information may be restricted if offerors identify it and the Freedom of Information Act (FOIA) does not require its release. For information to be protected, offerors must identify in the Notice of Proprietary Information (on the Proposal Cover Sheet) the page(s) on which such information appears. Any other Notice may be unacceptable to the Government and may constitute grounds for removing the proposal from further consideration without assuming any liability for inadvertent disclosure.

Unless disclosure is required by the FOIA, as determined by FOI officials of the DHHS, data contained in those portions of a proposal that have been identified as containing restricted information, in accordance with the Notice of Proprietary Information, shall not be used or disclosed except for evaluation purposes.

The DHHS may not be able to withhold data that has been requested pursuant to the FOIA, and the DHHS FOI officials must make that determination. The Government is not liable for disclosure if the DHHS has determined that disclosure is required by the FOIA.

If a contract is awarded to the offeror as a result of, or in connection with, the submission of a proposal, the Government shall have the right to use or disclose the data to the extent provided by law. Proposals not resulting in a contract remain subject to the FOIA.

Rights to Data Developed Under SBIR Funding Agreement. Rights to data, including software developed under the terms of any funding agreement resulting from a contract proposal submitted in response to this solicitation, shall remain with the awardee. However, the Government shall have the limited right to use such data for Government purposes only.

- (1) Each agency must refrain from disclosing SBIR technical data to outside the Government (except reviewers) and especially to competitors of the Small Business Concern (SBC), or from using the information to produce future technical procurement specifications that could harm the SBC that discovered and developed the innovation.
- (2) SBIR agencies must protect from disclosure and non-governmental use all SBIR technical data developed from work performed under an SBIR funding agreement for a period of not less than four years from delivery of the last deliverable under that agreement (either Phase I, Phase II, or Federally-funded SBIR Phase III) unless, subject to paragraph (3) of this section, the agency obtains permission to disclose such SBIR technical data from the awardee or SBIR offeror. Agencies are released from obligation to protect SBIR data upon expiration of the protection period except that any such data that is also protected and referenced under a subsequent SBIR award must remain protected through the protection period of that subsequent SBIR award. For example, if a Phase III award is issued within or after the Phase II data rights protection period and the Phase III award refers to and protects data developed and protected under the Phase II award, then that data must continue to be protected through the Phase III protection period. Agencies have discretion to adopt a protection period longer than four years. The Government retains a royalty-free license for Government use of any technical data delivered under an SBIR award, whether patented or not. This section does not apply to program evaluation.
- (3) SBIR technical data rights apply to all SBIR awards, including subcontracts to such awards, that fall within the statutory definition of Phase I, II, or III of the SBIR program, as described in Section 4 of the SBIR Policy Directive, dated September 24, 2002. The scope and extent of the SBIR technical data rights applicable to Federally-funded Phase III awards is identical to the SBIR data rights applicable to Phases I and II SBIR awards. The data rights protection period lapses only: (i) Upon expiration of the protection period applicable to the SBIR award, or (ii) by agreement between the awardee and the agency.

Copyrights. The awardee may normally copyright and publish (consistent with appropriate national security considerations, if any) material developed with PHS support. The awarding component receives a royalty-free license for the Federal Government and requires that each publication contain an acknowledgement of agency support and disclaimer statement, as appropriate. An acknowledgement shall be to the effect that: "This publication was made possible by contract number _____ from (DHHS awarding component)" or "The project described was supported by contract number _____ from (DHHS awarding component)."

Patents. Small business concerns normally retain the principal worldwide patent rights to any invention developed with Government support. Under existing regulations, 37 CFR 401, the Government receives a royalty-free license for Federal Government use, reserves the right to require the patent-holder to license others in certain circumstances, and requires that anyone exclusively licensed to sell the invention in the United States must normally manufacture it substantially in the United States.

To the extent authorized by 35 U.S.C. 205, the Government will not make public any information disclosing a Government-supported invention for a four year period to allow the awardee a reasonable time to file a patent application, nor will the Government release any information that is part of a patent application.

Inquiries or information about additional requirements imposed by 37 CFR 401 should be obtained from local counsel or from:

Office of Policy for Extramural
Research Administration
Division of Extramural Inventions and
Technology Resources
National Institutes of Health (NIH)
6705 Rockledge Drive, MSC 7980
Bethesda, MD 20892-7980
Phone: (301) 435-0679
Fax: (301) 480-0272
E-mail: jpkim@nih.gov

Inventions must be reported promptly—within two months of the inventor's initial report to the contractor organization—to the Division of Extramural Inventions and Technology Resources, NIH, at the address above. This should be done prior to any publication or presentation of the invention at an open meeting, since failure to report at the appropriate time is a violation of 35 U.S.C. 202, and may result in loss of the rights of the small business concern, inventor, and Federal Government in the invention. All foreign patent rights are immediately lost upon publication or other public disclosure unless a United States patent application is already on file. In addition, statutes preclude obtaining valid United States patent protection after one year from the date of a publication that discloses the invention.

Awardees are encouraged to submit reports electronically using Interagency Edison (<http://www.iedison.gov>). Information from these reports is retained by the NIH as confidential and submission does not constitute any public disclosure. Failure to report as described at 37 CFR Section 401.14 is a violation of 35 U.S.C. 202 and may result in loss of the rights of the recipient organization. In addition to fulfilling reporting requirements, Edison notifies the user of future time sensitive deadlines with enough lead-time to avoid the possibility of loss of patent rights due to administrative oversight. Edison can accommodate the invention reporting need of all organizations. For additional information about this invention reporting and tracking system, visit the Edison home page cited above or contact Edison via e-mail at Edison@od.nih.gov.

Resource Sharing Plan(s). NIH considers the sharing of unique research resources developed through NIH-sponsored research an important means to enhance the value of, and advance research. When resources have been developed with NIH funds and the associated research findings published or provided to NIH, it is important that they be made readily available for research purposes to qualified individuals within the scientific community. If the final data/resources are not amenable to sharing (for example, human subject concerns, the Small Business Act provisions, etc.), this must be explained in the Resource Sharing section of the proposal. See http://grants.nih.gov/grants/policy/data_sharing/data_sharing_faqs.htm.

(a) **Data Sharing Plan:** Investigators seeking \$500,000 or more in direct costs in any year are expected to include a brief 1-paragraph description of how final research data will be shared, or explain why data-sharing is not possible (for example human subject concerns, the Small Business Innovation Development Act provisions, etc.) Offerors are encouraged to discuss data-sharing plans with their program contact. See [Data-Sharing Policy](http://grants.nih.gov/grants/policy/data_sharing/) (http://grants.nih.gov/grants/policy/data_sharing/) or <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-032.html>.

(b) **Sharing Model Organisms:** Regardless of the amount requested, all proposals where the development of model organisms is anticipated are expected to include a description of a specific plan for sharing and distributing unique model organisms and related resources, or state appropriate reasons why such sharing is restricted or not possible. See [Sharing Model Organisms Policy](#)

(http://grants.nih.gov/grants/policy/model_organism/index.htm), and [NIH Guide NOT-OD-04-042 \(http://grants.nih.gov/grants/guide/notice-files/NOT-OD-04-042.html\)](http://grants.nih.gov/grants/guide/notice-files/NOT-OD-04-042.html).

(c) Genome Wide Association Studies (GWAS): Regardless of the amount requested, offerors seeking funding for a genome-wide association study are expected to provide a plan for submission of GWAS data to the NIH-designated GWAS data repository, or provide an appropriate explanation why submission to the repository is not possible. A genome-wide association study is defined as any study of genetic variation across the entire genome that is designed to identify genetic associations with observable traits (such as blood pressure or weight) or the presence or absence of a disease or condition. For further information see Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-Wide Association Studies, [NIH Guide NOT-OD-07-088 \(http://www.nih.gov/grants/guide/notice-files/NOT-OD-07-088.html\)](http://www.nih.gov/grants/guide/notice-files/NOT-OD-07-088.html), and <http://gwas.nih.gov/>.

Royalties. If royalties exceed \$1,500, you must provide the following information on a separate page for each separate royalty or license fee:

1. Name and address of licensor.
2. Date of license agreement.
3. Patent numbers.
4. Patent application serial numbers, or other basis on which the royalty is payable.
5. Brief description (including any part or model number of each contract item or component on which the royalty is payable).
6. Percentage or dollar rate of royalty per unit.
7. Unit price of contract item.
8. Number of units.
9. Total dollar amount of royalties.
10. If specifically requested by the Contracting Officer, a copy of the current license agreement and identification of applicable claims of specific patents (see FAR 27.204 and 31.205-37).

8.6 PERFORMANCE OF RESEARCH AND ANALYTICAL WORK

For Phase I projects, small business concerns must perform a minimum of two-thirds or 67% of the research and/or analytical effort (i.e., total contract price less profit/fee) conducted under the resulting contract.

For Phase II projects, small business concerns must perform a minimum of one-half or 50% of the research and/or analytical effort (i.e., total contract price less profit/fee) conducted under the resulting contract.

The Contracting Officer must approve deviations from these requirements in writing after consultation with the NIH SBIR Program Coordinator.

Contractor Commitments. Upon award of a contract, the contractor shall be required to make legal commitments through acceptance of Government contract clauses in the Phase I contract. The outline that follows is illustrative of the types of provisions required by the Federal Acquisition Regulations that shall be included in the Phase I contract. This is not a complete list of provisions to be included in Phase I contracts, nor does it contain specific wording of these clauses. Copies of complete terms and conditions applicable to your contract are available upon request.

1. **Standards of Work.** Work performed under the contract must conform to high professional standards.
2. **Inspection.** Work performed under the contract is subject to Government inspection and evaluation at all times.

3. **Termination for Convenience.** The Government may terminate the contract at any time for convenience if it deems termination to be in its best interest, in which case the contractor will be compensated for work performed and for reasonable termination costs.
4. **Disputes.** Any dispute concerning the contract that cannot be resolved by agreement shall be decided by the contracting officer with right of appeal.
5. **Equal Opportunity.** The contractor will not discriminate against any employee or applicant for employment because of race, color, religion, sex, or national origin.
6. **Affirmative Action for Veterans.** The contractor will not discriminate against any employee or applicant for employment because he or she is a disabled veteran or veteran of the Vietnam era.
7. **Affirmative Action for Handicapped.** The contractor will not discriminate against any employee or applicant for employment because he or she is physically or mentally handicapped.
8. **Gratuities.** The Government may terminate the contract if any gratuities have been offered to any representative of the Government to secure the contract.
9. **American-made Equipment and Products.** When purchasing equipment or products under an SBIR contract award, the contractor shall purchase only American-made items whenever possible.
10. **Examination of Records.** The Comptroller General (or a duly authorized representative) shall have the right to examine any directly pertinent records of the contractor involving transactions related to this contract.
11. **Default.** The Government may terminate the contract for default if the contractor fails to perform the work described in the contract and such failure is not the result of excusable delays.
12. **Contract Work Hours.** The contractor may not require an employee to work more than eight hours a day or forty hours a week unless the employee is compensated accordingly (i.e., overtime pay).
13. **Covenant Against Contingent Fees.** No person or agency has been employed to solicit or secure the contract upon an understanding for compensation except bona fide employees or commercial agencies maintained by the contractor for the purpose of securing business.
14. **Patent Infringement.** The contractor shall report each notice or claim of patent infringement based on the performance of the contract.

THE GENERAL CLAUSES FOR A RESEARCH AND DEVELOPMENT SBIR PHASE I OR PHASE II CONTRACT WILL BE APPLICABLE TO THE CONTRACT RESULTING FROM THIS SOLICITATION. HOWEVER, THE ORGANIZATIONAL STRUCTURE OF THE SUCCESSFUL OFFEROR WILL DETERMINE THE SPECIFIC GENERAL CLAUSE LISTING TO BE CONTAINED IN THE CONTRACT AWARDED FROM THIS SOLICITATION:

The complete listing of these clauses may be accessed at:

<http://rcb.cancer.gov/rcb-internet/appl/general-clauses/clausesDGS.jsp>

8.7 ELECTRONIC AND INFORMATION TECHNOLOGY (SECTION 508)

- a. Pursuant to Section 508 of the Rehabilitation Act of 1973 (29 U.S.C. 794d), as amended by the Workforce Investment Act of 1998, all electronic and information technology (EIT) products and services developed, acquired, maintained, or used under the resultant contract must comply with the "Electronic and Information Technology Accessibility Provisions" set forth by the Architectural and Transportation Barriers Compliance Board (also referred to as the "Access Board") in 36 CFR part 1194. Information about Section 508 provisions is available at <http://www.section508.gov/>. The complete text of Section 508 Final provisions can be accessed at <http://www.access-board.gov/sec508/provisions.htm>.
- b. The contractor shall submit electronic reports/documents that meet the requirements of Section 508 of the Rehabilitation Act of 1973, as amended by the Workforce Investment Act of 1998. Conformance shall be verified by producing electronic reports/documents that satisfy the HHS Section 508 Checklists and Standards. (See [HHS Section 508 Checklists and Standards](#).) For further guidance, please see <http://www.hhs.gov/web/508/index.html>.

8.8 ADDITIONAL INFORMATION

1. This solicitation is intended for informational purposes and reflects current planning. If there is any inconsistency between the information contained herein and the terms of any resulting SBIR contract, the terms of the contract are controlling.
2. Prior to award of an SBIR contract, the Government may request the offeror to submit certain organizational, management, personnel and financial information to assure responsibility of the offeror to receive an award.
3. The Government is not responsible for any expenditures of the offeror in advance and in anticipation of an award. In a cost reimbursement contract, reimbursement of costs by the Government may be made only on the basis of costs incurred by the contractor after award and during performance.
4. This solicitation is not an offer by the Government and does not obligate the Government to make any specific number of awards. Awards under this program are contingent upon the scientific/technical merit of proposals and the availability of funds.
5. The SBIR contract program is not intended as a mechanism to invite unsolicited proposals. Unsolicited SBIR contract proposals shall not be accepted under the SBIR program in either Phase I, Phase II, or Fast-Track.
6. If an award is made pursuant to a proposal submitted in response to this SBIR solicitation, the contractor will be required to certify that he or she has not previously been, nor is currently being, paid for essentially equivalent work by any agency of the Federal Government.
7. Prior to award of a contract, the contractor will be required to provide a Data Universal Numbering System (DUNS) number. A DUNS number may be obtained immediately, at no charge, by calling Dun and Bradstreet at 1-866-705-5711 or via the Internet at <https://eupdate.dnb.com/requestoptions/government/ccrreg/>. The contractor must also be registered in the Central Contractor Registry (CCR) prior to award of a contract. Registration can be made via the Internet at <http://www.ccr.gov>.

9. INSTRUCTIONS FOR PROPOSAL SUBMISSION

9.1 RECEIPT DATE

The deadline for receipt of all contract proposals submitted in response to this solicitation is:
3:00 p.m., Eastern Time
August 9, 2012

Any proposal, modification or revision received at the offices designated below after the exact time specified for receipt is "late" and will not be considered unless it is received before award is made, and

1. There is acceptable evidence to establish that it was received at the Government installation designated for receipt of offers and was under the Government's control prior to the time set for receipt of offers; or
2. It is the only proposal received.

Acceptable evidence to establish the time of receipt at the Government installation includes the time/date stamp of that installation on the proposal wrapper, other documentary evidence of receipt maintained by the installation, or oral testimony or statements of Government personnel.

If an emergency or unanticipated event interrupts normal Government processes so that proposals cannot be received at the office designated for receipt of proposals by the exact time specified in the solicitation, and urgent Government requirements preclude amendment of the solicitation, the time specified for receipt of proposals will be deemed to be extended to the same time of day specified in the solicitation on the first work day on which normal Government processes resume.

Proposals may be withdrawn by written notice received at any time before award. Notwithstanding above, a proposal received after the date and time specified for receipt may be considered if it offers significant cost or technical advantages to the Government and it was received before proposals were distributed for evaluation, or within 5 calendar days after the exact time specified for receipt, whichever is earlier.

Note: Modifications or revisions to proposals that result in the proposal exceeding the stated page limitations will not be considered.

9.2 NUMBER OF COPIES

For Phase I, submit the original and 5 copies of each proposal. The Principal Investigator and a corporate official authorized to bind the offeror must sign the original. The 5 copies of the proposal may be photocopies of the original.

For Fast-Track Phase II, submit the original and 9 copies.

For Phase I and Fast-Track Phase II business proposals, submit an original and 5 copies.

In addition to the paper submissions, offerors shall submit two CD-Rom's containing a PDF (Adobe Acrobat) copy of the entire proposal (Technical and Business). This does not replace the paper copies but is in addition to them. The paper copy is the official copy for recording timely receipt of proposals. By signing the proposal, the offeror certifies that, as part of the offer, the information in the paper copy is exactly the same as that which is contained on the electronic media.

9.3 BINDING AND PACKAGING OF PROPOSAL

Send all copies of a proposal in the same package. Do not use special bindings or covers. Staple the pages in the upper left corner of each proposal.

10. CONTRACTING OFFICER AND ADDRESSES FOR MAILING OR DELIVERY OF PROPOSALS

Any small business concern that intends to submit an SBIR contract proposal under this solicitation should provide the appropriate contracting officer(s) with early, written notice of its intent, giving its name, address, telephone, e-mail, and topic number(s). If the solicitation is modified or canceled before this solicitation closes, only those companies that have expressed such intent will be notified.

Proposals to the NHLBI, if mailed through the U.S. Postal Service, must be addressed as follows:

Yolanda Bursie
Contract Specialist
NHLBI Extramural Contracts Branch
6701 Rockledge Drive
Rockledge Building II, Room 6016
Bethesda, MD 20892-7902

Please mail, fax, or email Letters of Intent to the NHLBI Extramural Contracts Branch at the address below:

Yolanda Bursie
Contract Specialist
NHLBI Extramural Contracts Branch
6701 Rockledge Drive
Rockledge Building II, Room 6016
Bethesda, MD 20892-7902*
Phone: 301-435-0362 Fax: 301-480-0338

E-mail: bursieyl@nhlbi.nih.gov

**Change the zip code to 20817 if hand-delivered or delivered by an express or other courier service to the NHLBI.*

11. SCIENTIFIC AND TECHNICAL INFORMATION SOURCES

Health science research literature is available at academic and health science libraries throughout the United States. Information retrieval services are available at these libraries and Regional Medical Libraries through a network supported by the National Library of Medicine. To find a Regional Medical Library in your area, visit <http://nnlm.gov/> or contact the Office of Communication and Public Liaison at publicinfo@nlm.nih.gov, (301) 496-6308.

Other sources that provide technology search and/or document services include the organizations listed below. They should be contacted directly for service and cost information.

National Technical Information Service
1-800-553-6847
<http://www.ntis.gov>

National Technology Transfer Center
Wheeling Jesuit College
1-800-678-6882
<http://www.nttc.edu/>

12. RESEARCH TOPIC – SEE ATTACHMENT 1 FOR THE TOPIC DESCRIPTION

PART II HUMAN SUBJECTS RESEARCH GUIDANCE AND INFORMATION SUPPLEMENT

1. INTRODUCTION

A Protection of Human Subjects section of the Research Plan is required for all proposals. The information provided in the section on Protection of Human Subjects should be consistent with the information provided on the face page of the application.

For all research involving human subjects, the Scientific Review Group (SRG) will assess the adequacy of protections for research participants against research risks, and the appropriate inclusion of women, minorities, and children, based on the information provided in the application.

To assist in preparing the section on Protection of Human Subjects, six possible scenarios are provided in Section 2 below. All research projects will fall into one of these six scenarios (to help determine whether research that involves the use of human data or biological specimens is human subjects research, refer to this Web site <http://grants.nih.gov/grants/policy/hs>). Determine which scenario the proposed research falls into, then go to the specific instructions applicable to that scenario in Section 3 of the Supplement. Where appropriate, Section 3 provides instructions on addressing the Inclusion of Women and Minorities, the Targeted/Planned Enrollment Table, and the Inclusion of Children. All definitions related to human subjects research are linked to text found in Part I, Section 3, Definitions. Section 5 of this Part includes descriptions of and links to the DHHS Human Subjects Protections regulations and NIH policies that apply to clinical research.

2. SCENARIOS

Scenario A. No Human Subjects Research

If no human subjects research is proposed in the proposal, check the box marked “No” on the Proposal Cover Sheet (Appendix A) and indicate “No” on the Proposal Summary and Data Record (Appendix G). If your proposed research involves the use of human data and/or biological specimens, you must provide a justification for your claim that no human subjects are involved in the Protection of Human Subjects section of the Research Plan.

See the [instructions for Scenario A under Section 3](#).

Scenario B. Non-Exempt Human Subjects Research

If research involving human subjects is anticipated to take place under the award, check the box marked “Yes” on the Proposal Cover Sheet (Appendix A) and indicate “Yes” on the Proposal Summary and Data Record (Appendix G). Enter your Human Subjects Assurance Number.

In the Protection of Human Subjects section of the Research Plan, you must provide sufficient information for reviewers to determine that the proposed research meets (1) the requirements of the DHHS regulations to protect human subjects from research risks (45 CFR part 46), and (2) the requirements of NIH policies on inclusion of women, minorities, and children. Research involving a clinical trial will fall under either Scenario E or F below.

See the [instructions for Scenario B under Section 3](#).

Scenario C. Exempt Human Subjects Research

If **all** of the proposed human subjects research meets the criteria for one or more of the exemptions from the requirements in the DHHS regulations (46.101(b)), check the box marked “Yes” on the Proposal Cover Sheet (Appendix A). Indicate “Yes” on the Proposal Summary and Data Record and insert E-1, E-2, E-3, E-4, E-5, or E-6 as appropriate, in the field for Exemption Number (Appendix G). Leave IRB Approval Date field blank since a Human Subjects Assurance Number is not needed for exempt research. Check “N/A” in field for “example of informed consent” and “Clinical Protocol” as these are not required for exempt research.

In the section on Protection of Human Subjects in the Research Plan, provide a justification for the exemption(s) containing sufficient information about the involvement of the human subjects to allow a determination by peer reviewers and NIH staff that claimed exemption(s) is/are appropriate.

The PHS will make a final determination as to whether the proposed activities are covered by the regulations or are in an exempt category, based on the information provided in the Research Plan. When in doubt, consult with the Office for Human Research Protections (OHRP), Department of Health and Human Services by accessing their Web site <http://www.hhs.gov/ohrp/> for guidance and further information.

The [exemptions](#) appear in Part I, Section 3, Definitions.

Please note: If the proposed research involves only the use of human data or biological specimens, you should first determine whether the research involves human subjects. The exemptions do not apply if the research does not involve human subjects. For help determining whether research that involves the use of human data or biological specimens is human subjects research, please refer to this Web site <http://grants.nih.gov/grants/policy/hs/>.

See the [instructions for Scenario C under Section 3](#).

Scenario D. Delayed-Onset Human Subjects Research

If human subjects research is anticipated within the period of the award but plans for involvement of human subjects cannot be described in the application as allowed by the DHHS regulations (45 CFR part 46.118), check “Yes” to “This proposed project involves human subjects” on the Proposal Cover Sheet (Appendix A) and indicate “Yes” on the Proposal Summary and Data Record (Appendix G). In the section on Protection of Human Subjects in the Research Plan, you should either include an explanation of anticipated protections for human subjects or an explanation of why protections cannot be described.

Examples of delayed-onset of human subjects research include:

- Human subjects research is dependent upon the completion of animal or other studies; or
- Human subjects research protocols to be included will undergo an independent decision-making process (often defined by a FOA).

See [instructions for Scenario D under Section 3](#).

Scenario E. Human Subjects Research Involving a Clinical Trial

If research involving human subjects is anticipated to take place under the award, and you intend to conduct a clinical trial during the project period, check the boxes marked “Yes” on the Proposal Cover Sheet (Appendix A) to “This proposed project involves human subjects,” and “Clinical Trial?” Indicate “Yes” on the Proposal Summary and Data Record (Appendix G). In addition, complete the items regarding the Institution’s General Assurance, Institution’s Review Board, informed consent and clinical protocol.

In the section on Protection of Human Subjects in the Research Plan, you must provide sufficient information for reviewers to determine that the proposed research meets:

- 1) the requirements of the DHHS regulations to protect human subjects from research risks (45 CFR part 46);
- 2) NIH policy requirements for Data and Safety Monitoring for Clinical Trials;
- 3) the ClinicalTrials.gov requirements if applicable;
- 4) the requirements of NIH policies on inclusion of women, minorities, and children; and
- 5) the requirements of NIH policy on reporting race and ethnicity data for human subjects in clinical research.

See [instructions for Scenario E under Section 3](#).

Scenario F. Human Subjects Research Involving an NIH-Defined Phase III Clinical Trial

If research involving human subjects is anticipated to take place under the award, and you intend to conduct an NIH-defined Phase III clinical trial during the project period, check the boxes marked “Yes” to the following statement/questions on the Proposal Cover Sheet (Appendix A):

- This proposed project involves human subjects.
- Clinical Trial?
- Agency-Defined Phase III Clinical Trial?

Also indicate “Yes” on the Proposal Summary and Data Record (Appendix G) to the following question: Does this proposal involve human subjects research? In addition, complete the items regarding the Human Subjects Assurance Number, Institution’s Review Board, informed consent and Clinical Protocol.

In the section on Protection of Human Subjects in the Research Plan, you must provide sufficient information for reviewers to determine that the proposed research meets:

- 1) the requirements of the DHHS regulations to protect human subjects from research risks (45 CFR part 46);
- 2) NIH policy requirements for Data and Safety Monitoring for Clinical Trials;
- 3) the ClinicalTrials.gov requirements if applicable;
- 4) the requirements of NIH policies on inclusion of women, minorities, and children;
- 5) additional Requirements for NIH-defined Phase III clinical trials; and
- 6) the requirements of NIH policy on reporting race and ethnicity data for subjects in clinical research.

See [instructions for Scenario F under Section 3](#).

3. INSTRUCTIONS FOR PREPARING THE SECTION ON PROTECTION OF HUMAN SUBJECTS**Scenario A. No Human Subjects Research Proposed**

Criteria

Human Subjects Research	No
Exemption Claimed	No
Clinical Trial	N/A
NIH-Defined Phase III Clinical Trial	N/A

Instructions and Required Information

In the proposal narrative, create a heading labeled “Protection of Human Subjects” and include the following statement below the heading: “No Human Subjects Research is proposed in this proposal.”

If proposed studies using human data or biological specimens do not involve human subjects as described in the OHRP Guidance on Research Involving Coded Private Information or Biological Specimens (<http://www.hhs.gov/ohrp/policy/cdebiol.html>), provide an explanation of why the proposed studies do not constitute research involving human subjects.

The explanation could include: a description of the source of the data/biological specimens, and whether there is any intervention or interaction with the subjects in order to obtain the specimens and data; what identifiers will be associated; the role(s) of providers of the data/biological specimens in the proposed research; and the manner by which the privacy of research participants and confidentiality of data will be protected.

Research that does not involve intervention or interaction with living individuals, or identifiable private information, is not human subjects research (see Part I, Section 3, Definitions). Research involving the use of coded private information or biological specimens may not constitute human subjects research if the conditions of the OHRP Guidance on Research Involving Coded Private Information or Biological Specimens have been met (<http://www.hhs.gov/ohrp/policy/cdebiol.html>).

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

Scenario B. Non-Exempt Human Subjects Research

Criteria

Human Subjects Research	Yes
Exemption Claimed	No
Clinical Trial	No
NIH-Defined Phase III Clinical Trial	No

Instructions and Required Information

Although no specific page limitation applies to this section of the proposal, be succinct.

In the proposal narrative, create a section entitled “Protection of Human Subjects” and create a subheading for each of the following items.

Follow the instructions that are identified for each of the following topics and provide the information that is requested:

Protections for Human Subjects - Section 4.1 - 4.1.4

Inclusion of Women and Minorities - Section 4.2

Targeted/Planned Enrollment Table - Section 4.3

Inclusion of Children - Section 4.4

If the research involves collaborating sites or subprojects, provide the information identified above for each participating site.

Scenario C: Human Subjects Research Claiming Exemption 1, 2, 3, 4, 5, or 6

Criteria

Human Subjects Research	Yes
-------------------------	-----

Exemption Claimed	1, 2, 3, 4, 5, or 6
Clinical Trial	Yes or No
NIH-Defined Phase III Clinical Trial	No

Instructions and Required Information

Although no specific page limitation applies to this section of the proposal, be succinct. The exemptions appear in Part I, Section 3, Definitions.

Although the research may be exempt from the DHHS regulatory requirements, it is still research involving human subjects and the application must follow the instructions that are identified for each of the following topics and provide the information that is requested.

In the proposal narrative, create a heading entitled “Protection of Human Subjects” and include the following statement below the heading: “This Human Subjects Research falls under Exemption(s)”

Follow the instructions that are identified for each of the following topics and provide the information that is requested:

Justification for Claimed Exemption(s):

In this section, identify which exemption(s) (1, 2, 3, 4*, 5, or 6) you are claiming. Justify why the research meets the criteria for the exemption(s) that you have claimed.

If the research will include a clinical trial, even if exempt, include a Data and Safety Monitoring Plan – Section 4.1.5, and address the ClinicalTrials.gov requirements if applicable – Section 4.1.6.

Inclusion of Women and Minorities - Section 4.2

Targeted/Planned Enrollment Table - Section 4.3

Inclusion of Children - Section 4.4

*NOTE: If all the proposed research meets the criteria for Exemption 4, then the requirements for inclusion of women and minorities, targeted/planned enrollment table, and inclusion of children, do not need to be addressed.

Scenario D: Delayed-Onset Human Subjects Research

Criteria

Human Subjects Research	Yes
Exemption	Yes or No
Clinical Trial	Yes or No
NIH-Defined Phase III Clinical Trial	Yes or No

Instructions and Required Information

In rare situations, proposals are submitted with the knowledge that human subjects will be involved during the period of support, but plans are so indefinite that it is not possible to describe the involvement of human subjects

in the proposal. The kinds of activities that lack definite plans are often institutional awards where the selection of specific projects is the institution's responsibility, research training grants, and projects in which the involvement of human subjects depends upon completion of instruments, animal studies, or purification of compounds.

If the involvement of human subjects cannot be fully described, create a heading entitled "Protection of Human Subjects" and provide a detailed explanation why it is not possible to develop definite plans at this time. The explanation should be specific and directly related to the Specific Aims in the proposal. If the involvement of human subjects depends upon information that is not presently available (e.g., completion of instruments, animal studies, purification of compounds), be explicit about the information and the factors affecting the availability of the information. Describe the information that will be necessary in order to develop definite plans for the involvement of human subjects, why that information is not currently available, and when the information is expected to become available during the course of the project.

If an award is made, prior to the involvement of human subjects the awardee must submit to the NHLBI Contracting Officer for prior approval either (1) detailed information as required in the Research Plan, Protection of Human Subjects (addressing risks to the subjects, adequacy of protection against risks, potential benefits of the proposed research, importance of the knowledge to be gained, and data and safety monitoring plan if applicable) and certification of IRB approval, OR (2) if all of the research meets the criteria for one or more exemptions, identification of which exemption(s) is/are applicable to the research, and a justification for the exemption with sufficient information about the involvement of human subjects to allow a determination that the claimed exemption is appropriate. For clinical research, the request for prior approval must also address the inclusion of women and minorities, the inclusion of children, and provide completed targeted/planned enrollment tables as required in the Research Plan.

Under no circumstance may human subjects be involved in research until approval is granted by the Contracting Officer entity, and certification of IRB approval has been accepted by the NHLBI.

In the proposal narrative, create a section entitled Protection of Human Subjects and a subheading for each of the following items. Follow the instructions that are identified for each of the following topics and EITHER provide as much of the information that is requested as possible; OR describe why it is not possible to provide the information due to delayed-onset of human subjects research:

Protection of Human Subjects – Section 4.1 - 4.1.4

If the research will include a clinical trial, even if exempt, include a Data and Safety Monitoring Plan - Section 4.1.5, and address the ClinicalTrials.gov requirements if applicable – Section 4.1.6.

Inclusion of Women and Minorities – Section 4.2

Targeted/Planned Enrollment Table – Section 4.3

Inclusion of Children – Section 4.4

Scenario E: Clinical Trial

Criteria

Human Subjects Research	Yes
Exemption	Yes or No
Clinical Trial	Yes
NIH-Defined Phase III Clinical Trial	No

Instructions and Required Information

In the proposal narrative, create a section entitled "Protection of Human Subjects" and include the following statement below the heading: "This Human Subjects Research meets the definition of a clinical trial." (See definition of "clinical trial" in Part I.) Create a subheading for each of the following items. Follow the instructions that are identified for each of the following topics and provide the information that is requested:

Protection of Human Subjects – Section 4.1 - 4.1.6

Inclusion of Women and Minorities – Section 4.2

Targeted/Planned Enrollment Table – Section 4.3

Inclusion of Children – Section 4.4

If the research involves collaborating sites or subprojects, provide the information identified above for each participating site.

Scenario F: NIH Defined Phase III Clinical Trial

Criteria

Human Subjects Research	Yes
Exempt	No
Clinical Trial	Yes
NIH-Defined Phase III Clinical Trial	Yes

Instructions and Required Information

In the proposal narrative, create a section entitled "Protection of Human Subjects" and include the following statement below the heading: "This Human Subjects Research involves an NIH-Defined Phase III Clinical Trial." (See "NIH defined Phase III Clinical Trial" in Definitions)

Create a subheading for each of the following items. Follow the instructions that are identified for each of the following topics and provide the information that is requested:

Protection of Human Subjects - Section 4.1 - 4.1.6

Inclusion of Women and Minorities - Section 4.2

Additional Instructions and Requirements when NIH-Defined Phase III Clinical Trials are Proposed - Section 4.2.1

Targeted/Planned Enrollment Table - Section 4.3

Inclusion of Children - Section 4.4

If the research involves collaborating sites or subprojects, provide the information identified above for each participating site.

4. INSTRUCTIONS PERTAINING TO NON-EXEMPT HUMAN SUBJECTS RESEARCH

In your proposal narrative, **create a section entitled “Human Subjects.”** Although no specific page limitation applies to this section of the proposal, be succinct. Scientific Review Groups will assess each proposal as being acceptable or unacceptable with regard to the protection of human subjects. DHHS regulations and policies governing human subjects research are described and referenced in Section 5 below. **Use subheadings** to address the issues listed under items 4.1-4.4 below. If your research includes a clinical trial, include a subheading “Data and Safety Monitoring Plan” and follow the instructions in 4.2 below. If your research includes an NIH-Defined Phase III Clinical Trial, follow the additional instructions in 4.2.1 below.

4.1 PROTECTION OF HUMAN SUBJECTS

4.1.1 Risks to Human Subjects

a. *Human Subjects Involvement, Characteristics, and Design*

- Describe the proposed involvement of human subjects in the work outlined in the Human Subjects Research section.
- Describe and justify the characteristics of the subject population, including their anticipated number, age range, and health status if relevant.
- Describe and justify the sampling plan, as well as the recruitment and retention strategies and the criteria for inclusion or exclusion of any subpopulation.
- Explain the rationale for the involvement of special vulnerable populations, such as fetuses, neonates, pregnant women, children, prisoners, institutionalized individuals, or others who may be considered vulnerable populations. Note that ‘prisoners’ includes all subjects involuntarily incarcerated (for example, in detention centers) as well as subjects who become incarcerated after the study begins.
- If relevant to the proposed research, describe procedures for assignment to a study group. As related to human subjects protection, describe and justify the selection of an intervention’s dose, frequency, and administration.
- List any collaborating sites where human subjects research will be performed, and describe the role of those sites and collaborating investigators in performing the proposed research. Explain how data from the site(s) will be obtained, managed, and protected.

b. *Sources of Materials*

- Describe the research material obtained from living individuals in the form of specimens, records, or data.
- Describe any data that will be collected from human subjects for the project(s) described in the application.
- Indicate who will have access to individually identifiable private information about human subjects.
- Provide information about how the specimens, records, and/or data are collected, managed, and protected as well as whether material or data that include individually identifiable private information will be collected specifically for the proposed research project.

c. *Potential Risks*

- Describe the potential risks to subjects (physical, psychological, financial, legal, or other), and assess their likelihood and seriousness to the human subjects.
- Where appropriate, describe alternative treatments and procedures, including the risks and potential benefits of the alternative treatments and procedures, to participants in the proposed research.

4.1.2 Adequacy of Protection Against Risks

a. *Recruitment and Informed Consent*

- Describe plans for the recruitment of subjects (where appropriate) and the process for obtaining informed consent. If the proposed studies will include children, describe the process for meeting requirements for parental permission and child assent.
- Include a description of the circumstances under which consent will be sought and obtained, who will seek it, the nature of the information to be provided to prospective subjects, and the method of documenting consent. If a waiver of some or all of the elements of informed consent will be sought, provide justification for the waiver. Informed consent document(s) need not be submitted to the PHS agencies unless requested.

b. *Protections Against Risk*

- Describe planned procedures for protecting against or minimizing potential risks, including risks to privacy of individuals or confidentiality of data, and assess their likely effectiveness.
- Research involving vulnerable populations, as described in the DHHS regulations, Subparts B-D must include additional protections. Refer to DHHS regulations, and OHRP guidance:

Additional Protections for Pregnant Women, Human Fetuses and Neonates:

<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subpartb>

Additional Protections for Prisoners:

<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subpartc>

OHRP Subpart C Guidance: <http://www.hhs.gov/ohrp/policy/index.html#prisoners>

Additional Protections for Children:

<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subpartd>

OHRP Subpart D Guidance: <http://www.hhs.gov/ohrp/policy/index.html#children>

- Where appropriate, discuss plans for ensuring necessary medical or professional intervention in the event of adverse effects to the subjects. Studies that involve clinical trials (biomedical and behavioral intervention studies) must include a general description of the plan for data and safety monitoring of clinical trials and adverse event reporting to the IRB, the NIH and others, as appropriate, to ensure the safety of subjects.

4.1.3 Potential Benefits of the Proposed Research to Human Subjects and Others

- Discuss the potential benefits of the research to research participants and others.
- Discuss why the risks to subjects are reasonable in relation to the anticipated benefits to research participants and others.

4.1.4 Importance of the Knowledge to be Gained

- Discuss the importance of the knowledge gained or to be gained as a result of the proposed research.
- Discuss why the risks to subjects are reasonable in relation to the importance of the knowledge that reasonably may be expected to result.

NOTE: Test articles (investigational new drugs, devices, or biologics) including test articles that will be used for purposes or administered by routes that have not been approved for general use by the Food and Drug Administration (FDA) must be named. State whether the 30-day interval between submission of applicant certification to the FDA and its response has elapsed or has been waived and/or whether use of the test article has been withheld or restricted by the FDA, and/or the status of requests for an Investigational New Drug (IND) or Investigational Device Exemption (IDE) covering the proposed use of the test article in the Research Plan.

4.1.5 Data and Safety Monitoring Plan

The NIH Data and Safety Monitoring Plan Policy is described and referenced in Part I Section 5.3 of this solicitation.

- If the proposed research includes a clinical trial, create a heading entitled "Data and Safety Monitoring Plan."
- Provide a general description of a monitoring plan that you plan to establish as the overall framework for data and safety monitoring. Describe the entity that will be responsible for monitoring and the process by which Adverse Events (AEs) will be reported to the Institutional Review Board (IRB), the funding I/C, the NIH Office of Biotechnology Activities (OBA), and the Food and Drug Administration (FDA) in accordance with Investigational New Drug (IND) or Investigational Device Exemption (IDE) regulations. Be succinct. Contact the FDA (<http://www.fda.gov/>) and also see the following Web sites for more information related to IND and IDE requirements:
http://www.access.gpo.gov/nara/cfr/waisidx_01/21cfr312_01.html (IND)
http://www.access.gpo.gov/nara/cfr/waisidx_01/21cfr812_01.html (IDE)
- The frequency of monitoring will depend on potential risks, complexity, and the nature of the trial; therefore, a number of options for monitoring trials are available. These can include, but are not limited to, monitoring by a:
 - a. PD/PI (required)
 - b. Institutional Review Board (IRB) (required)
 - c. Independent individual/safety officer
 - d. Designated medical monitor
 - e. Internal Committee or Board with explicit guidelines
 - f. Data and Safety Monitoring Board (DSMB). NIH specifically requires the establishment of Data and Safety Monitoring Boards (DSMBs) for multi-site clinical trials involving interventions that entail potential risk to the participants, and generally for Phase III clinical trials. Although Phase I and Phase II clinical trials may also need DSMBs, smaller clinical trials may not require this oversight format, and alternative monitoring plans may be appropriate.
- A detailed Data and Safety Monitoring Plan must be submitted to the applicant's IRB and subsequently to the funding IC for approval prior to the accrual of human subjects (<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html>). For additional guidance on creating this Plan, see the above reference.

4.1.6 ClinicalTrials.gov Requirements

Public Law 110-85 (also known as the FDA Amendments Act (FDAAA) of 2007) mandates registration and results reporting of certain "applicable clinical trials" in ClinicalTrials.gov. Under the statute these trials generally include: (1) Trials of Drugs and Biologics: Controlled, clinical investigations, other than Phase 1 investigations, of a product subject to FDA regulation; and (2) Trials of Devices: Controlled trials with health outcomes, other than small feasibility studies, and pediatric postmarket surveillance. Review the statutory definition of applicable clinical trial to identify if registration is required to comply with the law (See [PL 110-85](#), Section 801(a), adding new 42 U.S.C. 282(j)(1)(A)).

NIH encourages registration of ALL clinical trials whether required under the law or not.

Registration is accomplished at the ClinicalTrials.gov Protocol Registration System Information Web site (<http://prsinfo.clinicaltrials.gov/>). A unique identifier called an NCT number, or ClinicalTrials.gov registry number, will be generated during the registration process.

The NIH implementation of FDAAA requires:

- the registration of applicable clinical trials in ClinicalTrials.gov no later than 21 days after the first subject is enrolled,
- the reporting of summary results information (including adverse events) no later than 1 year after the completion date for registered applicable clinical trials involving drugs that are approved under section

505 of the Food, Drug and Cosmetic Act (FDCA) or licensed under section 351 of the PHS Act, biologics, or of devices that are cleared under section 510k of FDCA, and

- if an “applicable clinical trial” is funded in whole or in part by an NIH grant or cooperative agreement, grant and progress report forms shall include a certification that the responsible party has made all required submissions to ClinicalTrials.gov.

For competing (new and renewal) applications that include applicable clinical trials which require registration and, in certain cases, require results reporting under FDAAA, provide the NCT number/s, Brief Title/s (protocol title intended for the lay public – see Definitions), and the identity (name, organization) of the responsible party (or parties) and their contact information (e-mail address is required for internal administrative use only) in the human subjects section of the Research Plan under a section heading entitled ClinicalTrials.gov. If a new applicable clinical trial is proposed or if the contract will support an applicable clinical trial that is ongoing but not yet required to register under FDAAA (e.g. less than 21 days have passed since enrollment of the first patient), under the heading ClinicalTrials.gov include a clear statement that the application includes an applicable clinical trial which will require registration in ClinicalTrials.gov.

The entity responsible for registering the trial is the “responsible party.” The statute defines the responsible party as:

(1) the sponsor of the clinical trial (as defined in 21 CFR 50.3)

(<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=50.3>), or

(2) the principal investigator of such clinical trial if so designated by a sponsor, grantee, contractor, or awardee (provided that “the principal investigator is responsible for conducting the trial, has access to and control over the data from the clinical trial, has the right to publish the results of the trial, and has the ability to meet all of the requirements” for submitting information under the law) (http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=110_cong_public_laws&docid=f:publ085.110.pdf). See PL 110-85, Section 801(a), (adding new 42 U.S.C. 282(j)(1)(A)(ix)).

For the complete statutory definitions of “responsible party” and “applicable clinical trial”, refer to [Elaboration of Definitions of Responsible Party and Applicable Clinical Trial](#).

The signature on the application of the Authorized Organizational Representative assures compliance with FDAAA.

Additional information can be found on the ClinicalTrials.gov Web site (http://grants.nih.gov/ClinicalTrials_fdaaa).

4.2 INCLUSION OF WOMEN AND MINORITIES

Create a section heading entitled “Inclusion of Women and Minorities” and place it immediately following the “Protection of Human Subjects” section. Although no specific page limitation applies to this section of the proposal, be succinct. The NIH Policy on the Inclusion of Women and Minorities in Clinical Research is described and referenced in Section 5.6.

Scientific Review Groups will assess each proposal as being acceptable or unacceptable with regard to the inclusion of women and minorities in clinical research.

In this section of the Research Plan, address, at a minimum, the following four points:

1. The targeted/planned distribution of subjects by sex/gender and racial/ethnic groups for each proposed study or protocol using the format in the Targeted/Planned Enrollment Table. (Instructions for completing this table are provided below in 4.3.) If using existing specimens and/or data without access to information on the distribution of women and minorities, so state and explain the impact on the goals of the research as part of the rationale that inclusion cannot be described (item 3 below). Alternatively, describe the gender and minority composition of the population base from whom the specimens and/or data will be obtained. Include the Targeted/Planned Enrollment Table in this section.

2. A description of the subject selection criteria and rationale for selection of sex/gender and racial/ethnic group members in terms of the scientific objectives and proposed study design. The description may include, but is not limited to, information on the population characteristics of the disease or condition under study.
3. A compelling rationale for proposed exclusion of any sex/gender or racial/ethnic group (see examples below).
4. A description of proposed outreach programs for recruiting sex/gender and racial/ethnic group members as subjects.

Examples of acceptable justifications for exclusion of:

A. *One gender:*

1. One gender is excluded from the study because:
 - inclusion of these individuals would be inappropriate with respect to their health;
 - the research question addressed is relevant to only one gender;
 - evidence from prior research strongly demonstrates no difference between genders; or
 - sufficient data already exist with regard to the outcome of comparable studies in the excluded gender, and duplication is not needed in this study.
2. One gender is excluded or severely limited because the purpose of the research constrains the applicant's selection of study subjects by gender (e.g., uniquely valuable stored specimens or existing datasets are single gender; very small numbers of subjects are involved; or overriding factors dictate selection of subjects, such as matching of transplant recipients, or availability of rare surgical specimens).
3. Gender representation of specimens or existing datasets cannot be accurately determined (e.g., pooled blood samples, stored specimens, or data-sets with incomplete gender documentation are used), and this does not compromise the scientific objectives of the research.

B. *Minority groups or subgroups:*

1. Some or all minority groups or subgroups are excluded from the study because:
 - inclusion of these individuals would be inappropriate with respect to their health;
 - the research question addressed is relevant to only one racial or ethnic group;
 - evidence from prior research strongly demonstrates no differences between racial or ethnic groups on the outcome variables;
 - a single minority group study is proposed to fill a research gap; or
 - sufficient data already exists with regard to the outcome of comparable studies in the excluded racial or ethnic groups and duplication is not needed in this study.
2. Some minority groups or subgroups are excluded or poorly represented because the geographical location of the study has only limited numbers of these minority groups who would be eligible for the study, and the investigator has satisfactorily addressed this issue in terms of:
 - the size of the study;
 - the relevant characteristics of the disease, disorder or condition; or
 - the feasibility of making a collaboration or consortium or other arrangements to include representation.
3. Some minority groups or subgroups are excluded or poorly represented because the purpose of the research constrains the applicant's selection of study subjects by race or ethnicity (e.g., uniquely valuable cohorts, stored specimens or existing datasets are of limited minority representation, very small numbers of subjects are involved, or overriding factors dictate selection of subjects, such as matching of transplant recipients or availability of rare surgical specimens).

4. Racial or ethnic origin of specimens or existing datasets cannot be accurately determined (e.g., pooled blood samples, stored specimens or data sets with incomplete racial or ethnic documentation are used) and this does not compromise the scientific objectives of the research.

4.2.1 Additional Instructions and Requirements When NIH-Defined Phase III Clinical Trials Are Proposed

If the proposed research includes an NIH-Defined Phase III Clinical Trial, the section on Inclusion of Women and Minorities also must address whether clinically important sex/gender and/or race/ethnicity differences are expected from the intervention effect. The discussion may include supporting evidence and/or data derived from animal studies, clinical observations, metabolic studies, genetic studies, pharmacology studies, and observational, natural history, epidemiology and other relevant studies. The discussion of expected sex/gender and/or race/ethnicity differences in intervention effect must include selection and discussion of one of the following analysis plans:

- Plans to conduct valid analyses to detect significant differences in intervention effect among sex/gender and/or racial/ethnic subgroups when prior studies strongly support these significant differences among subgroups, *or*
- Plans to include and analyze sex/gender and/or racial/ethnic subgroups when prior studies strongly support no significant differences in intervention effect between subgroups. (Representation of sex/gender and racial/ethnic groups is not required as subject selection criteria, but inclusion is encouraged.), *or*
- Plans to conduct valid analyses of the intervention effect in sex/gender and/or racial/ethnic subgroups (without requiring high statistical power for each subgroup) when the prior studies neither support nor negate significant differences in intervention effect among subgroups.

4.3 INSTRUCTIONS FOR COMPLETING THE TARGETED/PLANNED ENROLLMENT TABLES FOR REPORTING RACE AND ETHNICITY DATA FOR SUBJECTS IN CLINICAL RESEARCH

The NIH Policy on Reporting Race and Ethnicity Data for Subjects in Clinical Research is described and referenced in Section 5.8 below.

A. New Proposals

All new clinical research studies should collect and report information on participants with respect to two categories of ethnicity and five categories of race. The Inclusion Enrollment Report (http://grants.nih.gov/grants/funding/424/SF424R-R_enrollmentreport.doc) for reporting summary data on participants to NIH includes two categories of ethnicity and five categories of race and is based on the Office of Management and Budget (OMB) reporting standards for data on race and ethnicity. Investigators should review the instructions and Frequently Asked Questions about using the Enrollment Table format at <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-01-053.html>.

When reporting these data in the aggregate, investigators should report: (a) the number of research participants in each ethnic category; (b) the number of research participants who selected only one category for each of the five racial categories; (c) the total number of research participants who selected multiple racial categories reported as the “number selecting more than one race,” and (d) the number of research participants in each racial category who are Hispanic or Latino. Investigators may provide the detailed distributions, including all possible combinations, of multiple responses to the racial designations as additional information. However, more detailed data should be compiled in a way that they can be reported using the required categories.

Instructions for Completing Targeted/Planned Enrollment Table

(http://grants.nih.gov/grants/funding/424/SF424R-R_enrollment.doc)

Provide the study title.

The “Total Planned Enrollment” means the number of subjects that are expected to be enrolled in the study, consistent with the definition in ClinicalTrials.gov.

The “Total Planned Enrollment” will be reported in two ways in the table: by “Ethnic Category” and by “Racial Categories.”

“Ethnic Category”: Provide the numeric distribution of the Total Planned Enrollment according to ethnicity and sex/gender in the top part of the table.

“Racial Categories”: Provide the numeric distribution of the Total Planned Enrollment, this time by racial categories and sex/gender, in the bottom part of the table. Note that Hispanic is an ethnic, not a racial, category.

If there is more than one study/protocol, provide a separate table for each.

List any proposed racial/ethnic subpopulations below the table.

Submitting Applications or Proposals Using Existing Data in Clinical Research with No Plans for Collecting New/Additional Data:

Investigators are instructed to provide plans for the total number of subjects proposed for the study and to provide the distribution by ethnic/racial categories and sex/gender using the Targeted/Planned Enrollment Table. Under these circumstances, investigators are not required to re-contact subjects solely to comply with the newly revised categories.

If Data Collection is Ongoing, Such that New Human Subjects Will be Enrolled and/or Additional Data Will be Collected from Human Subjects:

Investigators should report ethnicity/race and sex/gender sample composition using the Inclusion Enrollment Report.

If Data Collection is Complete, Such that No New/Additional Subject Contact is Planned:

Investigators should use the Inclusion Enrollment Report.

Research Conducted at Foreign Sites:

If proposed studies involve a foreign site, investigators are encouraged to design culturally sensitive and appropriate data collection instruments that allow research participants to self-identify their racial and ethnic affiliation. However, these items should be designed in a way that they can be aggregated into the OMB-required categories. Also, the investigator can report on any racial/ethnic subpopulations by listing this information in an attachment to the required table. This may be particularly useful when distinctive subpopulations are relevant to the scientific hypotheses being studied.

When completing the tables that describe research in foreign sites, investigators should asterisk and footnote the table indicating that data include research participants in foreign sites. If the aggregated data only includes participants in foreign research sites, the investigator should provide information in one table with an asterisk and footnote. However, if the study includes both domestic and foreign sites, the investigator should complete two separate tables – one for domestic and another for foreign participants.

B. Progress Reports

The Inclusion Enrollment Report (http://grants.nih.gov/grants/funding/424/SF424R-R_enrollmentreport.doc) must be used for reporting accrual data to the NIH. In annual progress reports, investigators conducting clinical research are required to provide the cumulative total enrollment of subjects to-date, showing the distribution by ethnic/racial categories and sex/gender on the Inclusion Enrollment Report, and must update the Targeted/Planned Enrollment Table as needed.

4.4 INCLUSION OF CHILDREN

The NIH Policy on Inclusion of Children is referenced and described in Section 5.7. Instructions for this item under the “Human Subjects” heading of the Research Plan are as follows:

- Create a section entitled “Inclusion of Children” and place it immediately following the Targeted/Planned Enrollment Table.
- For the purpose of implementing these guidelines, a *child* is defined as an individual under the age of 21 years (for additional information see <http://grants.nih.gov/grants/funding/children/children.htm> and <http://grants.nih.gov/grants/guide/notice-files/not98-024.html>).
- Provide either a description of the plans to include children, or, if children will be excluded from the proposed research, application, or proposal, present an acceptable justification for the exclusion (see below).
- If children are included, the description of the plan should include a rationale for selecting a specific age range of children. The plan also must include a description of the expertise of the investigative team for working with children at the ages included, of the appropriateness of the available facilities to accommodate the children, and the inclusion of a sufficient number of children to contribute to a meaningful analysis relative to the purpose of the study.
- Scientific Review Groups will assess each proposal as being acceptable or unacceptable with regard to the age-appropriate inclusion or exclusion of children in the research project.
- When children are involved in research, the Additional Protections for Children Involved as Subjects in Research (45 CFR part 46 Subpart D (<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subpartd>)) apply and must be addressed under the Protections Against Risk subheading (4.1.2.b).

Justifications for Exclusion of Children

For the purposes of this policy, all individuals under 21 are considered children; however, exclusion of any specific age group, such as individuals under 18, should be justified in this section. It is expected that children will be included in all clinical research unless one or more of the following exclusionary circumstances apply:

1. The research topic to be studied is not relevant to children.
2. Laws or regulations bar the inclusion of children in the research.
3. The knowledge being sought in the research is already available for children or will be obtained from another ongoing study, and an additional study will be needlessly redundant. Documentation of other studies justifying the exclusions should be provided. NIH program staff can be contacted for guidance on this issue if the information is not readily available.
4. A separate, age-specific study in children is warranted and preferable. Examples include:
 - a. The condition is relatively rare in children, as compared to adults (in that extraordinary effort would be needed to include children, although in rare diseases or disorders where the applicant has made a particular effort to assemble an adult population, the same effort would be expected to assemble a similar child population with the rare condition); or
 - b. The number of children is limited because the majority are already accessed by a nationwide pediatric disease research network; or
 - c. Issues of study design preclude direct applicability of hypotheses and/or interventions to both adults and children (including different cognitive, developmental, or disease stages or different age-related metabolic processes). While this situation may represent a justification for excluding children in some instances, consideration should be given to taking these differences into account in the study design and

expanding the hypotheses tested, or the interventions planned, to allow inclusion of children rather than excluding them.

5. Insufficient data are available in adults to judge potential risk in children (in which case one of the research objectives could be to obtain sufficient adult data to make this judgment). Although children usually should not be the initial group to be involved in research studies, in some instances, the nature and seriousness of the illness may warrant their participation earlier based on careful risk and benefit analysis.
6. Study designs are aimed at collecting additional data on pre-enrolled adult study subjects (e.g., longitudinal follow-up studies that did not include data on children).
7. Other special cases can be justified by the investigator and found acceptable to the review group and the Institute/Center Director.

5. HUMAN SUBJECTS RESEARCH POLICY

Human Subjects Research Policy includes DHHS regulations for the protection of human subjects and the following NIH policies related to human subjects research.

5.1 PROTECTION OF HUMAN SUBJECTS

The Department of Health and Human Services (DHHS) regulations for the protection of human research subjects provide a systematic means, based on established, internationally recognized ethical principles, to safeguard the rights and welfare of individuals who participate as subjects in research activities supported or conducted by the DHHS. The regulations stipulate that the awardee organization, whether domestic or foreign, bears responsibility for safeguarding the rights and welfare of human subjects in DHHS-supported research activities. The regulations require that offeror organizations engaged in nonexempt human subjects research supported or conducted by the DHHS hold a Federal-wide Assurance (FWA) with the Office for Human Research Protections (OHRP), and establish appropriate policies and procedures for the protection of human subjects. These regulations, [45 CFR part 46 \(http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html\)](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html), Protection of Human Subjects, are available from OHRP, Department of Health and Human Services, The Tower Building, 1101 Wootton Parkway, Suite 200, Rockville, MD 20852; telephone: 1-866-447-4777 (toll-free) or (240) 453-6900; e-mail: ohrp@osophs.dhhs.gov. In general, OHRP considers organizations that receive direct support from DHHS for the conduct of nonexempt human subjects research to be engaged in human subjects research (for more information on whether an institution is engaged in human subjects research, refer to: <http://www.hhs.gov/ohrp/policy/engage08.html>). When a research project is conducted by multiple organizations, each organization that is engaged in nonexempt human subjects research must hold an FWA and comply with the regulations at 45 CFR 46.

Nonexempt research involving human subjects may only be conducted under a DHHS award if the engaged organization(s) is operating in accord with an approved FWA and provides verification that an Institutional Review Board (IRB) that is registered under the specific FWA has reviewed and approved the proposed activity in accordance with the DHHS regulations. No award to an individual will be made unless that individual is affiliated with an assured organization that accepts responsibility for compliance with the DHHS regulations. Foreign offeror organizations must also comply with the provisions of the regulations unless a determination of equivalent protections is made in accord with 45 CFR 46.101(h).

Under DHHS regulations to protect human subjects, certain research areas are [exempt](#). However, if an offeror makes inappropriate designations of the noninvolvement of human subjects or of exempt categories of research, this may result in delays in the review of an application or an application not being reviewed. The PHS will make a final determination as to whether the proposed activities are covered by the regulations or are in an exempt category, based on the information provided in the Research Plan. With the exception of research projects that meet the criteria for Exemption 4, studies that are exempt from the human subjects regulatory requirements must still address the inclusion of women, minorities and children in the study design.

Regulations of the Food and Drug Administration (21 CFR 50, 21 CFR 56) generally apply to biomedical research involving an unapproved drug, device or biologic and may apply to certain studies of approved products.

Additional information on FDA regulations is available at <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm>. If work falls under FDA's regulatory requirements, the awardee must follow both DHHS and FDA human subject protection regulations.

The *National Institutes of Health Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines)* apply to all projects (NIH-funded and non NIH-funded) involving recombinant DNA molecules that are conducted at or sponsored by an institution that receives NIH support for recombinant DNA research. As defined by the *NIH Guidelines*, recombinant DNA molecules are either: (1) molecules that are constructed outside living cells by joining natural or synthetic DNA segments to DNA molecules that can replicate in a living cell; or (2) DNA molecules that result from the replication of those described in (1). The *NIH Guidelines* set forth principles and standards for safe and ethical conduct of recombinant DNA research and apply to both basic and clinical research studies. The *NIH Guidelines* should be carefully reviewed and implemented to ensure that proper biosafety and containment practices are employed for all projects involving recombinant DNA research, including review by an Institutional Biosafety Committee that meets the requirements of the *NIH Guidelines*. Further, the *NIH Guidelines* include special review and reporting requirements for the conduct of human gene transfer studies (under Appendix M). Failure to comply with the *NIH Guidelines* may result in suspension, limitation, or termination of NIH funds for recombinant DNA research at the organization or a requirement for NIH prior approval of any or all recombinant DNA projects at the organization. A copy of the *NIH Guidelines* is posted at the following URL: http://oba.od.nih.gov/rdna/nih_guidelines_oba.html and may be obtained from the NIH Office of Biotechnology Activities, 6705 Rockledge Drive, Suite 750, Bethesda, MD 20892, 301-496-9838.

Federal requirements to protect human subjects apply to most research on human specimens (such as cells, blood, and urine), residual diagnostic specimens, and medical information. Research involving existing data, documents, records, pathological specimens, diagnostic specimens, or tissues that are individually identifiable is considered "research involving human subjects." The NIH Office of Extramural Research Human Subjects Web site contains additional information and Frequently Asked Questions to help investigators understand how these federal requirements apply to their research. See <http://grants.nih.gov/grants/policy/hs/index.htm>.

The DHHS regulations require the NIH to evaluate all proposals involving human subjects (<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46.120>). This independent evaluation is conducted at the NIH through the peer review system and NIH staff review, and, as required, will take into consideration the risks to the subjects, the adequacy of protection against these risks, the potential benefits of the research to the subjects and others, and the importance of the knowledge gained or to be gained. On the basis of this evaluation, the NIH may approve or disapprove the proposal, or enter into negotiations to develop an approvable one.

5.2 VULNERABLE POPULATIONS

Investigators who conduct research involving pregnant women, human fetuses and neonates, prisoners (or subjects who become prisoners after the research has started), or children, must follow the provisions of the regulations in Subparts B, C, and D of [45 CFR part 46](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html) (<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html>), respectively. The subparts describe the additional protections required for conducting research involving these populations. Relevant information may be obtained at the OHRP Web site (<http://www.hhs.gov/ohrp/policy/index.html>).

REMINDER: DHHS regulations at [45 CFR part 46, Subpart C](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subpartc) (<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subpartc>) describe requirements for additional protections for research involving prisoners as subjects or individuals who become prisoners after the research has started. Refer to: <http://www.hhs.gov/ohrp/policy/prisoner.html> for complete instructions.

[Exemptions 1-6](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subpartc) do **not** apply to research involving prisoners or subjects who become prisoners (see [Subpart C](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subpartc) (<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subpartc>)). Although Exemptions 1 and 3-6 apply to research involving children (see [Subpart D](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subpartd) (<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subpartd>)), [Exemption 2](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subpartd) can only be used for

research involving educational testing or observations of public behavior when the investigator(s) do not participate in the activities being observed.

5.3 DATA AND SAFETY MONITORING PLANS FOR CLINICAL TRIALS

For each proposed clinical trial, NIH requires a data and safety monitoring plan that describes oversight and monitoring to ensure the safety of participants and the validity and integrity of the data. The level of monitoring should be commensurate with the risks and the size and complexity of the clinical trial. Prior to the accrual of human subjects, a detailed data and safety monitoring plan must be submitted to the offeror's IRB and to the funding entity for approval. Adverse Events must be reported to the IRB, the NIH funding Institute or Center, and other appropriate offices or agencies. This policy requirement is in addition to any monitoring requirements imposed by [45 CFR part 46 \(http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html\)](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html). NIH policy specifically requires the establishment of a Data and Safety Monitoring Board (DSMB) for multi-site clinical trials involving interventions that entail potential risk to the participants, and generally for Phase III clinical trials.

5.4 IRB APPROVAL

NIH does not require certification of IRB approval of the proposed research prior to NIH peer review of a proposal. See <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-031.html>.

Following NIH peer review, the offeror organization will be notified of the need for review and approval of the proposed research by an IRB that is registered under the institutional assurance with OHRP. See <http://www.hhs.gov/ohrp/> to register an IRB. Certification of IRB approval must be sent to the Grants Management Office identified in the notice requesting documentation. Certification of IRB review and approval must include: the PHS SBIR proposal number, title of the project, name of the program director /principal investigator, date of IRB approval, and appropriate signatures. Offerors may also use the optional form "Protection of Human Subjects - Assurance Identification/IRB Certification/Declaration of Exemption (Common Rule)" (OMB Form No. 0990-0263 <http://www.hhs.gov/ohrp/assurances/forms/of310.rtf>) to meet this requirement.

According to OHRP policy, in general, an institution is considered to be engaged in human subjects research when it receives an NIH award to support nonexempt human subjects research. See <http://www.hhs.gov/ohrp/policy/engage08.html>. All institutions engaged in human subjects research must obtain a Federalwide Assurance (FWA) from OHRP. Instructions for applying for a Federalwide Assurance (FWA) are available from the OHRP Web site at <http://www.hhs.gov/ohrp/assurances/index.html>.

DHHS human subject regulations at 45 CFR 46.103(f) require that each application for non-exempt HHS-supported human subject research be reviewed and approved by an IRB (see also <http://www.hhs.gov/ohrp/policy/conditionalapproval2010.html>). Only the date of approval of the application should be submitted to NIH. However, the IRB must ensure that any corresponding protocol(s) are consistent with the application, and must maintain documentation of IRB approval of all corresponding protocols, including those reviewed by consortium participants. For multi-site research, the primary grantee is expected to collect the certification from each subrecipient.

Any modifications to the Research Plan in the proposal, required by either NIH or by the IRB, must be submitted with follow-up certification of IRB approval to the NIH before the competing award is made. It is the responsibility of the PD/PI and the offeror organization to submit the follow-up documentation.

If more than a year will have elapsed between the initial IRB review date and the anticipated award date, the NHLBI staff shall require re-review by the IRB prior to award.

5.5 REQUIRED EDUCATION IN THE PROTECTION OF HUMAN RESEARCH PARTICIPANTS

NIH requires education on the protection of human research participants for all individuals identified in PHS applications as senior/key personnel who will be involved in the design or conduct of human subjects research, before funds are awarded for applications or contract proposals involving human subjects. For information relating to this requirement, see the following notices <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html>

and <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-01-061.html>, and Frequently Asked Questions at: http://grants.nih.gov/grants/policy/hs_educ_faq.htm. Prior to award, offerors will be required to provide a description of education completed in the protection of human subjects for all senior/key personnel involved in the design or conduct of human subjects research. Although NIH does not endorse specific programs, there are curricula available that can provide guidance or that can be modified to provide training in this area. See <http://phrp.nihtraining.com/users/login.php> for computer-based training developed for NIH that can be downloaded at no charge. For information on facilitating education and developing curricula, see <http://www.nih.gov/sigs/bioethics>.

5.6 NIH POLICY ON THE INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH

NIH policy requires that women and members of minority groups and their subpopulations must be included in all NIH-supported biomedical and behavioral research projects involving [clinical research](#) unless a clear and compelling rationale and justification establishes to the satisfaction of the funding IC Director that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. Exclusion under other circumstances must be designated by the Director, NIH, upon the recommendation of an IC Director based on a compelling rationale and justification. Cost is not an acceptable reason for exclusion except when the study would duplicate data from other sources. Women of childbearing potential should not be routinely excluded from participation in clinical research. All NIH-supported biomedical and behavioral research involving human subjects is defined as clinical research. This policy applies to research subjects of all ages.

The inclusion of women and members of minority groups and their subpopulations must be addressed in developing a research design appropriate to the scientific objectives of the study. The Research Plan should describe the composition of the proposed study population in terms of sex/gender and racial/ethnic group, and provide a rationale for selection of such subjects. Such a plan should contain a description of the proposed outreach programs for recruiting women and minorities as participants. See http://grants.nih.gov/grants/funding/women_min/women_min.htm.

5.7 NIH POLICY ON INCLUSION OF CHILDREN

Research involving children (see definition of “[child](#)”) must comply with the NIH Policy and Guidelines on the Inclusion of Children in Clinical Research. Investigators should obtain full copies of the Policy and Guidelines from NIH staff, or from <http://grants.nih.gov/grants/funding/children/children.htm>.

NIH policy requires that children (i.e., individuals under the age of 21) must be included in all clinical research, conducted or supported by the NIH unless there are clear and compelling reasons not to include them. Therefore, proposals for clinical research must include a description of plans for including children. If children will be excluded from the research, the proposal must present an acceptable justification for the exclusion.

The involvement of children as subjects in research must be in compliance with all applicable subparts of [45 CFR part 46](#) (<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html>) as well as with other pertinent Federal laws and regulations.

IRBs have special review requirements to protect the well-being of children who participate in research. These requirements relate to risk, benefit, parental/guardian consent, and assent by children, and to research involving children who are wards of the state or of another institution. The local IRB approves research that satisfies the conditions set forth in the regulations.

5.8 NIH POLICY ON REPORTING RACE AND ETHNICITY DATA: SUBJECTS IN CLINICAL RESEARCH

The Office of Management and Budget (OMB) (http://www.whitehouse.gov/omb/fedreg_1997standards) defines minimum standards for maintaining, collecting and presenting data on race and ethnicity for all Federal reporting agencies (including NIH) in OMB Directive 15, http://www.whitehouse.gov/omb/fedreg_1997standards. The standards were revised in 1997 and include two ethnic categories (Hispanic or Latino and Not Hispanic or Latino) and five racial categories (American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, and White). Reports of data on race and ethnicity shall use these categories. The

categories in this classification are social-political constructs and should not be interpreted as being anthropological in nature. NIH is required to use these definitions to allow comparisons to other federal databases, especially the census and national health databases. The following definitions apply to the minimum standards for the ethnic and racial categories.

Ethnic Categories:

Hispanic or Latino: A person of Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish culture or origin, regardless of race. The term, "Spanish origin," can be used in addition to "Hispanic or Latino."

Not Hispanic or Latino

Racial Categories:

American Indian or Alaska Native: A person having origins in any of the original peoples of North, Central, or South America, and who maintains tribal affiliation or community attachment.

Asian: A person having origins in any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent including, for example, Cambodia, China, India, Japan, Korea, Malaysia, Pakistan, the Philippine Islands, Thailand, and Vietnam. (Note: Individuals from the Philippine Islands have been recorded as Pacific Islanders in previous data collection strategies.)

Black or African American: A person having origins in any of the black racial groups of Africa. Terms such as "Haitian" or "Negro" can be used in addition to "Black or African American."

Native Hawaiian or Other Pacific Islander: A person having origins in any of the original peoples of Hawaii, Guam, Samoa, or other Pacific Islands.

White: A person having origins in any of the original peoples of Europe, the Middle East, or North Africa.

Ethnic/Racial Subpopulations: In addition to OMB ethnic and racial categories, NIH uses the following definition for ethnic/racial subpopulations:

Subpopulations: Each ethnic/racial group contains subpopulations that are delimited by geographic origins, national origins, and/or cultural differences. It is recognized that there are different ways of defining and reporting racial and ethnic subpopulation data. The subpopulation to which an individual is assigned depends on self-reporting of specific origins and/or cultural heritage. Attention to subpopulations also applies to individuals who self identify with more than one race. These ethnic/racial combinations may have biomedical, behavioral, and/or social-cultural implications related to the scientific question under study.

Guidance on Collecting Race and Ethnicity Data from Human Subjects

When an investigator is planning to collect data on ethnicity and race, the categories identified above should be used. The collection of greater detail is encouraged, for example on ethnic/racial subpopulations. However, any collection that uses more detail must be designed in a way that data can be aggregated into these minimally required categories. Use self-report or self-identification to collect this information by asking two separate questions – one on ethnicity and one on race. Collect ethnicity information first followed by the question on race and provide subjects with the option to select more than one racial category.

See NIH Policy on [Inclusion of Women and Minorities](http://grants.nih.gov/grants/funding/women_min/women_min.htm) and http://grants.nih.gov/grants/funding/women_min/women_min.htm.

5.9 RESEARCH ON TRANSPLANTATION OF HUMAN FETAL TISSUE

In signing the proposal Cover Page, the Authorized Organizational Representative/Corporate Official of the offeror organization certifies that if research on the transplantation of human fetal tissue is conducted, the offeror organization will make available, for audit by the Secretary, DHHS, the physician statements and informed

consents required by section 498A (b)(2) and (c) of the Public Health Service Act, 42 U.S.C. 289g (b)(2) and (c), or ensure DHHS access to those records, if maintained by an entity other than the offeror organization.

5.10 RESEARCH USING HUMAN EMBRYONIC STEM CELLS

In signing the proposal Cover Page, the Authorized Organizational Representative/Corporate Official of the offeror organization certifies that if research using human embryonic stem cells (hESCs) is proposed, the offeror organization will identify hESCs to be used from the NIH Registry (<http://stemcells.nih.gov/research/registry/>), or, if a specific cell line cannot be referenced at the time of application, certify that one from the NIH Registry will be used, in accord with the NIH Guidelines on Human Stem Cell Research (<http://stemcells.nih.gov/policy/2009guidelines.htm>) . See <http://stemcells.nih.gov/index.asp> for additional information on stem cells, and <http://stemcells.nih.gov/policy/guidelines.asp> for Federal policy statements and guidelines on federally funded stem cell research.

5.11 CLINICALTRIALS.GOV REQUIREMENTS

In signing the proposal Cover Page, the Authorized Organizational Representative/Corporate Official of the offeror organization certifies that if the research includes an applicable clinical trial under Public Law 110-85, the offeror organization will be in compliance with the registration and reporting requirements of Public Law 110-85, if applicable (http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=110_cong_public_laws&docid=f:publ085.110.pdf). The law, enacted 09/27/2007, amends the Public Health Service Act to expand the scope of clinical trials that must be registered in ClinicalTrials.gov. It also increases the number of registration fields that must be submitted, requires certain results information to be included, and sets penalties for noncompliance.

The trials that must be registered are called “applicable clinical trials.” Under the statute these trials generally include: (1) Trials of Drugs and Biologics: Controlled, clinical investigations, other than Phase 1 investigations, of a product subject to FDA regulation; and (2) Trials of Devices: Controlled trials with health outcomes, other than small feasibility studies, and pediatric postmarket surveillance. NIH encourages registration of ALL trials whether required under the law or not.

Additional information can be found on the ClinicalTrials.gov Web site (http://grants.nih.gov/ClinicalTrials_fdaaa/).

Transcatheter cerclage mitral valve annuloplasty for secondary mitral regurgitation (NHLBI SBIR TT)

Fast-track proposals: Accepted

Number of anticipated awards: 1

Budget (total costs): Phase I: \$200,000 for 6 months; Phase II: The NHLBI will support Phase II budgets appropriate to the complexity and scope of this solicitation and within the guidelines of the SBIR program. These budget guidelines normally do not exceed \$1,500,000 for 2 years. Offerors proposing budgets in excess of this amount should contact the NHLBI Contracting Officer listed in the solicitation.

It is strongly suggested that proposals adhere to the above budget amounts and project periods. Proposals with budgets exceeding the above amounts and project periods may not be funded.

Summary

Secondary mitral valve regurgitation is a common contributor to heart failure, and is caused by annular expansion and papillary muscle traction. Secondary mitral valve regurgitation may be amenable to surgical annuloplasty, which reduces mitral valve annular size to enhance coaptation of the otherwise normal leaflets.

NHLBI intramural laboratories have developed a novel non-surgical catheter-based approach to annuloplasty called “cerclage annuloplasty.” Using enhanced image guidance, catheter tools traverse a trajectory including the coronary sinus, a basal septal perforator vein, a short transmyocardial pathway through the interventricular septum, and the right ventricular inflow tract. Once this pathway is established, circumferential tension is applied to reduce annular dimensions. Serendipitous features of cerclage annuloplasty include preservation of mitral annular deformation throughout the cardiac cycle, and reciprocal entrapment of the left ventricular outflow tract to enhance coaptation of the anterior mitral leaflet during systole.

The NHLBI has established the potential utility of cerclage annuloplasty in a porcine model of ischemic cardiomyopathy. To translate the project into humans will require development of commercial-grade interventional tools to make a clinical procedure simple and safe, including device and regulatory development, followed by early clinical testing. NHLBI has four patent applications filed related to cerclage annuloplasty.

A catheter-based annuloplasty like cerclage may have value as a primary therapy for secondary mitral regurgitation. Alternatively cerclage annuloplasty may have value as an adjunctive therapy combined, for example, with leaflet clip procedures. It may also have value in less-severe disease not justifying surgical morbidity, or to relieve symptoms accompanied by severe comorbidity precluding surgical therapy.

Relevant NIH Publications and Patent Applications

- Kim JH, Kocaturk O, Ozturk C, Faranesh AZ, Sonmez M, Sampath S, Saikus C, Kim AH, Raman VK, Derbyshire JA, Schenke WH, Wright VJ, Berry C, McVeigh ER, Lederman RJ, Journal of the American College of Cardiology. 2009;54(7):638-651, Pubmed ID 19660696, posted at <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3034128>.

- Device for protecting coronary arteries against compression during transcatheter mitral valve annuloplasty (“Transcatheter Coronary Sinus Mitral Valve Annuloplasty Procedure and Coronary Artery and Myocardial Protection Device”). JH Kim, RJ Lederman, O Kocaturk. Assignee: The United States of America. U.S. Provisional Patent Applications 60/858,716 and 60/932,611 filed November 14, 2006 and May 31, 2007 respectively (expired); International Patent Application PCT/US2007/023876 filed November 13, 2007 (expired), U.S. Patent Application 12/514,990 filed May 15, 2009, European Patent Application 07861997. NIH reference no. E-249-2006.
- Cerclage locking device and delivery system (“Tensioning Device and Methods of Use”). O Kocaturk. Assignee: The United States of America. U.S. Provisional Patent Application 61/157,267 filed March 4, 2009 (expired), International Patent Application PCT/US2010/026245 filed March 4, 2010 (expired), U.S. Patent Application 13/254,160 filed August 31, 2011. NIH reference no. E-048-2009.
- An expandable mesh target and capture device for transcatheter cerclage annuloplasty. (“Method and Devices for Transcatheter Cerclage Annuloplasty”). RJ Lederman, O Kocaturk. Assignee: The United States of America. U.S. Provisional Patent Application 61/383,061 filed September 15, 2010 (expired), International Patent Application PCT/US2011/51748 filed September 15, 2011. NIH reference no. E-108-2010.

NHLBI will share any unpublished patent applications with offerors willing to sign confidential disclosure agreements.

Technology Transfer

This is an SBIR TT (Technology Transfer) contract topic from the NHLBI. This is a new program whereby inventions from the NHLBI Division of Intramural Research are licensed to qualified small businesses with the intent that those businesses develop these inventions into commercial products that benefit the public. The contractor funded under this NHLBI SBIR contract topic shall work closely with the NHLBI inventor(s) of this technology, who will assist in pre-clinical experiments and will perform a clinical trial using offeror’s product. The NHLBI inventor(s) will provide assistance in a collaborative manner with catheter designs, procedure techniques, clinical considerations, and discussions during the entire award period. Between the time this contract topic is published and the time an offeror submits a contract proposal for this Topic, no contact will be allowed between the offeror and the NHLBI inventor. However, a pre-submission public briefing and/or webinar will be given by NHLBI staff to explain in greater detail the technical and licensing aspects of this program.

The awarded contractor will automatically be granted a royalty-free, non-exclusive license to use NIH-owned and patented background invention(s) only within the scope and term of the award. However, an SBIR offeror or SBIR contractor can apply for an exclusive or non-exclusive commercialization license to make, use, and sell products or services incorporating the NIH background invention(s). Offerors submitting an SBIR contract proposal in response to this solicitation are strongly encouraged to submit concurrently an application for a commercialization license to such background invention(s). Under the NHLBI SBIR TT program, the SBIR contract award process will be conducted in parallel with, but distinct from, the review of any applications for a commercialization license.

To apply for a commercialization license to develop the NIH invention(s), an SBIR offeror or SBIR contractor must submit a license application to the NIH Licensing and Patenting Manager: Michael Shmilovich, <mailto:shmilovm@mail.nih.gov> or (301) 435-5019. A license application and model license agreements are available at <http://www.ott.nih.gov/pdfs/LicApp.pdf> and http://www.ott.nih.gov/forms_model_agreements/forms_model_agreements.aspx#LAP. This license application provides NIH with information about the potential licensee, some of the terms desired, and the potential licensee's plans for development and/or commercialization of the invention. License applications will be treated in accordance with Federal patent licensing regulations as provided in 37 CFR Part 404. A further description of the NIH licensing process is available at http://www.ott.nih.gov/licensing_royalties/intra_techlic.aspx. NIH will notify an SBIR offeror who has submitted an application for an exclusive commercialization license if another application for an exclusive license to the background invention is received at any time before such a license is granted.

Any invention developed by the contractor during the course of the SBIR TT contract period of performance will be owned by the contractor subject to the terms of Section 8.5, Limited Rights Information and Data of the solicitation and the contractor must abide by the terms of the award for administering any subject inventions (including all invention reporting requirements), consistent with applicable laws, regulations, and NIH policies.

Specifications

Transcatheter cerclage annuloplasty is a new procedure requiring purpose-built devices. It uses devices and techniques typical of transcatheter arterial interventional procedures, such as catheter guides, subselective vascular instrumentation, target tissue traversal, and device snare-recovery. It is, however, a new procedure that requires an understanding of the functional anatomy of the heart including venous, myocardial, and conduction system.

The awardee will undertake clinical development of a system of devices to allow transcatheter cerclage annuloplasty to treat secondary mitral regurgitation due to mitral annular dilation. Several devices will be needed for serial procedural steps, and are likely to include:

1. A device or system to engage a target septal perforator coronary vein via the coronary sinus. One option would be a coronary sinus catheter with an outer balloon to pressurize the coronary veins, to be used along with a coaxial microcatheter selectively to engage the septal perforator vein.
2. A device or system positioned in the right ventricular outflow tract to serve as a target for septal traversal and to capture the traversal device without allowing for trabecular or subvalvar entrapment. One option would resemble a snare device, and should accommodate variable reentry sites. Both the coronary sinus and right ventricular elements probably should return through a common introducer sheath, for example through a single jugular, axillary, or femoral vein. The venous access system should be suitable for non-surgical access to the jugular, axillary, and/or femoral vein and therefore should be 10-12Fr or smaller if possible.
3. A device to traverse the myocardium between the target septal perforator vein and the right ventricular target and capture device. This has been accomplished using coronary guidewires. The myocardial traversal system should be small enough that inadvertent venous perforation would be well tolerated, and therefore ideally approximately 0.014"

before larger devices are introduced. The device should be visible to the operator using the selected image guidance modality. A successful traversal device must accommodate reliable and safe capture/ensnarement/retrieval, without mechanical disruption, once it has reentered the right heart.

4. A permanent cerclage tension or suture device. This includes a system to exchange the captured traversal device for the permanent tension device or suture. The device or suture must not erode through myocardium after deployment. The myocardial tension device or suture should distribute erosive radial forces and should probably be at least 1mm in width. Novel biocompatible materials/ solutions are invited, that are suitable for FDA Class III devices. The tension or suture device must have a mechanism to apply graded tension interactively under imaging guidance. A preclinical performance criterion is the ability to impart 800g linear cerclage tension force without causing angiographic obstruction of an entrapped coronary artery. A second preclinical performance criterion is the ability to reduce the septal-lateral dimension of a dilated mitral annulus by 20% in vivo. This tension should be reversible during the procedure, and should be fixed at the conclusion of the procedure. The tension fixation system should assure no circumferential displacement or loss of tension during application of fixation. The choice of a flexible versus rigid tension element or suture should be justified.
5. A device deployed along the tension device to protect entrapped coronary arteries against unintended compression during application of cerclage tension, and a mechanism to deploy it and to guard against inadvertent displacement.

Key user requirements include (1) Non-surgical procedure conduct. (2) A procedure that can be completed in less than approximately one hour after vascular access is obtained. Solutions are encouraged to minimize the number of procedural steps and reduce procedural complexity. For example, the myocardial traversal system could be combined with the tension delivery/exchange device. (3) Clear imaging/visual targets for skill-driven procedure steps such as myocardial tissue traversal. (4) Reversibility of tension delivery until the conclusion of the procedure to assure success and freedom from immediate complications. (5) Freedom from immediate complications including coronary artery compression, tricuspid valve regurgitation, and iatrogenic atrioventricular conduction block.

Concept drawings shall accompany proposals.

The use of marketed devices as procedural adjuncts is acceptable.

Pre-submission Meeting for Offerors

A pre-submission meeting will be conducted at the NHLBI offices (6701 Rockledge Dr., Rm 9112/9116, Bethesda, MD) on June 14th, 2012, from 2pm to 3pm EST. NHLBI staff will explain the objectives of the solicitation, describe the applicable NIH technology, and answer questions related to licensing and the acquisitions process. For offerors that cannot participate in person the event will be webcast at <https://webmeeting.nih.gov/cerclagerfp/>. NHLBI requests that participants register by June 7 via email at NHLBI_SBIR@mail.nih.gov and indicate whether they will attend in person or via the webcast. Participants can submit questions in advance of the

event at NHLBI_SBIR@mail.nih.gov or during the meeting. Answers to all questions will be available after the event at www.nhlbi.nih.gov/funding/sbir/funding/cerclagerfp.htm. Additional information about the event is available at www.nhlbi.nih.gov/funding/sbir/funding/cerclagerfp.htm.

Phase I Deliverables

Phase I deliverables include a mature system of devices that allow transcatheter cerclage annuloplasty in a large animal model, that satisfies all the above Specifications, and that is near a final design lock. The sponsoring NHLBI laboratory is prepared to teach the awardee about the procedure, and is willing to perform in vivo proof-of-principle experiments in a limited number of NHLBI swine experiments. Individual prototypes shall include solutions for the five procedure steps outlined in the preceding “Specifications” Section. Offerors shall include a timeline with milestones in order to produce the specific Phase I deliverables, in sequence, which include each of the following:

1. Concept prototype devices for initial review within 2 months of award. These may be preceded by refined concept drawings. A strategy for final concept selection shall be outlined clearly.
2. Prototypes for simulated use testing in an anatomic model, and for tissue testing if applicable.
3. Prototypes for simulated use in ex vivo tissue specimens such as pig hearts, within 4 months of award.
4. Prototypes for *non-survival* large animal testing, with attention to materials biocompatibility.
5. Report of pre-Investigational Device Exemption (IDE) interaction with the US Food and Drug Administration (FDA) to establish an initial plan for clinical device development. This plan shall include a comprehensive description of the Bill of Materials, Quality System, and plan for addressing clinical development issues raised in interactions with the FDA.

At the conclusion of Phase I, there shall be a complete system of prototype devices able to successfully and reliably complete cerclage annuloplasty procedure in a large animal model (such as swine) within a reasonable period of time (such as 30 minutes), as assessed by NIH operators. This shall be a complete procedure including myocardial traversal, coronary artery protection, reversibility of tension, and fixation of tension with a permanent implant that is near final clinical design lock. The result shall be durable as demonstrated in animal survival for at least 4 weeks.

Phase II Deliverables

Offerors are instructed to provide a clear development timeline that include design iterations and the milestones needed to produce the Phase II deliverables. These deliverables shall be at the level of final device development suitable for use in humans, and include:

1. Prototype devices for human cadaver testing. The applicant must obtain cadaver specimens as required.
2. Mature prototypes for *survival* large animal testing.
3. Final finished product for pre-clinical regulatory testing to support IDE application to the FDA. The awardee is expected to perform or obtain safety-related in vivo experiments and data to support the IDE application, including testing for mechanical fatigue and biocompatibility. The sponsoring NHLBI laboratory is willing to perform in vivo proof-of-principal experiments in swine and is willing to design the clinical protocol for the IDE.
4. An IDE for a First in Human clinical test of cerclage annuloplasty to be performed at NIH, to allow site initiation within 12 months of conclusion of Phase II.
5. A supply of devices (Final finished product) for the IDE clinical trial at NIH, to include at least 10 subjects.
6. The awardee shall be prepared to implement design and manufacturing changes required for safe completion of the proposed First in Human protocol.

Upon delivering Final Finished Product devices and an Investigational Device Exemption, the sponsoring NHLBI laboratory will perform the First in Human research protocol, including subject recruitment, selection, procedure conduct, endpoint assessment, and data capture without additional resources from the awardee. We anticipate that this protocol would be initiated within 12 months of conclusion of Phase II.