BROAD AGENCY ANNOUNCMENT

1. **REQUISITION OR OTHER PURCHASE AUTHORITY:** 15 U.S.C. 631, et seq., as amended		
2. **Solicitation Number:** BAA N44CM47014-11	3. **Issue Date:** December 18, 2014	4. **Set Aside:** [ ] No [X] Yes, See Part 1.2 on page 4
5. **Title**: FY 2015 SBIR Phase II Solicitation		
6. **ISSUED BY**: Office of Acquisitions National Cancer Institute National Institutes of Health 9609 Medical Center Drive Building 9609, Room 1E558 Rockville, Maryland 20850	7. **SUBMIT OFFERS TO**: See Part 6 Submission of Proposals	
8. Proposals for furnishing the supplies and/or services in THE SCHEDULE will be received at the place, and in the number of copies, specified in Part 6, "Submission of Proposals" before 3:00 PM EST on February 3, 2015. Offers must remain valid through September 30, 2015. All questions must be received by 12 NOON EST on January 16, 2014 to allow adequate time to prepare and issue responses prior to the receipt of proposals. Questions received after that time and date will not be answered. All questions must be submitted in writing to ncioasbir@mail.nih.gov. No inquiries submitted via E-mail to any other address will be answered.		
9. This solicitation requires delivery of proposals as specified in Part 6 of this solicitation. IF THE OFFEROR'S PROPOSAL IS NOT RECEIVED BY THE CONTRACTING OFFICE AT THE PLACE AND TIME SPECIFIED, THEN IT WILL BE CONSIDERED LATE AND HANDLED IN ACCORDANCE WITH HHSAR Clause 352.215-70, "Late Proposals and Revisions" LOCATED IN PART 3 OF THIS SOLICITATION.		
10. Offerors must be registered in the System for Award Management (SAM) at http://www.sam.gov prior to award of a contract.		
11. FOR INFORMATION E-MAIL: ncioasbir@mail.nih.gov. No inquiries submitted via E-mail to any other address will be answered. NO TELEPHONE CALLS WILL BE ACCEPTED.		
Solicitation of the National Cancer Institute SMALL BUSINESS INNOVATION RESEARCH (SBIR) PHASE II CONTRACT PROPOSALS	Rosemary Hamill Contracting Officer Office of Acquisitions National Cancer Institute	

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1 PROGRAM DESCRIPTION

1.1 OBJECTIVES

This solicitation is for Phase II contract proposals only. Included are instructions for Offerors to prepare Phase II 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 a research topic listed in PART 8 of this solicitation. 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 Research/Research & Development (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 basic design of the NIH/CDC SBIR program is in accordance with the Small Business Administration (SBA) SBIR Program Policy Directive (February 24, 2014). This SBIR contract solicitation strives to encourage scientific and technical innovation in areas specifically identified by the NIH. 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 NIH and the private sector.

1.2 THE SBIR PROGRAM CONSISTS OF THREE SEPARATE PHASES:

Phase I: Feasibility

The objective of Phase I is to determine the scientific of 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 I awards normally may not exceed $150,000 for direct costs, indirect costs, and profit (fixed fee) for a period not to exceed 6 months.

Phase II: Full R/R&D Effort

The objective of Phase II is to continue 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 awards normally may not exceed $1,000,000 for direct costs, indirect costs, and profit (fixed fee) for a period normally not to exceed two years.

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 Phase 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 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. 3303(b). The NIH 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 Executive Order 13329, encouraging innovation in manufacturing-related research and development, NIH seeks, through the SBIR program, biomedical research related to advanced processing, manufacturing process, equipment and systems; or manufacturing workforce skills and protection. This solicitation includes some topic areas that are considered relevant to manufacturing-related R&D. Additional information will be posted on the NIH Small Business Research Funding Opportunities Website and in the NIH Guide for Grants and Contracts as it becomes available.

1.3 SBIR PROGRAM ELIGIBILITY

Only United States owned small businesses are eligible to participate in the SBIR program. An SBIR awardee shall meet the following criteria at the time of Phase I and II awards:

i. Organized for profit, with a place of business located in the United States;

ii. More than 50 percent owned and controlled by one or more individuals who are citizens of, or permanent resident aliens in, the United States, or by another for-profit business concern that is more than 50% owned and controlled by one or more individuals who are citizens of, or permanent resident aliens in, the United States; and

iii. No more than 500 employees, including affiliates.

iv. For awards from agencies using the authority under 15 U.S.C. 638(dd)(1), an awardee may be owned and controlled by more than one VC, hedge fund, or private equity firm so long as no one such firm owns a majority of the stock.

v. Phase I awardees with multiple prior awards shall meet the benchmark requirements for progress toward commercialization.

See the Eligibility Guide provided at http://sbir.gov/sites/default/files/elig_size_compliance_guide.pdf

1.4 AGENCY CONTACT

For general information on the SBIR Program solicitation please email:
Rosemary Hamill
Contracting Officer Office
of Acquisitions National
Cancer Institute
9609 Medical Center Drive
Building 9609, Room 1E560
Rockville, Maryland 20850
(240) 276-5405
ncioasbir@mail.nih.gov

1.5 DEFINITIONS

1.5.1 General Definitions

The following definitions apply for the purposes of this solicitation. Additional applicable definitions can be found in the SBA Policy Directive (http://sbir.gov/sites/default/files/sbir_pd_with_1-8-14_amendments_2-24-14.pdf) and the Federal Acquisition Regulation (FAR) (https://acquisition.gov/far/current/html/Subpart%202_1.html):

(a) **Consultant**. An individual who provides professional advice or services for a fee, but not as an employee of the engaging party. To prevent apparent or actual conflicts of interest, **grantees** and consultants shall establish written guidelines indicating the conditions of payment of consulting fees. Consultants may also include firms that provide paid professional advice or services.
(b) **Contract.** An award instrument that establishes a mutually binding legal relationship obligating the seller to furnish the supplies or services and the buyer to pay for them.
(c) **Fraud, Waste, and Abuse**

1. Fraud includes any false representation about a material fact or any intentional deception designed to deprive the United States unlawfully of something of value or to secure from the United States a benefit, privilege, allowance, or consideration to which an individual or business is not entitled.
2. Waste includes extravagant, careless or needless expenditure of Government funds, or the consumption of Government Property, that results from deficient practices, systems, controls, or decisions.
3. Abuse includes any intentional or improper use of Government resources, such as misuse of rank, position, authority, or resources.

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

(e) **Proprietary Information**. Proprietary information is information that the Offeror provides which constitutes a trade secret, proprietary commercial or financial information, confidential personal information, or data affecting the national security.

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

1. A systematic, intensive study directed toward greater knowledge or understanding of the subject studied;
2. A systematic study directed specifically toward applying new knowledge to meet a recognized need; or
3. 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.

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

(h) **Service-Disabled Veteran-Owned Small Business Concern**. A small business concern not less than 51 percent of which is owned by one or more service-disabled veterans or, in the case of any publically owned business, not less than 51 percent of the stock of which is owned by one or more service-disabled veterans; and the management and daily business operations of which are controlled by one or more service-disabled veterans or, in the case of a service-disabled veteran with permanent and severe disability, the spouse or permanent caregiver of such veteran. Status as a Service-Disabled Veteran-Owned Small Business Concern is determined in accordance with 13 CFR Parts 125.8 through 125.13; also see 19.307.

(i) **Small Business Concern (SBC).** A concern that meets the requirements set forth in 13 C.F.R. §121.702 (available at http://ecfr.gpoaccess.gov/cgi/t/text/text-idx?c=ecfr;sid=03878acee7c064a02cac0d870e00ef43;rgn=div8;view=text;node=13%3A1.0.1.1.17.1.273.45;idno=13;cc=ecfr).

(j) **SBIR Technical Data**. All data generated during the performance of an SBIR award.

(k) **SBIR Technical Data Rights.** The rights an SBIR awardee 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.

1.5.2 R&D Related Definitions

(a) **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.

(b) **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 shall be included in NIH conducted or supported clinical research unless there are scientific or ethical reasons not to include them.

HHS Regulations (45 CFR part 46, Subpart D, Sec.401-409) 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.

(c) **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.

(d) **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 (if completed)* 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.

(e) **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 shall 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 shall 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.

(f) **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*.

(g) **Gender**. Refers to the classification of research subjects in 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 specification.

(h) **Human Subjects**. The HHS regulations "Protection of Human Subjects" 45 CFR part 46, 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

(i) **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 system.

(j) **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)).

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

(l) **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.)

(m) **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 exisϴng manufacturing processes that deliver substanϴal productivity, quality, or environmental benefits.
   - development of new manufacturing processes, including new materials, coaϴngs, 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 addiϴve and subtracϴve 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 informaϴon technologies that improve the quality and productivity of manufacturing cells, lines, systems, and facilities.
   - innovaϴon in extended enterprise funcϴons criϴcal to manufacturing, such as quality systems, resource management, supply change integration, and distribution, scheduling and tracking.
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.
   - technologies that enable integrated and collaboraϴve 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.

(n) **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 shall 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)).

(o) **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 HHS human subjects regulations (45 CFR 46) if:

- the specimens and/or informaϴon/data are not obtained from an interacϴon/ intervenϴon with the subject specifically for the research; and
- the invesϴgator(s) cannot readily ascertain the idenϴty 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.)

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

1. A systematic, intensive study directed toward greater knowledge or understanding of the subject studied;
2. A systematic study directed specifically toward applying new knowledge to meet a recognized need; or
3. 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.

(q) **Research Institution.** Any organization located in the United States that is:

- A university.
- A nonprofit institution as defined in Section 4(5) of the Stevenson-Wydler Technology Innovation Act of 1980.

(r) **Research Involving Animal Subjects**

All research involving live, vertebrate animals shall be conducted in accordance with the Public Health Service Policy on Humane Care and Use of Laboratory Animals (PHS Policy).

In addition, the research involving live vertebrate animals shall be conducted in accordance with the description set forth in the Vertebrate Animal Section (VAS) of the contractor's technical proposal, as modified in the Final Proposal Revision (FPR), which is incorporated by reference.

(s) **Research Involving Human Subjects**

All research involving human subjects, to include use of human biological specimens and human data, shall comply with the applicable federal and state laws and agency policy/guidelines for human subject protection.

Exemptions.

The six categories of research exempt from the HHS human subject regulations are:

(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.

(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.

(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.

(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.

(5) Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which 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.

(6) Taste and food quality evaluation and consumer acceptance studies,

(i) if wholesome foods without additives are consumed or

a. (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.

(t) **Research Involving Recombinant DNA Molecules.** Any recipient performing research involving recombinant DNA molecules and/or organisms and viruses containing recombinant DNA molecules shall comply with the National Institutes of Health Guidelines for Research Involving Recombinant DNA Molecules, dated March 2013 as amended. The guidelines can be found at: http://oba.od.nih.gov/rdna/nih_guidelines_oba.html. Recombinant DNA is defined as (i) molecules that are constructed outside living cells by joining natural or synthetic DNA segments to DNA molecules that can replicate in living cells or (ii) molecules that result from the replication of those described in (i) above. A listing of the cited regulations is available at: http://www.acq.osd.mil/osbp/sbir/sb/resources/deskreference/quickref/researchrecombinantdna.shtml

(u) **SIGNIFICANT DIFFERENCE**. For the 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 difference between the effects in two groups achieves statistical difference. Statistical difference 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.

1.6 Reporting Matters Involving Fraud, Waste, and Abuse

Anyone who becomes aware of the existence or apparent existence of fraud, waste and abuse in NIH funded programs is encouraged to report such matters to the HHS Inspector General's Office in writing or on the Inspector General's Hotline. The toll free number is **1-800-HHS-TIPS (1-800-447-8477).** All telephone calls will be handled confidentially. The website to file a complaint on-line is: http://oig.hhs.gov/fraud/hotline/ and the mailing address is:

US Department of Health and Human Services
Office of Inspector General
ATTN: OIG HOTLINE OPERATIONS
P.O. Box 23489
Washington, D.C. 20026

2 CERTIFICATIONS

2.1 Certification for Offerors that are Majority-Owned by Multiple Capital Operating Companies, Hedge Fund or Private Equity Firms

Each Offeror that is majority-owned by multiple venture capital operating companies, hedge funds, or private equity firms shall register with SBA in the Company Registry Database at www.SBIR.gov and submit a certification with its proposal. See PART 9 for certification document.

2.2 SBIR Funding Agreement Certification

Each Offeror shall register in SBA's Company Registry Database and submit a pdf document of the registration with its proposal. See PART 9 for certification document.

2.3 Human Subjects Certifications/Assurances/Clearances- If Applicable.

a. Certificate of Completion for Protection of Human Research Participants Education - required prior to award.
b. Federalwide Assurance (FWA) - required to prior to research involving human subjects.
c. Institutional Review Board (IRB) registration - required prior to research with human subjects.

2.4 Animal Assurance and Inter-Institutional Assurance – If Applicable.

a. Animal Welfare Assurance – required prior to award.
b. Inter-Institutional Assurance – required prior to award. An Inter-Institutional Assurance is required when animal work is being performed by a subcontractor.
c. Institutional Animal Care and Use Committee (IACUC) approval – required prior to award.

2.5 SBIR Funding Agreement Certification – Life Cycle Certification

Each offeror is required to certify their eligibility as a Small Business prior to receipt of final payment for the Phase II portion of the contract. Therefore, the Contractor shall certify their eligibility as a small business for the research and development purposes under the SBIR program in their final invoice submission under the contract. The SBIR Funding Agreement form is included as an attachment in PART 9.

3 PROPOSAL PREPERATION INSTRUCTIONS AND REQUIREMENTS

3.1 Introduction

3.1.1 General Information

3.1.1.1 Definitions. As used in this provision-

"Discussions" are negotiations that occur after establishment of the competitive range that may, at the Contracting Officer's discretion, result in the Offeror being allowed to revise its proposal.

"In writing", "writing", or "written" means any worded or numbered expression that can be read, reproduced, and later communicated, and includes electronically transmitted and stored information.

"Proposal modification" is a change made to a proposal before the solicitation's closing date and time, or made in response to an amendment, or made to correct a mistake at any time before award.

"Proposal revision" is a change to a proposal made after the solicitation closing date, at the request of or as allowed by a Contracting Officer as the result of negotiations.

"Time," if stated as a number of days, is calculated using calendar days, unless otherwise specified, and will include Saturdays, Sundays, and legal holidays. However, if the last day falls on a Saturday, Sunday, or legal

holiday, then the period shall include the next working day.

3.1.1.2 *Amendments to solicitations. If this solicitation is amended, all terms and conditions that are not amended remain unchanged.*

3.1.1.3 *Submission, modification, revision, and withdrawal of proposals.*

Unless other methods (e.g., electronic commerce or facsimile) are permitted in the solicitation, proposals and modifications to proposals shall be submitted in paper media in sealed envelopes or packages (i) addressed to the office specified in the solicitation, and (ii) showing the time and date specified for receipt, the solicitation number, and the name and address of the Offeror. Offerors using commercial carriers should ensure that the proposal is marked on the outermost wrapper with the information as specified in PART 6.

1. *Offerors are responsible for submitting proposals, and any modifications or revisions, so as to reach the Government office designated in the solicitation by the time specified in the solicitation. The original hardcopy of the proposal will be considered the official document of receipt and will be time stamped upon receipt.*

   (A) *Any proposal, modification, or revision received at the Government office designated in the solicitation after the exact time specified for receipt of offers is "late" and will not be considered unless it is received before award is made, the Contracting Officer determines that accepting the late offer would not unduly delay the acquisition; 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.*

   (B) However, a late modification of an otherwise successful proposal that makes its terms more favorable to the Government will be considered at any time it is received and may be accepted.

2. *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. 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.*

3. *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.*

4. *Proposals may be withdrawn by written notice received at any time before award. Proposals may be withdrawn in person by an Offeror or an authorized representative, if the identity of the person requesting withdrawal is established and the person signs a receipt for the proposal before award.*

5. *Offerors shall submit proposals in response to this solicitation in English and in U.S. dollars. .*

6. *Offerors may submit modifications to their proposals at any time before the solicitation closing date and time, and may submit modifications in response to an amendment, or to correct a mistake at any time before award.*

7. *Offerors may submit revised proposals only if requested or allowed by the Contracting Officer.*

3.1.1.4 *Proposals may be withdrawn at any time before award. Withdrawals are effective upon receipt of notice by the Contracting Officer.*

3.1.1.5 *Offer expiration date. Proposals in response to this solicitation will be valid for the number of days specified on the solicitation cover sheet (unless a different period is proposed by the Offeror).*

A. *Restriction on disclosure and use of data.*
The proposal submitted in response to this request may contain data (trade secrets; business data (e.g., commercial information, financial information, cost and pricing data); and technical data) which the Offeror, including its prospective subcontractor(s), does not want used or disclosed for any purpose other than for evaluation of the proposal. The use and disclosure of any data may be so restricted; provided, that the Government determines that the data is not required to be disclosed under the Freedom of Information Act, 5 U.S.C. 552, as amended, and the Offeror marks the cover sheet of the proposal with the following statements, specifying the particular portions of the proposal which are to be restricted:

"Unless disclosure is required by the Freedom of Information Act, 5 U.S.C. 552, as amended, (the Act) as determined by Freedom of Information (FOI) officials of the Department of Health and Human Services (HHS), data contained in the portions of this proposal which the Offeror has specifically identified by page number, paragraph, etc. as containing restricted information shall not be used or disclosed except for evaluation purposes. The Offeror acknowledges that HHS may not be able to withhold a record (e.g. data, document, etc.) nor deny access to a record requested pursuant to the Act and that the HHS's FOI officials shall make that determination. The Offeror hereby agrees that the Government is not liable for disclosure if HHS has determined that disclosure is required by the Act. If a contract is awarded to the Offeror as a result of, or in connection with, the submission of this proposal, the Government shall have right to use or disclose the data to the extent provided in the contract. Proposals not resulting in a contract remain subject to the Act. The Offeror also agrees that the Government is not liable for disclosure or use of unmarked data and may use or disclose the data for any purpose, including the release of the information pursuant to requests under the Act. The data subject to this restriction are contained
in pages (insert page numbers, paragraph designations, etc. or other identification)."

B. *In addition, the Offeror shall mark each page of data it wishes to restrict with the following statement:*

"Use or disclosure of data contained on this page is subject to the restriction on the cover sheet of this proposal or quotation."

3.1.1.6 *Offerors are cautioned that proposals submitted with restrictive statements or statements differing in substance from those cited above may not be considered for award. The Government reserves the right to reject any proposal submitted with a nonconforming statement(s).*

3.1.1.7 *Contract Award*
The Government intends to award a contract or contracts resulting from this solicitation to the responsible Offeror(s) whose proposal(s) represents the best value after evaluation in accordance with the factors and

subfactors in the solicitation (See PART 4).

1. The Government intends to evaluate proposals and award a contract without discussions with Offerors (except clarifications as described in FAR 15.306(a)). Therefore, the Offeror's initial proposal should contain the Offeror's best terms from a cost or price and technical standpoint. The Government reserves the right to conduct discussions if the Contracting Officer later determines them to be necessary. If the Contracting Officer determines that the number of proposals that would otherwise be in the order of merit ranking exceeds the number at which an efficient competition can be conducted, the Contracting Officer may limit the number of proposals to the greatest number that will permit an efficient competition among the most highly rated proposals.

2. The Government reserves the right to make multiple awards if, after considering the additional administrative costs, it is in the Government's best interest to do so.

3. Exchanges with Offerors after receipt of a proposal do not constitute a rejection or counteroffer by the Government.

4. The Government may determine that a proposal is unacceptable if the prices proposed are materially unbalanced between line items or sub line items. Unbalanced pricing exists when, despite an acceptable total evaluated price, the price of one or more contract line items is significantly overstated or understated as indicated by the application of cost or price analysis techniques. A proposal may be rejected if the Contracting Officer determines that the lack of balance poses an unacceptable risk to the Government.

5. The Government will perform a cost realism analysis and the cost realism will be considered by the source selection authority in evaluating performance or schedule risk.

3.1.2 NAICS CODE AND SIZE STANDARD

Note: The following information is to be used by the Offeror in preparing its Representations and Certifications (See PART 9 of this RFP); specifically in completing the provision entitled, SMALL BUSINESS PROGRAM REPRESENTATION, FAR Clause 52.219-1.

(a) The North American Industry Classification System (NAICS) code for this acquisition is 541711.
(b) The small business size standard is 500 employees.

***3.1.3* TYPE OF CONTRACT AND NUMBER OF AWARDS**

(a) It is anticipated that multiple awards will be made from this solicitation as specified in Part 8 per SBIR RESEARCH TOPICS and that the awards will be made on/about September 2015.

(b) It is anticipated that the award(s) from this solicitation will be a fully funded, Cost-Reimbursement type Completion contract with a Period of Performance of twenty-four months.

(c) FAR 16.301-3 limits use of any contract type, other than firm-fixed price, to a contractor whose accounting system is adequate for determining costs applicable to the contract. To be considered for an award under this solicitation, the Offeror is required to certify, in its Business Proposal, the adequacy of its accounting system. See the paragraph entitled, Adequate Accounting System in PART 3.7 Business Proposal Instructions in this solicitation for additional information about this certification.

3.1.4 COMMITMENT OF PUBLIC FUNDS

The Contracting Officer is the only individual who can legally commit the Government to the expenditure of public

funds in connection with the proposed procurement. Any other commitment, either explicit or implied, is invalid.

3.1.5 COMMUNICATIONS PRIOR TO CONTRACT AWARD

Offerors shall direct all communications to the attention of the Contract Specialist and Contracting Officer cited on the face page of this SOLICITATION. Communications with other officials may compromise the competitiveness of this acquisition and result in cancellation of the requirement.

3.1.6 RELEASE OF INFORMATION

Contract selection and award information will be disclosed to Offerors in accordance with regulations applicable to negotiated acquisition. Prompt written notice will be given to unsuccessful Offerors as they are eliminated from the competition, and to all Offerors following award.

3.1.7 PREPARATION COSTS

The Government shall not pay for the preparation and submission of a proposal.

3.1.8 SERVICE OF PROTEST (SEPTEMBER 2006) - FAR 52.233-2

(a) Protests, as defined in section 33.101 of the Federal Acquisition Regulation, that are filed directly with an agency, and copies of any protests that are filed with the Government Accountability Office (GAO), shall be served on the Contracting Officer (addressed as follows) by obtaining written and dated acknowledgment of receipt from:

Contracting Officer Office
of Acquisitions National
Cancer Institute
9609 Medical Center Drive
Building 9609, Room 1E560
Rockville, Maryland 20850

(b) The copy of any protest shall be received in the office designated above within one day of filing a protest with the GAO.

(End of Provision)

3.1.9 Contract Type and General Clauses

It is contemplated that a cost-reimbursement completion type contract will be awarded. Any resultant contract shall include the clauses applicable to the selected Offeror's organization and type of contract awarded as required by Public Law, Executive Order, or acquisition regulations in effect at the time of execution of the proposed contract.

3.1.10 Binding and Packaging of Proposal

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

3.1.11 Separation of Technical and Business Proposals

The proposal shall be prepared in two parts: a "Technical Proposal" and a "Business Proposal." Each of the parts shall be separate and complete in itself so that evaluation of one may be accomplished independently of, and concurrently with, evaluation of the other. The technical proposal shall include direct cost and resources information, such as labor-hours and categories and applicable rates, materials, subcontracts, travel, etc., and associated costs so that the Offeror's understanding of the project may be evaluated (See **PART 9**, Attachment entitled, TECHNICAL PROPOSAL COST SUMMARY.) However, the technical proposal should not include pricing data relating to individual salary information, indirect cost rates or amounts, fee amounts (if any), and total costs. The technical proposal should disclose the Offeror’s technical approach in as much detail as possible, including, but not

limited to, the requirements of the technical proposal instructions. See 3.6 Technical Proposal and 3.7 Business Proposal.

3.1.12 Evaluation of Proposals

The Government will evaluate proposals in accordance with the factors set forth in PART 4-Method of Selection and Evaluation Criteria of this RFP.

3.1.13 Potential Award Without Discussions

The Government reserves the right to award a contract without discussions if the Contracting Officer determines that the initial prices are fair and reasonable and that discussions are not necessary.

3.1.14 Use of the Metric System of Measurement

It is the policy of the Department of Health and Human Services to support the Federal transition to the metric system and to use the metric system of measurement in all procurements, grants, and other business related activities unless such use is impracticable or is likely to cause significant inefficiencies. The Offeror is encouraged to prepare their proposal using either "Hard Metric," "Soft Metric," or "Dual Systems" of measurement. The following definitions are provided for the Offeror's information:

Hard Metric - The replacement of a standard inch-pound size with an accepted metric size for a particular purpose. An example of size substitution might be: selling or packaging liquids by the liter instead of by the pint or quart (as for soft drinks), or instead of by the gallon (as for gasoline).

Soft Metric - The result of a mathematical conversion of inch-pound measurements to metric equivalents for a particular purpose. The physical characteristics are not changed.

Dual Systems - The use of both inch-pound and metric systems. For example, an item is designed, produced, and described in inch-pound values with soft metric values also shown for information or comparison purposes.

3.1.15 Privacy Act – Treatment of Proposal Information

The Privacy Act of 1974 (P.L. 93-579) requires that a Federal agency advise each individual whom it asks to supply information, the authority which authorizes the solicitation, whether disclosure is voluntary or mandatory, the principal purpose or purposes for which the information is intended to be used, the uses outside the agency which may be made of the information, and the effects on the individual, if any, of not providing all or any part of the requested information.

The NIH is requesting the information called for in this SOLICITATION pursuant to the authority provided by Sec. 301(a)(7) of the Public Health Service Act, as amended, and P.L. 92-218, as amended.

Providing the information requested is entirely voluntary. The collection of this information is for the purpose of conducting an accurate, fair, and adequate review prior to a discussion as to whether to award a contract.

Failure to provide any or all of the requested information may result in a less than adequate review.

In addition, the Privacy Act of 1974 (P.L. 93-579, Section 7) requires that the following information be provided when individuals are requested to disclose their social security number.

Provision of the social security number is voluntary. Social security numbers are requested for the purpose of accurate and efficient identification, referral, review and management of NIH contracting programs. Authority for requesting this information is provided by Section 301 and Title IV of the PHS Act, as amended.

The information provided by the Offeror may be routinely disclosed for the following purposes:

- to the cognizant audit agency and the Government Accountability Office for auditing.
- to the Department of Justice as required for litigation.
- to respond to congressional inquiries.
- to qualified experts, not within the definition of Department employees, for opinions as a part of the review process.

3.1.16 Institutional Responsibility Regarding Investigator Conflicts of Interest

45 CFR Part 94 promotes objectivity in research by establishing standards to ensure there is no reasonable expectation that the design, conduct, or reporting of research to be performed under NIH contracts will be biased by any Investigator financial conflicts of interest. The Institution shall comply with all requirements of 45 CFR Part 94 at: http://www.ecfr.gov/cgi-bin/text-idx?c=ecfr&SID=0af84ca649a74846f102aaf664da1623&rgn=div5&view=text&node=45:1.0.1.1.51&idno=45.

3.1.17 Solicitation Provisions Incorporated by Reference, FAR 52.252-1 (February 1998)

This Solicitation incorporates one or more solicitation provisions by reference, with the same force and effect as if they were given in full text. Upon request, the Contracting Officer will make their full text available. The Offeror is cautioned that the listed provisions may include blocks that shall be completed by the Offeror and submitted with its quotation or offer. In lieu of submitting the full text provisions, the Offeror may identify the provision by paragraph identifier and provide the appropriate information with its quotation or offer. Also, the full text of a solicitation provision may be accessed electronically at this address: http://www.acquisition.gov/far/index.html.

FEDERAL ACQUISITION REGULATION (48 CFR CHAPTER 1):

a. Data Universal Numbering System Number, FAR Provision 52.204-6 (July 2013).

b. Order of Precedence-Uniform Contract Format, FAR Clause 52.215-8, (October 1997).

3.2 Proposal Limitations

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, letters from collaborators and consultants, and the Offeror's Phase I Final Report.

3.3 Proposal Cover Sheet

Use Attachment 3 SBIR Proposal Cover Sheet found in PART 9 of this Solicitation.

Every Offeror is required to provide a copy of its registration information printed from the Company Registry unless the information can be transmitted automatically to the NCI. Every Offeror shall also include at least the following information on the first page of proposals:

A. Agency and Solicitation number.

B. Topic Number or Letter.

C. Subtopic Number or Letter.

D. Topic Area.

E. Project Title.

F. Name and complete address of firm.

G. Disclose permission (by statement of checkbox), such as follows, shall be included at the discretion of the funding agency:

"Will the Offeror permit the Government to disclose the Offeror's name, address, and telephone number of the corporate official of the Offeror's concern, if the Offeror's proposal does not result in award, to appropriate local and state-level economic development organizations that may be interested in contacting the Offeror for further information? Yes ____No _____"

H. Signature of a company official of the proposing SBC and that individual's typed name, title, address, telephone number, and date of signature.

The proposal shall be signed by an official authorized to bind the Offeror's organization and shall stipulate that it is predicated upon all the terms and conditions of this RFP.

I. Signature of Principal Investigator or Project Manager within the proposing SBC and that individual's typed name, title, address, telephone number, email address and date of signature.

J. Legend for proprietary information as described in Part 5, Considerations. It may also be noted by asterisks in the margins on proposal pages.

3.4 DATA COLLECTION REQUIREMENT

Each offeror is required to provide financial disclosure information in the SBA database (www.SBIR.gov). The following are examples of the data to be entered into the database:

A. Any business concern or subsidiary established for the commercial application of a product or service for which an SBIR award is made.

B. Revenue from the sale of new products or services resulting from the research conducted under each Phase II award;

C. Additional investment from any source, other than Phase I or Phase II awards, to further the research and development conducted under each Phase II award.

D. Update the information in the database for any prior Phase II award received by the SBC. The SBC may apportion sales or additional investment information relating to more than one Phase II award among those awards, if it notes the apportionment for each award.

NOTE: Each Phase II awardee is required to update the appropriate information on the award in the database upon completion of the last deliverable under the funding agreement and is requested to voluntarily update the information in the database annually thereafter for a minimum period of 5 years.

3.5 ABSTRACT SUMMARY

Use Attachment 5 Abstract of Research Plan found in PART 9 of this Solicitation.

Offerors shall provide a one-page project summary of the proposed R&D including at least the following:

1. Name and Address of SBC.
2. Name and Title of principal investigator or project manager
3. Agency name, solicitation number, solicitation topic, and subtopic.
4. Title of project.
5. Technical abstract limited to two hundred words.
6. Summary of the anticipated results and implications of the approach and the potential commercial applications of the research.

3.6 TECHNICAL PROPOSAL

A detailed work plan shall be submitted indicating how each aspect of the statement of work is to be accomplished. The Offeror's technical approach should be in as much detail as the Offeror consider necessary to fully explain the Offeror's proposed technical approach or method. The technical proposal should reflect a clear understanding of the nature of the work being undertaken. The technical proposal shall include information on how the project is to be organized, staffed, and managed. Information should be provided which will demonstrate the Offerors understanding and management of important events or tasks.

Note to Offerors: Beginning May 25, 2008, the Offeror shall include the applicable PubMed Central (PMC) or NIH Manuscript Submission reference number when citing publications that arise from its NIH funded research.

3.6.1 Technical Proposal Composition

3.6.1.1 Technical Proposal Cover Sheet

Use Attachment 3, SBIR Proposal Cover Sheet found in PART 9 of this Solicitation.

3.6.1.2 Table of Contents

3.6.1.3 Abstract of Research Plan

Use Attachment 5, Abstract of Research Plan found in PART 9 of this solicitation. 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.

3.6.1.4 Achieved Results of Phase I Effort

In addition to including a copy of the Offeror's SBIR Phase I Final Report, briefly discuss and summarize the results of the Offeror's Phase I effort so the reviewers can assess the achievements of the Offeror's Phase I contract.

3.6.1.5 Technical Discussions

3.6.1.5.1 Research Plan

Detailed Approach and Methodology - provide an explicitly detailed description of the Phase II approach. This section should be the major portion of the proposal and shall clearly show advancement in the project appropriate for Phase II. Indicate not only what is planned, but also show how and where the work will be carried out. List all Technical Objectives and 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; and (3) describe end products and deliverables including progress reports not otherwise described in PART 5.2 of this solicitation. Offerors using Human Subjects or Vertebrate Animals in their research should refer to the specific instructions provided in the solicitation.

3.6.1.5.2 Personnel

List by name, title, department, and organization, the extent of commitment to this Phase II effort, as well as the experience and qualifications of each personnel who will be assigned for direct work on this program. Information is required which will show the composition of the task or work group, its general qualifications, and recent experience with similar equipment or programs. Special mention shall be made of direct technical supervisors and key technical personnel, and the approximate percentage of the total time each will be available for this program. **OFFERORS ARE REQUIRED TO ASSURE THAT THE PRINCIPAL INVESTIGATOR, AND ALL OTHER PERSONNEL PROPOSED, SHALL NOT BE COMMITTED ON FEDERALGRANTS AND CONTRACTS FOR MORE THAN A TOTAL OF 100% OF THEIR TIME. IF THE SITUATION ARISES WHERE IT IS DETERMINED THAT A PROPOSED EMPLOYEE IS COMMITTED FOR MORE THAN 100% OF HIS OR HER TIME, THE GOVERNMENT WILL REQUIRE ACTION ON THE PART OF THE OFFEROR TO CORRECT THE TIME COMMITMENT.** Salaries of all personnel shall adhere to the Salary Rate Limitation as stated in PART 3.7.4, section 2.a.8.

i. Single Principal Investigator/Project Director

List the name of the Principal Investigator/Project Director responsible for overall implementation of the contract and key contact for technical aspects of the project. In the event that there are co-investigators proposed, identify the Principal Investigator/Project Director who will be responsible for the overall implementation of any awarded contract. Discuss the qualifications, experience, and accomplishments of the Principal Investigator/Project Director. State the estimated time to be spent on the project, his/her proposed duties, and the areas or phases for which he/she will be responsible.

i. Multiple Principal Investigators

The NIH now provides Offerors the opportunity to propose a multiple Principal Investigator (PI) model on research and development contracts. The multiple PI model is intended to supplement, and not replace, the traditional single PI model. The NIH chose this RFP as a candidate for the multiple PI model. Ultimately, the decision to submit a proposal using the multiple PI versus single PI is the decision of the investigators and their institutions. The decision should be consistent with and justified by the scientific goals of the project.

It is essential that organizations consider all aspects of this approach before submitting a proposal. While there are some projects that clearly are appropriate for the multiple PI model, the "fit" of other projects may not be so clear. Offerors should base the selection of either the single PI or multiple PI option on the research proposed, to ensure optimal facilitation of the science. Projects suitable for the multiple PI model could include as few as two PIs who are jointly responsible for the scientific and technical direction of the project. The multiple PI option is based on the proposed project, not on the number of performance sites or the number of participating institutions.

Multiple PIs under research contracts shall use the Subcontract Model. In this approach, Offerors submit a single proposal, and a single award is made to the prime contractor. The prime contractor, when appropriate, will award subcontracts to fund the components of the project at the other institutions. The relationship between the contractor and subcontractors shall be designed to support all components of the project.

To facilitate communication with the NIH, the Offeror shall designate a Contact PI at the time of proposal submission. The Contact PI shall be employed at the prime contractor's organization. The designation of the Contact PI may rotate on an annual basis. However, this rotation is restricted to PIs located at the prime contractor's organization. The Contact PI is responsible for: relaying

communications between all of the PIs and the NIH, and coordinating progress reports for the project. Being named Contact PI does not confer any special authority for the project.

Leadership Plan

Offerors proposing multiple PIs will need to submit a Leadership Plan as part of the Technical Proposal. The Leadership Plan shall describe the governance and organizational structure of the research project including communication plans, process for making decisions on scientific direction, allocation of resources, publications, intellectual property issues, and procedures for resolving conflicts. The Leadership Plan shall follow the Table of Contents provided below:

A. Rationale

   Include a discussion of how the project will be enhanced by the multiple PI approach.

B. Identification of all proposed PIs

   Identify the proposed PIs, their point of contact information and affiliated organizations, and the percentages of time proposed for this project. Identify the Contact PI and plans for rotation of that role, if any.

C. Roles and Responsibilities

   Identify both the scientific and administrative roles and responsibilities of all named PIs.

D. Approach to Fiscal and Management Coordination

   Describe how the project will be performed and monitored from a fiscal and management perspective. Discuss organizational administrative coordination and support.

E. Project Direction and Resource Allocation

   Address how decisions will be made regarding scientific direction, and, how resources will be allocated and redistributed if needed during performance. Address plans for shared resources such as IT or other shared data considerations. If joint standard operating procedures will be developed, describe this process.

F. Communication and Lines of Authority

   Address communication and lines of authority within and among PIs and within and among organizations.

G. Data sharing, Intellectual Property, Publication, and other Proprietary Considerations

   Data sharing plans, intellectual property considerations, publication agreements, and any other proprietary or confidential information sharing should be addressed in this section.

H. Conflict Resolution

   Address how conflicts will be avoided, identified, and resolved.

ii. Other
Address any other information relative to the leadership approach to Multiple PI projects.

Offerors submitting single PI proposals do not need to submit a Leadership Plan.

iii. Other Investigators
List all other investigators/professional personnel who will be participating in the project. Discuss the qualifications, experience, and accomplishments. State the estimated time each will spend on the project, proposed duties on the project, and the areas or phases for which each will be responsible.

iv. Additional Personnel
List names, titles, and proposed duties of additional personnel, if any, who will be required for full-time employment, or on a subcontract or consultant basis. The technical areas, character, and extent of subcontract or consultant activity will be indicated and the anticipated sources will be specified and qualified. For all proposed personnel who are not currently members of the Offeror's staff, a letter of commitment or other evidence of availability is required. A resume does not meet this requirement. Commitment letters for use of consultants and other personnel to be hired shall include:

- The specific items or expertise they will provide.
- Their availability to the project and the amount of time anticipated.
- Willingness to act as a consultant.
- How rights to publications and patents will be handled.

Subcontractors and Consultants

Describe in detail any involvement of subcontractors and/or consultants, and provide resumes for all key subcontractor personnel. Refer to section 1.3 Definition for definition of Senior/Key Personnel. Also, provide a letter from each consultant proposed which includes: name, rate, the number of hours proposed, and a statement confirming that the rate being proposed is their standard rate charged to all.

v. Resumes
Resumes of all key personnel are required. Each shall indicate educational background, recent experience, specific or technical accomplishments, and a listing of relevant publications. Where vitae are extensive, summaries that focus on the most relevant experience or publications are desired.

3.6.1.5.3 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 the project. Briefly state their capacities, relative proximity and extent of availability to this effort. (Any equipment specifically proposed as a cost to the contract shall 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 in compliance with FAR 25.1 Buy American Act. Title to all equipment will vest in the Government.

3.6.1.5.4 Work Plan

The Offeror shall develop a Statement of Work similar in format to the sample provided in PART 9 of this solicitation entitled “Sample Statement of Work”. The Statement of Work should detail the Offeror’s approach and methodology. The plan should indicate what will be done, where it will be done, and how the R&D will be carried out. Phase II R&D should address the objectives from 3.6.1.5.1 above and the methods planned to achieve each objective or task should be discussed in detail. It will be incorporated into the final contract document. For this reason, do not include proprietary information as the contract and all contents therein are subject to the Freedom of Information Act and shall be disclosed should a FOIA request be submitted.

3.6.1.5.5 Commercialization Plan

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

i. 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.

ii. Company.

Give a brief description of the Offeror's 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 short description of the origins of the company. Indicate the Offeror's vision for the future, how the Offeror will grow/maintain a sustainable business entity, and how the Offeror will meet critical management functions as the Offeror's company evolves from a small technology R&D business to a successful commercial entity.

iii. Market, Customer, and Competition.

Describe the market and/or market segments the Offeror are targeting and provide a brief profile of the potential customer. Tell what significant advantages the Offeror's innovation will bring to the market, e.g., better performance, lower cost, more efficient or effective, new capability. Explain the hurdles the Offeror will have to overcome in order to gain market/customer acceptance of the Offeror's innovation. Describe any strategic alliances, partnerships, or licensing agreements the Offeror have in place to get FDA approval (if required) and to market and sell the Offeror's product. Briefly describe the Offeror's 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 the Offeror understand and know the competition.)

iv. Intellectual Property (IP) Protection.

Describe how the Offeror is going to protect the IP that results from the Offeror's innovation. Also note other actions the Offeror may consider taking that will constitute at least a temporal barrier to others aiming to provide a solution similar to the Offeror's.

v. Finance Plan.

Describe the necessary financing the Offeror will require, and when it will be required, as well as the Offeror's plans to raise the requisite financing to launch the Offeror's 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 the Offeror are going to take to secure Phase III funding.

vi. Production and Marketing Plan.

Describe how the production of the Offeror's product/service will occur (e.g., in-house manufacturing, contract manufacturing). Describe the steps the Offeror will take to market and sell the Offeror's product/service. For example, explain plans for licensing, internet sales, etc.

vii. Revenue Stream.

Explain how the Offeror plan to generate a revenue stream for the Offeror's 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 the Offeror's staffing will change to meet the Offeror's 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. The Offeror's 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 Federal agency with the intention that the results will be used by the United States Government; or other industrial firms.

3.6.1.5.6 Other Considerations

Record and discuss specific factors not included elsewhere which support the Offeror's proposal. Using specifically titled subparagraphs, items may include:

a. Any agreements and/or arrangements with subcontractor(s). Provide as much detail as necessary to explain how the statement of work will be accomplished within this working relationship.

b. Unique arrangements, equipment, etc., which none or very few organizations are likely to have which is advantageous for effective implementation of this project.

c. Equipment and unusual operating procedures established to protect personnel from hazards associated with this project.

d. Other factors the Offeror feel are important and support the Offeror's proposed research.

e. Recommendations for changing reporting requirements if such changes would be more compatible with the Offeror's proposed schedules.

3.6.1.5.7 Summary of Related Activities

Use Summary of Related Activities as provided in PART 9 of this solicitation.

3.6.1.5.8 Related R/R&D

Describe significant R/R&D that is directly related to the proposal including any conducted by the project manager/principal investigator or by the proposing SBC. Describe how it relates to the proposed effort, and

any planned coordination with outside sources. The Offeror shall persuade reviewers of his or her awareness of key, recent R/R&D conducted by others in the specific topic area.

3.6.1.5.9 Relationship with Future R/R&D

1. State the anticipated results of the proposed approach if the project is successful (Phase II).

2. Discuss the significance of the Phase I effort in providing a foundation for the Phase II R/R&D effort.

3.6.1.5.10 Special Technical Proposal Instructions/Requirements by Topic Number

Offerors shall comply with any special technical proposal instructions/requirements by Topic Number provided in PART 8 of this Solicitation.

3.6.1.5.11 Similar Proposals or Awards

WARNING-While it is permissible with proposal notification to submit identical proposals or proposals containing a significant amount of essentially equivalent work for consideration under numerous Federal program solicitations, it is unlawful to enter into funding agreements requiring essentially equivalent work. If there is any question concerning this, it must be disclosed to the soliciting agency or agencies before award. If an applicant elects to submit identical proposals or proposals containing a significant amount of essentially equivalent work under the Federal program solicitations, a statement must be included in each such proposal indicating:

i. The name and address of the agencies to which proposals were submitted or from which awards were received.
ii. Date of proposal submission or date of award.
iii. Title, number, and date of solicitations under which proposals were submitted or awards received.
iv. The specific applicable research topics for each proposal submitted or award received.
v. Titles of research projects.
vi. Name and title of principal investigator or project manager for each proposal submitted or award received.

3.6.1.5.12 Prior SBIR Phase II Awards.

If the SBC has received more than 15 Phase II awards in the prior 5 fiscal years, the SBC must submit in its proposal: name of the awarding agency; date of award; funding agreement number; amount of award; topic or subtopic title; follow-on agreement amount; source and date of commitment; and current commercialization status for each Phase II award. (This required proposal information will not be counted toward the proposal page limitation).

3.6.1.5.13 Cost Breakdown/Proposed Budget

Offeror shall submit a completed Technical Proposal Cost Summary, see Attachment 7 in PART 9 of this Soliciation.

3.6.1.5.14 Human Subjects

IMPORTANT NOTE TO OFFERORS: The following subparagraphs shall be addressed, as applicable, in a SEPARATE SECTION of the Technical Proposal entitled, "HUMAN SUBJECTS."

a. Human Subjects Decision Chart Reference

http://grants.nih.gov/grants/funding/424/SupplementalInstructions.pdf#Part_IIhttp://www.hhs.gov/

ohrp/policy/checklists/decisioncharts.html

b. **Notice to Offerors of Requirements of 45 CFR Part 46, Protection of Human Subjects, HHSAR 352.270-4(a) (January 2006)**

1. Copies of the Department of Health and Human Services (HHS) regulations for the protection of human subjects, 45 CFR Part 46, are available from the Office for Human Research Protections (OHRP), Bethesda, Maryland 20892. The regulations 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 HHS.

2. The regulations define a human subject as a living individual about whom an investigator (whether professional or student) conducting research obtains data through intervention or interaction with the individual, or identifiable private information. The regulations extend to the use of human organs, tissue, and body fluids from individually identifiable human subjects as well as to graphic, written, or recorded information derived from individually identifiable human subjects. The use of autopsy materials is governed by applicable State and local law and is not directly regulated by 45 CFR Part 46.

3. Activities in which the only involvement of human subjects will be in one or more of the categories set forth in 45 CFR 46.101(b)(1-6) are exempt from coverage.

4. Inappropriate designations of the noninvolvement of human subjects or of exempt categories of research in a project may result in delays in the review of a proposal. The Government's Project Officer will make a final determination of whether the proposed activities are covered by the regulations or are in an exempt category, based on the information provided in the proposal. In doubtful cases, the Project Officer will consult with OHRP.

5. In accordance with 45 CFR Part 46, prospective Contractors being considered for award shall be required to file with OHRP an acceptable Assurance of Compliance with the regulations, specifying review procedures and assigning responsibilities for the protection of human subjects. The initial and continuing review of a research project by an institutional review board shall assure that: the rights and welfare of the human subjects involved are adequately protected; the risks to the subjects are reasonable in relation to both the potential benefits, if any, to the subjects and the importance of the knowledge to be gained; and informed consent will be obtained by methods that are adequate and appropriate. HHS regulations for the protection of human subjects (45 CFR Part 46), information regarding OHRP registration and assurance requirements/processes, and OHRP contact information can be accessed at the OHRP Web site (at http://www.hhs.gov/ohrp/).

6. Offerors may consult with OHRP for advice or guidance concerning either regulatory requirements or ethical issues pertaining to research involving human subjects.

c. **Instructions to Offerors Regarding Protection of Human Subjects**

Offerors shall address the following human subjects protections issues if this contract will be for research involving human subjects (note: under each of the following points below, the Offeror should indicate whether the information provided relates to the primary research site, or to a collaborating performance site(s), or to all sites:

1. Risks to the subjects

- Human Subjects Involvement and Characteristics:
    - Describe the proposed involvement of human subjects in response to the solicitation.
    - Describe the characteristics of the subject population, including their anticipated number, age range, and health status.
    - Identify the criteria for inclusion or exclusion of any subpopulation. Explain the rationale for the involvement of special classes of subjects, such as fetuses, pregnant women, children, prisoners, institutionalized individuals, or others who are likely to be vulnerable populations.
- Sources of Materials:

  Identify the sources of research material obtained from individually identifiable living human subjects in the form of specimens, records, or data. Indicate whether the material or data will be obtained specifically for research purposes or whether use will be made of existing specimens, records, or data.

  Potential Risks:
    - Describe the potential risks to subjects (physical, psychological, social, legal, or other) and assess their likelihood and seriousness to the subjects.
    - Describe alternative treatments and procedures, including the risks and benefits of the alternative treatments and procedures, to participants in the proposed research, where appropriate.

2. Adequacy of Protection Against Risks

- Recruitment and Informed Consent:
    - Describe plans for the recruitment of subjects and the procedures for obtaining informed consent. 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. The informed consent document for the Contractor and any collaborating sites should be submitted only if requested elsewhere in the solicitation. Be aware that an IRB-approved informed consent document for the Contractor and any participating collaborative sites shall be provided to the Government prior to patient accrual or participant enrollment.
- Protection Against Risk:
    - Describe the procedures for protecting against or minimizing potential risks, including risks to confidentiality, and assess their likely effectiveness.
    - Discuss provisions for ensuring necessary medical or professional intervention in the event of adverse effects to the subjects where appropriate.
    - In studies that involve interventions, describe the provisions for data and safety

monitoring of the research to ensure the safety of subjects.

3. Potential Benefits of the Proposed Research to the Subjects and Others

   - Discuss the potential benefits of the research to the subjects and others.

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

   - Describe treatments and procedures that are alternatives to those provided to the participants by the proposed research, where appropriate.

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 may reasonably be expected to result.

     Note: If a test article (investigational new drug, device, or biologic) is involved, name the test article and state whether the 30-day interval between submission of Offeror's certification to the Food and Drug Administration (FDA) and its response has elapsed or has been waived and/or whether the FDA has withheld or restricted use of the test article.

     Collaborating Site(s)

     When research involving human subjects will take place at collaborating site(s) or other performance site(s), the Offeror shall provide in this section of its proposal a list of the collaborating sites and their assurance numbers. Further, if the Offeror is awarded a contract, the Offeror shall obtain in writing, and keep on file, an assurance from each site that the previous points have been adequately addressed at a level of attention that is at least as high as that documented at the Offeror's organization. Site(s) added after an award is made shall also adhere to the above requirements.

d. **Required Education in the Protection of Human Research Participants**

NIH policy requires education on the protection of human subject participants for all investigators submitting NIH proposals for contracts for research involving human subjects. This policy announcement is found in the NIH Guide for Grants and Contracts Announcement dated June 5, 2000 at the following website: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html. Offerors should review the policy announcement prior to submission of their proposals as certification of course completion will be a deliverable of a resultant contract. The following is a summary of the Policy Announcement:

For any solicitation for research involving human subjects, the Offeror shall provide in its technical proposal the following information: (1) a list of the names of the principal investigator and any other individuals proposed under the contract who are responsible for the design and/or conduct of the research; (2) the title of the education program completed(or to be completed prior to the award of the contract) for each named personnel; (3) a one sentence description of the program(s) listed in (2)

above. This requirement extends to investigators and all individuals responsible for the design and/or conduct of the research who are working as subcontractors or consultants under the contract.

Curricula that are readily available and meet the educational requirement include the NIH Office of Extramural Research (OER) on-line tutorial, entitled "Protecting Human Research Participants" at: http://phrp.nihtraining.com. This course is also available in Spanish under the title "Protección de los participantes humanos de la investigación" at: http://pphi.nihtraining.com. The Offeror may take the tutorials on-line or download the information in PDF form at no cost. The University of Rochester has made its training program available for individual investigators. Completion of this program will also satisfy the educational requirement. The University of Rochester manual, entitled, "Protecting Study Volunteers in Research," can be obtained through Centerwatch, Inc. at: http://store.centerwatch.com/c-29-training-guides.aspx. **Certificate of Completion from the online tutorial is required prior to contract award.**

If an institution already has developed educational programs on the protection of research participants, completion of these programs also will satisfy the educational requirement.

In addition, prior to the substitution of the principal investigator or any other individuals responsible for the design and/or conduct of the research under the contract, the Contractor shall provide the contracting officer with the title of the education program and a one sentence description of the program that the replacement has completed.

e. **Inclusion of Women and Minorities in Research Involving Human Subjects**

It is NIH policy that women and members of minority groups and their sub-populations shall be included in all NIH-supported clinical research projects involving human subjects, unless a clear and compelling rationale and justification establishes to the satisfaction of the relevant Institute/Center Director that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. The Director, NIH, may determine that exclusion under other circumstances is acceptable, upon the recommendation of an Institute/Center 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. This policy results from the NIH Revitalization Act of 1993(Section 492B of Public Law 103-43), **and applies to research subjects of all ages.** All investigators proposing research involving human subjects should read the UPDATED"NIH Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research, Amended October 2001," published in the NIH Guide for Grants and Contracts on October 9, 2001 at the following web site:

http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm

These guidelines contain a definition of **clinical research** adopted in June 2001, as:"(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 trials, and (d) development of new technologies; (2)Epidemiologic and behavioral studies; and (3) Outcomes research and health services research."

Information Required for ALL Clinical Research Proposals

This solicitation contains a review criterion addressing the adequacy of: (1) the Offeror's plans for inclusion of women and minorities in the research proposed; or (2) the Offeror's justification(s) for exclusion of one or both groups from the research proposed. Provide information on the composition of the proposed study population in terms of sex/gender and racial/ethnic groups and provide a rationale for selection of such subjects in response to the requirements of the solicitation. The description may include (but is not limited to) information on the population characteristics of the disease or condition being studied in the planned research, and/or described in the statement of work, national and local demography, knowledge of the racial/ethnic/cultural characteristics of the population, prior experience and collaborations in recruitment and retention of the populations and subpopulations to be studied, and the plans, arrangements and letters of commitment from relevant community groups and organizations for the planned research.

The proposal shall include the following information:

- A description of the subject selection criteria
  The proposed dates of enrollment (beginning and end)

- A description of the proposed outreach programs for recruiting women and minorities as subjects

- A compelling rationale for proposed exclusion of any sex/gender or racial/ethnic group

- The proposed sample composition using the "Planned Enrollment Report, PHS 398/2590"(see PART 9, Submission Forms and Certifications)

NOTE 1: *For all proposals, use the ethnic and racial categories and complete the "Planned Enrollment Report" in accordance with the Office of Management and Budget (OMB) Directive No. 15, which may be found at*: http://www.whitehouse.gov/omb/fedreg_notice_15.

Standards for Collecting Data. When the Offeror, as a contractor, are planning data collection items on race and ethnicity, the Offeror shall use, at a minimum, the categories identified in OMB Directive No. 15. The collection of greater detail is encouraged. However, the Offeror should design any additional, more detailed items so that they can be aggregated into these required categories. Self-reporting or self-identification using two separate questions is the preferred method for collecting data on race and ethnicity. When the Offeror collect race and ethnicity separately, the Offeror shall collect ethnicity first. The Offeror shall offer respondents the option of selecting one or more racial designations. When the Offeror collect data on race and ethnicity separately, the Offeror shall also make provisions to report the number of respondents in each racial category who are Hispanic or Latino. In the event that the Offeror presents aggregate data, the Offeror shall provide the number of respondents who selected only one category, for each of the five racial categories. If the Offeror collapse data on multiple responses, the Offeror shall make available at a minimum, the total number of respondents reporting "more than one race." Federal agencies shall not present data on detailed categories if doing so would compromise data quality or confidentiality standards.

In addition to the above requirements, solicitations for **NIH defined Phase III clinical trials** require that: a) all proposals and/or protocols provide a description of plans to conduct analyses, as appropriate, to detect significant differences in intervention effect (see NIH Guide: http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm, Definitions - Significant Difference *The definition of an " **NIH-Defined Phase III clinical trial**" can also be found at this website.) by sex/gender, racial/ethnic groups, and relevant subpopulations, if applicable; and

b)all contractors to report annually cumulative subject accrual, and progress in conducting analyses for sex/gender and race/ethnicity differences. Offerors may obtain copies of the Updated Guidelines from the sources above or from the contact person listed in the solicitation.

Also, the proposal shall include one of the following plans:

- Plans to conduct valid analysis 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,

  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 between subgroups.

Use the form entitled, "Planned Enrollment Report," when preparing the Offeror's response to the solicitation requirements for inclusion of women and minorities. (See PART 9 Submission Forms and Certifications)

Unless otherwise specified in this solicitation, the Government has determined that the work required by this solicitation does not involve a sex/gender specific study or a single or limited number of minority population groups. Therefore, the NIH believes that the inclusion of women and minority populations is appropriate for this project. (See PART 4 of this RFP for more information about evaluation factors for award.)

Use the form entitled, "Cumulative Inclusion Enrollment Report," for reporting in the resultant contract.

f. Inclusion of Children in Research Involving Human Subjects

It is NIH policy that children (defined below) shall be included in all human subjects research, including, but not limited to, clinical trials, conducted under a contract funded by the NIH, unless there are clear and compelling reasons not to include them. (See examples of Justifications for Exclusion of Children below). For the purposes of this policy, contracts involving human subjects include categories that would otherwise be exempt from the DHHS Policy for Protection of Human Research Subjects (sections 101(b) and401(b) of 45 CFR 46), such as surveys, evaluation of educational interventions, and studies of existing data or specimens that should include children as participants. This policy applies to both domestic and foreign research contracts.

For purposes of this policy, a child is defined as an individual under the age of 21 years.

All Offerors proposing research involving human subjects should read the "NIH Policy and Guidelines on the Inclusion of Children as Participants in Research Involving Human Subjects" which was published in the NIH Guide for Grants and Contracts on March 6,1998 and is available at the following URL address:

http://www.nih.gov/grants/guide/notice-files/not98-024.html

Offerors also may obtain copies from the contact person listed in the RFP.

Inclusion of children as participants in research shall be in compliance with all applicable subparts of 45 CFR 46 as well as other pertinent laws and regulations whether or not such research is otherwise exempted from 45 CFR 46. Therefore, any proposals shall include a description of plans for including children, unless the Offeror presents clear and convincing justification for exclusion. The "Human Subjects" section of the Offeror's technical proposal should provide either a description of the plans to include children and a rationale for selecting or excluding a specific age range of child, or an explanation of the reason(s) for excluding children as participants in the research. This solicitation contains a review criterion addressing the adequacy of: (1) the plans for including children as appropriate for the scientific goals of the research; and/or (2) the justification of exclusion of children or exclusion of a specific age range of children.

When children are included, the plan also shall include a description of: (1) the expertise of the investigative team for dealing with children at the ages included; (2) the appropriateness of the available facilities to accommodate the children; and, (3) the inclusion of a sufficient number of children to contribute to a meaningful analysis relative to the purpose/objective of the solicitation.

Justifications for Exclusion of Children

- It is expected that children will be included in all research involving human subjects unless one or more of the following exclusionary circumstances can be fully justified: The objective of the solicitation is not relevant to children.
    - There are laws or regulations barring the inclusion of children in the research to be conducted under the solicitation.
    - 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 redundant. The Offeror should provide documentation of other studies justifying the exclusion.
    - A separate, age-specific study in children is warranted and preferable. Examples include:
        - The relative rarity of the condition in children, as compared with adults (in that extraordinary effort would be needed to include children); or
        - The number of children is limited because the majority are already accessed by a nationwide pediatric disease research network; or
        - Issues of study design preclude direct applicability of hypotheses and/or interventions to both adults and children (including different cognitive, developmental, or disease stages of different age-related metabolic processes); or
        - 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). While 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; or
        - Study designs aimed at collecting additional data on pre-enrolled adult study subjects (e.g., longitudinal follow-up studies that did not include data on children);

- Other special cases justified by the Offeror and found acceptable to the review group and the Institute Director

Definition of a Child

For the purpose of this solicitation, a child is defined as an individual under the age of 21 years. The definition of child described above will pertain to this solicitation (notwithstanding the FDA definition of a child as an individual from infancy to 16 years of age, and varying definitions employed by some states). Generally, State laws define what constitutes a "child," and such definitions dictate whether or not a person can legally consent to participate in a research study. However, State laws vary, and many do not address when a child can consent to participate in research. Federal Regulations (45 CFR 46, subpart D, Sec.401-409) address DHHS protections for children who participate in research, and rely on State definitions of "child" for consent purposes. Consequently, the children included in this policy (persons under the age of 21) may differ in the age at which their own consent is required and sufficient to participate in research under State law. For example, some states consider a personage 18 to be an adult and therefore one who can provide consent without parental permission.

Research Involving Prisoners as Subjects

a. HHS Regulations at 45 CFR Part 46, Subpart C provide additional protections pertaining to biomedical and behavioral research involving prisoners or those individuals who, during the period of the contract become prisoners, as subjects. These regulations also set forth the duties of the Institutional Review Board (IRB) where prisoners are involved in their search. HHS funded research involving prisoners as subjects may not proceed until the Office for Human Research Protections (OHRP) issues approval, in writing, as required by 45 CFR 46.306(a)(2). In addition, OHRP Guidance on the Involvement of Prisoners in Research may be found at: http://www.hhs.gov/ohrp/policy/prisoner.html.

b. HHS Waiver for Epidemiological Research Involving Prisoners as Subjects

On June 20, 2003 the Secretary of HHS waived the applicability of certain provisions of Subpart C of 45 CFR Part 46, (Additional DHHS Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects) to specific types of epidemiological research involving prisoners as subjects.

The applicability of 45 CFR 46.305(a)(1) and 46.306(a)(2) for certain epidemiological research conducted or funded by DHHS is waived when:

1. The sole purposes are:
   - to describe the prevalence or incidence of a disease by identifying all cases, or
   - to study potential risk factor associations for a disease, and
2. The Institution responsible for the conduct of the research certifies to the OHRP that the Institutional Review Board (IRB) approved the research and fulfilled its duties under 45 CFR 46.305(a)(2 7) and determined and documented that:
   - the research presents no more than minimal risk, and

- no more than inconvenience to the prisoner subjects, and
- prisoners are not a particular focus of the research. For more information about this Waiver see http://www.gpo.gov/fdsys/pkg/FR-2003-06-20/html/03-15580.htm

g. Research Involving Human Fetal Tissue

Human Fetal Tissue means tissue or cells obtained from a dead human fetus, including human embryonic stem cells, human pluripotent stem cells and human embryonic germ cells.

The governing federal statute is the Public Health Service Act, 42 U.S.C. 289g 1 and 289g2. Implementing regulations and guidance for conducting research on human fetal tissue may be found at 45 CFR 46, Subpart B and http://grants1.nih.gov/grants/guide/notice-files/not93-235.html and any subsequent revisions to this NIH Guide to Grants and Contracts ("Guide") Notice.

By signing the face page of the proposal, the Offeror (authorized institutional official) certifies that researchers using human fetal tissue are in compliance with 42 USC 289g2. This statute specifically prohibits any person from knowingly acquiring, receiving, or transferring any human fetal tissue for valuable consideration. "Valuable consideration" is a concept similar to profit, and does not include reasonable payment for costs associated with the collection processing, preservation, storage, quality control or transportation of these tissues.

Research involving the transplantation of human fetal tissue shall be conducted in accordance with applicable Federal, State and local law.

h. Human Embryonic Germ Cell (HEGC) Research

a. Guidelines.

Research use of human embryonic germ cells derived from fetal tissue with Federal funds requires review of compliance with the NIH Guidelines for Research Using Human Pluripotent Stem Cells (http://stemcells.nih.gov/policy/guidelines.asp) (only the information regarding human embryonic germ cells is relevant). Embryonic germ cells are pluripotent stem cells derived from human embryos. See NIH Guide for Grants and Contracts Notice NOT OD 02 049, requiring that Offerors/contractors submit certain documents to the Human Pluripotent Stem Cell Review Group(HPSCRG), which will be reviewed in a public meeting. Research using human embryonic germ cells may not be performed prior to approval by the HPSCRG.

All Offerors should read the "NIH Guidelines" (http://stemcells.nih.gov/policy/guidelines.asp) if they either: (1) propose to respond to the Statement of Work requirements by conducting research that uses human embryonic germ cells or, (2)are responding to a Statement of Work that requires the use of human embryonic germ cells.

Offerors may obtain copies of these Guidelines from the website above or from the contact person listed in this solicitation.

b. Procedure for Review by Human Pluripotent Stem Cell Review Group (HPSCRG)

The _____has determined that human embryonic germ cells are required to be used

for the conduct of this research. The Offeror shall submit an original and two copies of the documentation and assurances that address the areas covered the "Procedures for Submission of Compliance Documents to the Human Pluripotent Stem Cell Review Group (HPSCRG) for the Research Use of Human Embryonic Germ Cells," at:
(http://grants2.nih.gov/grants/guide/notice-files/NOT-OD-02-049.html)

as a separate attachment in its proposal. Prior to any award made under this solicitation, the documentation and assurances will be subject to review by the HPSCRG, which meets in a public meeting. No research involving the use of human embryonic germ cells may begin prior to HPSCRG approval.

Offerors are encouraged to review issues pertaining to informed consent processes described in Section II.B.2.b of the NIH Guidelines, at:(
http://stemcells.nih.gov/staticresources/news/newsArchives/fr25au00-136.asp).
Offerors should also review the March 19, 2002, DHHS Office of Human Research Protection's document titled, "Guidance for Investigators and Institutional Review Boards Regarding Research Involving Human Embryonic Stem Cells, Germ Cells, and Stem Cell Derived Test Articles,"(
http://stemcells.nih.gov/StaticResources/news/newsArchives/stemcell.pdf)

OR

b. Procedure for Review by Human Pluripotent Stem Cell Review Group (HPSCRG)

If, in response to the solicitation, the Offeror proposes to use human embryonic germ cells, it shall submit, as a separate attachment to its proposal, an original and two copies of the documentation and assurances that address the areas covered in the "Procedures for Submission of Compliance Documents to the Human Pluripotent Stem Cell Review Group (HPSCRG) for the Research Use of Human Embryonic Germ Cells" at:
(http://grants2.nih.gov/grants/guide/notice-files/NOT-OD-02-049.html).
Prior to any award made under this solicitation, the documentation and assurances will be subject to review by the HPSCRG, which meets in a public meeting. No research involving the use of human embryonic germ cells may begin prior to HPSCRG approval.

Offerors are encouraged to review issues pertaining to informed consent processes described in Section II.B.2.b of the NIH Guidelines. Offerors should also review the March 19, 2002, DHHS Office of Human Research Protection's document titled" Guidance for Investigators and Institutional Review Boards Regarding Research Involving Human Embryonic Stem Cells, Germ Cells, and Stem Cell Derived Test Articles," at
(http://stemcells.nih.gov/StaticResources/news/newsArchives/stemcell.pdf)

OR

b. Procedure for Review by Human Pluripotent Stem Cell Review Group (HPSCRG)

The _____has determined that human embryonic germ cells are required to be used for the conduct of this research. The Offeror shall confirm in its proposal that it plans to use human embryonic germ cells as a part of its research. If the Offeror receives a contract award, the Contractor may not perform any research using human embryonic germ cells until the Human Pluripotent Stem Cell Review Group(HPSCRG) has reviewed and approved the documentation furnished as prescribed in the "Procedures for Submission of Compliance Documents to the Human Pluripotent Stem Cell Review Group (HPSCRG) for the Research Use of Human Embryonic

Germ Cells" (http://grants2.nih.gov/grants/guide/notice-files/NOT-OD-02-049.html)and the Contracting Officer has notified the Contractor of the approval in writing.

Offerors are encouraged to review issues pertaining to informed consent processes described in Section II.B.2.b of the NIH Guidelines at:
(http://stemcells.nih.gov/staticresources/news/newsArchives/fr25au00-136.asp).Offerors should also review the March 19, 2002, DHHS Office of Human Research Protection's document titled "Guidance for Investigators and Institutional Review Boards Regarding Research Involving Human Embryonic Stem Cells, Germ Cells, and Stem Cell Derived Test Articles," at:
(http://stemcells.nih.gov/StaticResources/news/newsArchives/stemcell.pdf)

The resultant contract will be divided into discrete phases or option periods. During Option Period(s)/Phase(s)_____* of the contract, the Contractor shall submit the original and two copies of the required documentation and assurances that address the areas covered in "Procedures for Submission of Compliance Documents to the Human Pluripotent Stem Cell Review Group (HPSCRG) for the Research Use of Human Embryonic Germ Cells," at:
(http://grants2.nih.gov/grants/guide/notice-files/NOT-OD-02-049.html)to the Contracting Officer. This documentation will be forwarded for review and approval to the HPSCRG.

If the HPSCRG disapproves the documentation presented by the Contractor, the Contracting Officer may elect to either terminate the contract in accordance with the Termination for Convenience clause of the contract OR determine not to exercise subsequent option(s) as appropriate based the terms of the specific contract. Otherwise, when the HPSCRG approves the documentation, the Contracting Officer will notify the Contractor in writing that research using the human embryonic germ cells may commence.

Research involving the use of human embryonic germ cells shall not be conducted under the contract until the HPSCRG review and approval have been obtained, and the Contracting Officer has provided written notice of such approval to the Contractor.

OR

<u>b. Procedure for Required Review by Human Pluripotent Stem Cell Review Group(HPSCRG)</u>

If the Offeror intends to fulfill the requirements of the Statement of Work by performing research using human embryonic germ cells, it shall so state in its proposal.

If the Offeror's proposal includes research using human embryonic germ cells and it receives a contract award, the Contractor may not perform any research using these human embryonic germ cells until the Human Pluripotent Stem Cell Review Group(HPSCRG) has reviewed and approved the documentation furnished as prescribed in "Procedures for Submission of Compliance Documents to the Human Pluripotent Stem Cell Review Group (HPSCRG) for the Research Use of Human Embryonic Germ Cells" (http://grants2.nih.gov/grants/guide/notice-files/NOT-OD-02-049.html)and the Contracting Officer has notified the Contractor of the approval in writing.

The resultant contract will be divided into discrete phases or option period(s). During Option Period(s)/Phase(s) _____* of the contract, the Contractor shall submit the original and two copies of the required documentation and assurances that address the areas covered in "Procedures for Submission of Compliance Documents to the Human Pluripotent Stem Cell Review Group (HPSCRG) for the Research Use of Human Embryonic Germ Cells,"

at:(http://grants2.nih.gov/grants/guide/notice files/NOT OD 02 049.html) to the Contracting Officer. This documentation will be forwarded for review and approval to the HPSCRG.

If the HPSCRG disapproves the documentation presented by the Contractor, the Contracting Officer may elect to either terminate the contract in accordance with the Termination for Convenience clause of the contract OR determine not to exercise subsequent option(s) as appropriate based the terms of the specific contract. Otherwise, when the HPSCRG approves the documentation, the Contracting Officer will notify the Contractor in writing that research using the human embryonic germ cells may commence.

Research involving the use of human embryonic germ cells shall not be conducted under the contract until the HPSCRG review and approval have been obtained, and the Contracting Officer has provided written notice of such approval to the Contractor.

i. Human Embryonic Stem Cell (hESC) Research

On March 9, 2009, the President issued Executive Order (EO) 13505: *Removing Barriers to Responsible Scientific Research Involving Human Stem Cells*. The NIH has published Guidelines on Human Stem Cell Research at: http://stemcells.nih.gov/policy/pages/2009guidelines.aspx. The Guidelines implement EO 13505 with regard to extramural NIH-funded stem cell research, establish policy and procedure under which the NIH will fund such research, and help ensure that NIH-funded research in this area is ethically responsible, scientifically worthy, and conducted in accordance with applicable law. Specific eligibility requirements for NIH funding of hESCs are included in Section II, *Eligibility of Human Embryonic Stem Cells for Research with NIH Funding*. Ineligible sources and uses of hESCs are addressed in Section IV, *Research Using hESCs and/or Human Induced Pluripotent Stem Cells That, Although the Cells May Come from Eligible Sources, is Nevertheless Ineligible for NIH Funding*, and Section V, *Other Research Not Eligible for NIH Funding*.

To facilitate research using human embryonic stem cells, the NIH has established a Human Embryonic Stem Cell Registry ("the NIH Registry") that lists the human embryonic stem cells that are currently eligible for use in NIH-funded research. This registry is available at: http://stemcells.nih.gov/research/registry/. Proposed human embryonic stem cell line(s) shall be on the NIH Registry at the time of proposal submission. Any possible changes to the proposed cell line shall be discussed in the proposal. Offerors wishing to have Human Embryonic Stem Cell Lines added to the NIH Human Embryonic Stem Cell Registry shall submit the request on Form NIH 2890 through the following website: http://hescregapp.od.nih.gov/NIH_Form_2890_Login.htm.

Research involving the derivation of new stem cells from human embryos or the use of human embryonic stem cells that are not listed on the NIH Registry may not be conducted with Federal funding.

j. Data and Safety Monitoring in Clinical Trials

All Offerors are directed to the full text of the NIH Policies regarding Data and Safety Monitoring and Reporting of Adverse Events that are found in the NIH Guide for Grants and Contracts Announcements at the following web sites:

http://grants.nih.gov/grants/guide/notice-files/not98-084.html
http://grants.nih.gov/grants/guide/notice-files/not99-107.html
http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html

All Offerors receiving an award under this solicitation shall comply with the NIH Policy cited in these NIH Announcements and any other data and safety monitoring requirements found elsewhere in this solicitation.

The following is a brief summary of the Data and Safety Monitoring and Adverse Event Reporting Requirements:

Data and Safety Monitoring is required for every clinical trial. Monitoring shall be performed on a regular basis and the conclusions of the monitoring reported to the Contracting Officer's Representative (COR).

The type of data and safety monitoring required will vary based on the type of clinical trial and the potential risks, complexity and nature of the trial. A plan for data and safety monitoring is required for all clinical trials. A general description of a monitoring plan establishes the overall framework for data and safety monitoring. It should describe the entity that will be responsible for the monitoring, and the policies and procedures for adverse event reporting. Phase III clinical trials generally require the establishment of a Data Safety Monitoring Board (DSMB). The establishment of a DSMB is optional for Phase I and Phase II clinical trials.

The DSMB/Plan is established at the time the protocol is developed and shall be approved by both the Institutional Review Board (IRB) and the Government and in place before the trial begins. If the protocol will be developed under the contract awarded from this solicitation, a general description of the data and safety monitoring plan shall be submitted as part of the proposal and will be reviewed by the scientific review group (Technical Evaluation Panel, (TEP)) convened to evaluate the proposal. If the protocol is developed and is included as part of the submitted proposal, a complete and specific data and safety monitoring plan shall be submitted as part of the proposal.

Monitoring Plans, at a minimum, shall include the prompt reporting of adverse events to the IRB, the NIH Office of Biotechnology Activities (OBA), and the Food and Drug Administration (FDA). Also, in the plan the Offeror should describe the frequency of reporting of the conclusions of the monitoring activities. The overall elements of each plan may vary depending on the size and complexity of the trial. The NIH Policy for Data and Safety Monitoring at http://grants.nih.gov/grants/guide/notice-files/not98-084.html describes examples of monitoring activities to be considered.

The frequency of monitoring will depend upon 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:

- Principal Investigator (required)
- Independent individual /Safety Officer
- Designated medical monitor
- Internal Committee or Board with explicit guidelines
- Data and Safety Monitoring Board (DSMB - required for multisite trials)
- Institutional Review Board (IRB - required)

For multi-site Phase I and Phase II trials, a central reporting entity that will be responsible for preparing timely summary reports of adverse events for distribution among sites and IRBs should be

considered.

Organizations with a large number of clinical trials may develop standard monitoring plans for Phase I and Phase II trials. In this case, such organizations may include the IRB-approved monitoring plan as part of the proposal submission.

k. **Registration of and Results Reporting for Applicable Clinical Trials in ClinicalTrials.gov**

The Food and Drug Administration Amendments Act of 2007(FDAAA) at: http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=110_cong_public_laws&docid=f:publ085.110.pdf, Title VIII, expands the National Institutes of Health's (NIH's) clinical trials registry and results database known asClinicalTrials.gov (http://www.clinicaltrials.gov/) and imposes new requirements that apply to certain applicable clinical trials, including those supported in whole or in part by NIH funds. FDAAA requires:

a. The registration of certain "applicable clinical trials" in ClinicalTrials.gov no later than 21 days after the first subject is enrolled; and

b. The reporting of summary results information (including adverse events) no later than1 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.

The resultant contract will support one or more applicable clinical trial subject to FDAAA.

The "responsible party" is the entity responsible for registering and reporting trial results inClinicalTrials.gov.

- Where the Contractor is the IND/IDE holder, the Contractor will be considered the Sponsor, therefore the "Responsible Party."

- Where there is no IND/IDE holder or where the Government is the IND/IDE holder, the Government will generally be considered the "Sponsor" and may designate the contractor's Principal Investigator (PI) as the "Responsible Party."

- For Multi-Center trials where there is no IND/IDE holder or where the Government is the IND/IDE holder, the "Responsible Party" will be designated at one site (generally the lead clinical site) and all other sites will be responsible for providing necessary data to the "Responsible Party" for reporting in the database.

Additional information is available at http://prsinfo.clinicaltrials.gov

3.6.1.5.15 Care of Live Vertebrate Animals

The following notice is applicable when contract performance is expected to involve care of live vertebrate animals:

Notice to Offerors of Requirement for Compliance with the Public Health Service Policy on Humane Care and Use of Laboratory Animals, HHSAR 352.270-5(a) (January 2006)

The Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals (PHS Policy) establishes

a number of requirements for research activities involving animals. Before award may be made to an offeror organization, the organization shall file, with the Office of Laboratory Animal Welfare (OLAW), National Institutes of Health (NIH), a written Animal Welfare Assurance (Assurance) which commits the organization to comply with the provisions of the PHS Policy, the Animal Welfare Act, and the Guide for the Care and Use of Laboratory Animals (National Academy Press, Washington, DC). In accordance with the PHS Policy, offeror organizations shall establish an Institutional Animal Care & Use Committee (IACUC), qualified through the experience and expertise of its members, to oversee the institution's animal program, facilities and procedures. Offeror organizations are required to provide verification of IACUC approval prior to release of an award involving live vertebrate animals. No award involving the use of animals shall be made unless OLAW approves the Assurance and verification of IACUC approval for the proposed animal activities has been provided to the Contracting Officer. Prior to award, the Contracting Officer will notify Contractor(s) selected for projects that involve live vertebrate animals that an Assurance and verification of IACUC approval are required. The Contracting Officer will request that OLAW negotiate an acceptable Assurance with those Contractor(s) and request verification of IACUC approval. For further information contact OLAW, at NIH, 6705 Rockledge Drive, RKL1, Suite 360,MSC 7982 Bethesda, Maryland 20892-7982 (E-mail: olaw@od.nih.gov; Phone: 301-496-7163).

(End of Provision)

The PHS Policy is available on the internet at: http://www.grants.nih.gov/grants/olaw/olaw.htm.

3.6.1.5.16 Research Involving Live Vertebrate Animals

It is intended that live vertebrate animals will be used during performance of this contract. The Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals (authority derived from the Health Research Extension Act of 1985) specifies that certain information is required from Offerors in contract proposals submitted to the NIH that will use live vertebrate animals.

The following five points shall be addressed in a separate section of the Technical Proposal titled "Vertebrate Animal Section" (VAS):

a. Detailed description of the proposed use of the animals, including species, strains, ages, sex and number to be used.

b. Justification for the use of animals, choice of species, and numbers to be used.

c. Information on the veterinary care of the animals.

d. Description of procedures for minimizing discomfort, distress, pain and injury.

e. Method of euthanasia and the reasons for the selection.

A concise (no more than 1-2 pages), complete description addressing these five points shall be provided. The description shall be cohesive and include sufficient information to allow evaluation by reviewers and NIH staff. For more discussion regarding the five points in the VAS, see NIH Guide Notice NOT-OD-10-049 at: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-10-049.html.

If a subcontract is proposed, an InterInstitutional Agreement shall be established with the Office of Laboratory Animal Welfare (OLAW) prior to award.

The Contract Proposal VAS Worksheet is provided as an Attachment in PART 9 of this solicitation to assist in the preparation of the VAS as part of the Technical Proposal. It can be accessed at: http://grants.nih.gov/grants/olaw/VAScontracts.pdf.

3.6.1.5.17 Obtaining and Disseminating Biomedical Research Resources

As a public sponsor of biomedical research, the National Institutes of Health (NIH) has a dual interest in accelerating scientific discovery and facilitating product development. Intellectual property restrictions can stifle the broad dissemination of new discoveries and limit future avenues of research and product development. At the same time, reasonable restrictions on the dissemination of research tools are sometimes necessary to protect legitimate proprietary interests and to preserve incentives for commercial development. To assist NIH contractors achieve an appropriate balance, the NIH has provided guidance in the form of a two-part document, consisting of Principles setting forth the fundamental concepts and Guidelines that provide specific information to patent and license professionals and sponsored research administrators for implementation.

The purpose of these Principles and Guidelines is to assist NIH funding recipients in determining: 1) Reasonable terms and conditions for making NIH-funded research resources available to scientists in other institutions in the public and private sectors (disseminating research tools); and 2) Restrictions to accept as a condition of receiving access to research tools for use in NIH-funded research (acquiring research tools). The intent is to help recipients ensure that the conditions they impose and accept on the transfer of research tools will facilitate further biomedical research, consistent with the requirements of the Bayh-Dole Act and NIH funding policy.

This policy, entitled, "SHARING BIOMEDICAL RESEARCH RESOURCES: Principles and Guidelines for Recipients of NIH Research Grants and Policy," (Federal Register Notice, December 23, 1999[64 FR 72090] will be included in any contract awarded from this solicitation. It can be found at the following website:

http://www.gpo.gov/fdsys/pkg/FR-1999-12-23/pdf/99-33292.pdf

1. **Sharing Research Data**

   [Note: This policy applies to **all** NIH contracts, regardless of dollar value, that are expected to generate research data.]

   The NIH endorses the sharing of final research data to expedite the translation of research results into knowledge, products, and procedures to improve human health. This contract is expected to generate research data. Therefore, the Offeror shall submit a plan in its technical proposal for data sharing or state why data sharing is not possible. If data sharing is limited, the Offeror should explain such limitations in its data sharing plan. NIH's data sharing policy may be found at the following Web site:

   http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-032.html

   [If the resultant contract is part of a collaborative program involving multiple sites, the data sharing will be governed by a dissemination plan to be developed jointly following award. Offerors shall include in their proposals a statement of willingness to work collaboratively after award with the other funded sites to

prepare a joint dissemination plan. Coordinating Center proposals should describe methods to coordinate the dissemination planning and implementation. The Coordinating Center shall include a budget and justification for any additional costs of this collaborative effort.]

2. **Sharing of Model Organisms for Biomedical Research**

The NIH Research Tools Policy (http://www.gpo.gov/fdsys/pkg/FR-1999-12-23/pdf/99-33292.pdf) also referred to as NIH Principles and Guidelines for Sharing of Biomedical Resources: Final Notice, December 1999, supports the concept of timely sharing and distribution of research resources. In accordance with NIH Guide Notice NOT-OD-04-042 at:(http://grants.nih.gov/grants/guide/notice-files/NOT-OD-04-042.html), dated May 7, 2004,and the September 10, 2004 extension of this policy NOT-OD-04-066 at:(http://grants.nih.gov/grants/guide/notice-files/NOT-OD-04-066.html),the NIH provides further sharing guidance with particular attention on model organisms for biomedical research. Such organisms include, but are not limited to: mammalian models such as the mouse and rat, and non-mammalian models, such as budding yeast, social amoebae, round worm, fruit fly, zebra fish, and frog. Research resources to be shared include genetically modified or mutant organisms, sperm, embryos, protocols for genetic and phenotypic screens, mutagenesis protocols, and genetic and phenotypic data for all mutant strains.

Offerors shall include in their technical proposal a description of a specific plan for sharing and distributing unique model organism research resources generated using NIH funding so that other researchers can benefit from these resources, OR provide appropriate reasons why such sharing is restricted or not possible. A reasonable time frame for periodic disposition of material and associated data shall be specified in the proposal. In addition, the plan shall address if, or how, Offerors will exercise their intellectual property rights while making model organisms and research resources available to the broader scientific community. At a minimum, the plan should address the following:

- Will material transfers be made with no more restrictive terms than in a Simple Letter Agreement (SLA) at: http://www.ott.nih.gov/mta-policy; for the transfer of materials or the Uniform Biological Material Transfer Agreement (UBMTA) (http://www.autm.net/UBMTA/8847.htm)

- How will inappropriate "reach-through" requirements (as discussed in the NIH Research Tools Policy) on materials transferred be discussed?

- How will technologies remain widely available and accessible to the research community, for example, if any intellectual property rights arise for which a patent application may be filed?

Offerors may request funds in their cost proposal to defray reasonable costs associated with sharing materials or data or transfer of model organisms and associated data to appropriate repositories.

3. **Data Sharing Policy for Genome-Wide Association Studies**

NIH is interested in advancing genome-wide association studies (GWAS) to identify common genetic factors that influence health and disease through a centralized GWAS data repository. For the purposes of this policy, a genome-wide association study is defined as any study of genetic variation across the entire human 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.

All Offerors proposing 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. Contractors submitting GWAS data are expected to:

- Provide descriptive information about their studies;
- Submit coded genotypic and phenotypic data to the NIH GWAS data repository; and
- Submit a certification that the institution or organization has reviewed and approved submission to the NIH, noting any limitations on data use based on the relevant informed consents and providing assurance that all data are submitted to the NIH in accord with applicable laws and regulations and that the identities of research participants will not be disclosed to the NIH GWAS data repository and an IRB and/or Privacy Board, as applicable, has reviewed and verified that:
    - The submission of data to the NIH GWAS data repository and subsequent sharing for research purposes are consistent with the informed consent of study participants from whom the data were obtained;
    - The investigator's plan for de-identifying datasets is consistent with the standards outlined above;
    - It has considered the risks to individuals, their families, and groups or populations associated with data submitted to the GWAS data repository; and
    - The genotype and phenotype data to be submitted were collected in a manner consistent with 45 C.F.R. Part 46.

Contractors requesting access to GWAS data in the NIH repository are expected to:

- Submit a data access request, including a brief description of the proposed research and a Data Use Certification that is co-signed by the designated Institutional Official(s) at their sponsoring institution;
- Use the data only for the approved research project described in the data access request;
- Protect data confidentiality;
- Not attempt to use the requested datasets to re-identify or contact individual study participants;
- Retain control of the data and not distribute it to any entity or individual not covered in the data access request;
- Ensure that data security measures are in place;
- Notify the appropriate Data Access Committee of policy violations; and
- Submit annual progress reports detailing significant research findings.

Additionally, Contractors requesting access to the data are also expected to abide by the dbGaP Approved User Code of Conduct (https://dbgap.ncbi.nlm.nih.gov/aa/GWAS_Code_of_Conduct.html).

Data repository management (submission and access) is governed by the Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-Wide Association Studies, NIH Guide NOT-OD-07-088 located at: http://grants.nih.gov/grants/guide/notice-files/NOTA-OD-07-088.html. For additional information see:

http://gwas.nih.gov/ .

3.7 BUSINESS PROPOSAL

3.7.1 Required Certifications

The Offeror shall submit a certification at the time of submission of the offer. The certification requires the Offeror to state that it intends to meet the size, ownership and other requirements of the SBIR Program at the time of award of the funding agreement, if selected for award.

1. The Offeror shall submit a certification at the time of award, and at any other time set forth in SBA's regulations at 13 CFR 121.701-121.705. The certification will require the Offeror to state that it meets the size, ownership and other requirements of the SBIR Program at the time of award of the funding agreement.

2. The SBIR awardee shall also submit certifications during funding agreement life cycle. A Phase II funding agreement shall state that the awardee shall submit a new certification as to whether it qualifies as a SBC and that is in compliance with specific SBIR Program requirements prior to receiving more than 50% of the total award amount and prior to final payment or disbursement.

3. Agencies may require additional certifications at other points in time during the life cycle of the funding agreement, such as at the time of each payment or disbursement.

   Each Offeror that is majority-owned by multiple venture capital operating companies, hedge funds, or private equity firms shall register with SBA in the Company Registry Database atwww.SBIR.gov and submit a certification with its SBIR proposal to the SBIR agency (see PART 9-Submission Forms and Certifications of this solicitation for the certification documents).

   Lifecycle Certifications

   In addition to the standard federal procurement certifications, the SBA SBIR/STTR Policy Directive requires the collection of certain information from firms at time of award and during the award life cycle. Please go to the NIH SBIR/STTR Forms Website at: http://grants.noih.gov/grants/forms.htm#contracts to access the forms required to be submitted during the award lifecycle. At a minimum, the Lifecycle certifications are required prior to receiving 50% of the total award amount, and prior to final payment on the Phase II award. These certifications will be identified as contract deliverables and incorporated into the contract delivery schedule.

3.7.2 Basic Cost/Price Information

The business proposal shall contain sufficient information to allow the Government to perform a basic analysis of the proposed cost or price of the work. This information shall include the amounts of the basic elements of the proposed cost or price. These elements will include, as applicable, direct labor, fringe benefits, travel, materials, subcontracts, purchased parts, shipping, indirect costs and rate, fee, and profit.

3.7.3 Proposal Cover

The Offeror shall complete the Form NIH-2043, with particular attention to the length of time the proposal is firm and the designation of those personnel authorized to conduct negotiations. (See PART 9, Attachment 13 entitled, NIH Form 2043, PROPOSAL SUMMARY AND DATA RECORD).

3.7.4 Certified Cost or Pricing Data

1. General Instructions

a. The Offeror shall provide the following information on the first page of the Offeror's pricing proposal:

1. Solicitation, contract, and/or modification number;
2. Name and address of Offeror;
3. Name and telephone number of point of contact;
4. Name of contract administration office (if available);
5. Type of contract action (that is, new contract, change order, price revision/redetermination, letter contract, unpriced order, or other);
6. Proposed cost; profit or fee; and total;
7. Whether the Offeror will require the use of Government property in the performance of the contract, and, if so, what property. See Item 16. Other Administrative Data, subparagraph a.2. Government Property of this PART 3.2.a.16.d.10 of this solicitation;
8. Whether the Offeror's organization is subject to cost accounting standards; whether the Offeror's organization has submitted a CASB Disclosure Statement, and if it has been determined adequate; whether the Offeror have been notified that the Offeror are or may be in noncompliance with the Offeror's Disclosure Statement or CAS, and, if yes, an explanation; whether any aspect of this proposal is inconsistent with the Offeror's disclosed practices or applicable CAS, and, if so, an explanation; and whether the proposal is consistent with the Offeror's established estimating and accounting principles and procedures and FAR Part 31, Cost Principles, and, if not, an explanation;
9. The following statement: This proposal reflects our estimates and/or actual costs as of this date and conform to the instructions in FAR 15.403 5(b)(1) and Table15 2. By submitting this proposal, we grant the Contracting Officer and authorized representative(s) the right to examine, at any time before award, those records, which include books, documents, accounting procedures and practices, and other data, regardless of type and form or whether such supporting information is specifically referenced or included in the proposal as the basis for pricing, that will permit an adequate evaluation of the proposed price;
10. Date of submission; and
11. Name, title and signature of authorized representative.

b. In submitting the Offeror's proposal, the Offeror shall include an index, appropriately referenced, of all the certified cost or pricing data and information accompanying or identified in the proposal. In addition, the Offeror shall annotate any future additions and/or revisions, up to the date of agreement on price, or an earlier date agreed upon by the parties, on a supplemental index.

c. As part of the specific information required, the Offeror shall submit, with the Offeror's proposal, certified cost or pricing data (as defined at FAR 2.101). The Offeror shall clearly identify on the Offeror's coversheet that certified cost or pricing data are included as part of the proposal. In addition, the Offeror shall submit with the Offeror's proposal any information reasonably required to explain the Offeror's estimating process, including
    1. The judgmental factors applied and the mathematical or other methods used in the estimate, including those used in projecting from known data; and
    2. The nature and amount of any contingencies included in the proposed price.

d. The Offeror shall show the relationship between contract line item prices and the total contract price. The Offeror shall attach cost element breakdowns for each proposed line item, using the appropriate format prescribed in the "Formats for Submission of Line Item Summaries'' section of this table. The Offeror shall furnish supporting breakdowns for each cost element, consistent with the Offeror's cost accounting system.

e. When more than one contract line item is proposed, the Offeror shall also provide summary total amounts covering all line items for each element of cost.

f. Whenever the Offeror have incurred costs for work performed before submission of a proposal, the Offeror shall identify those costs in the Offeror's cost/price proposal.

g. If the Offeror have reached an agreement with Government representatives on use of forward pricing rates/factors, identify the agreement, include a copy, and describe its nature.

h. As soon as practicable after final agreement on price or an earlier date agreed to by the parties, but before the award resulting from the proposal, the Offeror shall, under the conditions stated in FAR 15.406 2, submit a Certificate of Current Cost or Pricing Data.

2. **Cost Elements**

Depending on the Offeror's system, the Offeror shall provide breakdowns for the following basic cost elements, as applicable:

a. Materials and services.

Provide a consolidated priced summary of individual material quantities included in the various tasks, orders, or contract line items being proposed and the basis for pricing (vendor quotes, invoice prices, etc.). Include raw materials, parts, components, assemblies, and services to be produced or performed by others. For all items proposed, identify the item and show the source, quantity, and price. Conduct price analyses of all subcontractor proposals. Conduct cost analyses for all subcontracts when certified cost or pricing data are submitted by the subcontractor. Include these analyses as part of the Offeror's own certified cost or pricing data submissions for subcontracts expected to exceed the appropriate threshold in FAR 15.403-4. Submit the subcontractor certified cost or pricing data as part of the Offeror's own certified cost or pricing data as required in paragraph a.2. below. These requirements also apply to all subcontractors if required to submit certified cost or pricing data.

1. *Adequate Price Competition*. Provide data showing the degree of competition and the basis for establishing the source and reasonableness of price for those acquisitions (such as subcontracts, purchase orders, material order, etc.) exceeding, or expected to exceed, the appropriate threshold set forth at FAR 15.403-4 priced on the basis of adequate price competition. For inter organizational transfers priced at other than the cost of comparable competitive commercial work of the division, subsidiary, or affiliate of the contractor, explain the pricing method (see FAR 31.20526(e)).

2. *All Other*. Obtain certified cost or pricing data from prospective sources for those acquisitions (such as subcontracts, purchase orders, material order, etc.) exceeding the threshold set forth in FAR 15.403-4 and not otherwise exempt, in accordance with FAR 15.403-1(b) (i.e., adequate price competition, commercial items, prices set by law or regulation or waiver). Also provide data showing the basis for establishing source and reasonableness of price. In addition, provide a summary of the Offeror's cost analysis and a copy of certified cost or pricing data submitted by the prospective source in support of each subcontract, or purchase order that is the lower of either$12.5 million or more, or both more than the pertinent cost or pricing data threshold and more than 10 percent of the prime contractor's proposed price. Also submit any information reasonably required to explain the Offeror's estimating process (including the judgmental factors applied and the mathematical or other methods used in the estimate, including those used in projecting from known data, and the nature and amount of any contingencies included in the price). The Contracting Officer may require the Offeror to submit certified cost or pricing data in support of proposals in lower amounts. Subcontractor certified cost or pricing data shall be

accurate, complete and current as of the date of final price agreement, or an earlier date agreed upon by the parties, given on the prime contractor's Certificate of Current Cost or Pricing Data. The prime contractor is responsible for updating a prospective subcontractor's data. For standard commercial items fabricated by the Offeror that are generally stocked in inventory, provide a separate cost breakdown, if priced based on cost. For inter organizational transfers priced at cost, provide a separate breakdown of cost elements. Analyze the certified cost or pricing data and submit the results of the Offeror's analysis of the prospective source's proposal. When submission of a prospective source's certified cost or pricing data is required as described in this paragraph, it shall be included, along with the Offeror's own certified cost or pricing data submission ,as part of the Offeror's own certified cost or pricing data. The Offeror shall also submit any other certified cost or pricing data obtained from a subcontractor, either actually or by specific identification, along with the results of any analysis performed on that data.

b. **Direct Labor**

Provide a time phased (e.g., monthly, quarterly, etc.) breakdown of labor hours, rates, and cost by appropriate category, and furnish bases for estimates.

c. **Indirect Costs**

Indicate how the Offeror has computed and applied the Offeror's indirect costs, including cost breakdowns. An example is provided in attachment entitled IDC Two Tier Example (See PART 9) or can be found at http://oamp.od.nih.gov/sites/default/files/DFAS/IDCTwoTierExample_508.xlsx . Show trends and budgetary data to provide a basis for evaluating the reasonableness of proposed rates. Indicate the rates used and provide an appropriate explanation.

d. **Other Costs**

List all other costs not otherwise included in the categories described above(e.g., special tooling, travel, computer and consultant services, preservation, packaging and packing, spoilage and rework, and Federal excise tax on finished articles) and provide bases for pricing.

e. **Royalties**

If royalties exceed $1,500, the Offeror shall 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 numbers 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 27.202and 31.205-37).

f. **Facilities Capital Cost of Money**

When the Offeror elect to claim facilities capital cost of money as an allowable cost, the Offeror shall submit Form CASB CMF and show the calculation of the proposed amount (see FAR 31.205 10).

3. **Formats for Submission of Line Item Summaries**

The detailed breakdown shall be in the format as shown on the form **Breakdown of Proposed Estimated Cost (plus fee) w/excel spreadsheet** (PART 9, List of Attachments). For each separate cost estimate, the Offeror shall furnish a breakdown by cost element as indicated above. In addition, summary total amounts shall be furnished. In the event the RFP cites specific line items, by number, a cost breakdown for each line item shall be furnished.

4. **General Information**

a. There is a clear distinction between submitting certified cost or pricing data and merely making available books, records, and other documents without identification. The requirement for submission of certified cost or pricing data is met when all accurate cost or pricing data reasonably available to the Offeror have been submitted, either actually or by specific identification, to the Contracting Officer or an authorized representative. As later information comes into the Offeror's possession, it should be submitted promptly to the Contracting Officer in a manner that clearly shows how the information relates to the Offeror's price proposal. The requirement for submission of certified cost or pricing data continues up to the time of agreement on price, or an earlier date agreed upon between the parties if applicable.

b. By submitting the Offeror's proposal, the Offeror grant the Contracting Officer or an authorized representative the right to examine records that formed the basis for the pricing proposal. That examination can take place at any time before award. It may include those books, records, documents, and other types of factual information (regardless of form or whether the information is specifically referenced or included in the proposal as the basis for pricing) that will permit an adequate evaluation of the proposed price.

5. **Requirements for Certified Cost or Pricing Data and Data Other than Certified Cost or Pricing Data, FAR Clause 52.215-20** (October 2010)

a. Exceptions from certified cost or pricing data.

1. In lieu of submitting certified cost or pricing data, Offerors may submit a written request for exception by submitting the information described in the following subparagraphs. The Contracting Officer may require additional supporting information, but only to the extent necessary to determine whether an exception should be granted, and whether the price is fair and reasonable.

A. Identification of the law or regulation establishing the price offered. If the price is controlled under law by periodic rulings, reviews, or similar actions of a governmental body, attach a copy of the controlling document, unless it was previously submitted to the contracting office.

B. Commercial item exception. For a commercial item exception, the Offeror shall submit, at a minimum, information on prices at which the same item or similar items have previously been sold in the commercial market that is adequate for evaluating the reasonableness of the price for this acquisition. Such information may include:

A. For catalog items, a copy of or identification of the catalog and its date, or the appropriate pages for the offered items, or a statement that the catalog is on file in the buying office to which the proposal is being submitted. Provide a copy or describe current discount policies and price lists (published or unpublished), e.g., wholesale, original equipment manufacturer, or reseller. Also explain the basis of each offered price and its relationship to the established catalog price, including how the proposed price relates to the price of recent sales in quantities similar to the proposed quantities;

B. For market priced items, the source and date or period of the market quotation or other basis for market price, the base amount, and applicable discounts. In addition, describe the nature of the market;

C. For items included on an active Federal Supply Service Multiple Award Schedule contract, proof that an exception has been granted for the schedule item.

2. The Offeror grants the Contracting Officer or an authorized representative the right to examine, at any time before award, books, records, documents, or other directly pertinent records to verify any request for an exception under this provision, and the reasonableness of price. For items priced using catalog or market prices, or law or regulation, access does not extend to cost or profit information or other data relevant solely to the Offeror's determination of the prices to be offered in the catalog or marketplace.

b. Requirements for certified cost or pricing data. If the Offeror is not granted an exception from the requirement to submit certified cost or pricing data, the following applies:

6. **Certification for Offerors that are Majority-Owned by Multiple Capital Operating Companies, Hedge Funds, or Private Equity Firms.**

If applicable the offeror shall provide a copy of this certification (See PART 9) with its proposal.

7. **SBIR Funding Agreement Certification**

Each offeror shall register in SBA's Company Registry Database and submit a pdf document of the registration with its proposal. See SBIR Funding Certification, PART 9.

8. **Salary Rate Limitation in Fiscal Year 2014**

Offerors are advised that pursuant to P.L. 113-76, signed into law on January 17, 2014, no NIH Fiscal Year 2014 (until September 30, 2014) funds may be used to pay the direct annual salary of an individual through any contract awarded as a result of this solicitation at a rate in excess of the Executive Schedule, Level II* (direct salary is exclusive of Overhead, Fringe Benefits and General and Administrative expenses, also referred to as "indirect cost" or "facilities and administrative (F&A)costs"). Direct salary has the same meaning as the term "institutional base salary." An individual's direct salary (or institutional base salary) is the annual

compensation that the Contractor pays for an individual's appointment whether that individual's time is spent on research, teaching, patient care or other activities. Direct salary (or institutional base salary) excludes any income that an individual maybe permitted to earn outside of duties to the Contractor.

This does not preclude the Offeror from absorbing that portion of an employee's annual salary(plus the dollar amount for fringe benefits and associated indirect costs) that exceeds a rate of the Executive Schedule, Level II*. The salary rate limitation set by P.L 113-76 applies only to Fiscal Year 2014 funds, however, salary rate ceilings for subsequent years may be included in future DHHS appropriation acts. Multi-year contracts awarded pursuant to this solicitation may be subject to unilateral modifications by the Government if an individual's annual salary exceeds any salary rate ceiling established in future appropriations acts. The Executive Schedule, Level II* annual salary rate limitation also applies to individuals proposed under subcontracts; however it does not apply to consultants. P.L. 113-76 states:

"None of the funds appropriated in this title shall be used to pay the salary of an individual through a grant or other extramural mechanism, at a rate in excess of Executive Level II."

LINK TO EXECUTIVE SCHEDULE RATES OF PAY: http://www.opm.gov/oca/*(For current year rates, click on Salaries and Wages/Executive Schedule/Rates of Pay for the Executive Schedule. For prior year rates, click on Salaries and Wages/select Another Year at the top of the page/Executive Schedule/Rates of Pay for the Executive Schedule. Rates are effective January1 of each calendar year unless otherwise noted.)*

***Note to Offerors**: The current Fiscal Year Executive Level II Salary Rate shall be adhered to in the preparation of the Offeror's proposal. All costs associated with any resultant contract award shall be incompliance with the current Fiscal Year Executive Level II Salary rates.

9. **Total Compensation Plan**

a. Instructions

1. Total compensation (salary and fringe benefits) of professional employees under service contracts may, in some cases, be lowered by recompetition of these contracts. Lowering of compensation can be detrimental in obtaining the necessary quality of professional services needed for adequate performance of service contracts. It is, therefore, in the best interest of the Government that professional employees, as defined in 29 CFR Part 541, be properly compensated in these contracts. All Offerors as a part of their Business Proposal will submit a "Total Compensation Plan" (salaries and fringe benefits) for these professional employees for evaluation purposes.

2. The Government will evaluate the Total Compensation Plan to ensure that this compensation reflects a sound management approach and an understanding of the requirements to be performed. It will include an assessment of the Offeror's ability to provide uninterrupted work of high quality. The total compensation proposed will be evaluated in terms of enhancing recruitment and retention of personnel and its realism and consistency with a total plan for compensation (both salaries and fringe benefits).

3. Evaluation for award, therefore, will include an assessment of the Total Compensation Plan submitted by each Offeror.

b. Evaluation

1. **Total Compensation Plan (Professional Employees)**
   In establishing compensation levels for professional employees, the total compensation(both salaries

and fringe benefits) proposed shall reflect a clear understanding of the requirements of the work to be accomplished and the suitability of the proposed compensation structure to obtain and retain qualified personnel to meet mission objectives. The salary rates or ranges shall recognize the distinct differences in professional skills and the complexity of varied disciplines as well as job difficulty. Proposals offering total compensation levels less than currently being paid by the predecessor Contractor for the same work will be evaluated, in addition to the above, on the basis of maintaining program continuity, uninterrupted work of high quality, and availability of required competent professional employees. Offerors are cautioned that instances of lowered compensation for essentially the same professional work may be considered a lack of sound management judgment in addition to indicating a lack of understanding of the requirement. Provide supporting salary documentation for all individuals proposed (i.e. personnel documents, pay stubs, balance sheets).

2. **Cost (Professional Compensation)**
   Proposals which are unrealistically low or do not reflect a reasonable relationship of compensation to the professional job categories so as to impair the Contractor's ability to recruit and retain competent professional employees, may be viewed as reflecting a failure to comprehend the complexity of the contract requirements. The Government is concerned with the quality and stability of the work force to be employed on this contract. The compensation data required will be used in evaluation of the Offeror's understanding of the contract requirements.

3. **Other (Labor Relations)**
   An assessment of the potential for adverse effect upon performance and maintenance of the required number of professional employees with requisite skills resulting from an unrealistically low compensation structure will also be made.

4. **Federal Acquisition Regulation Clauses incorporated by Reference**
   FAR Clause 52.222-46, Evaluation of Compensation for Professional Employees.

10. **Other Administrative Data**

a. Property

1. It is HHS policy that Contractors will provide all property necessary for contract performance. Exception may be granted to provide Government property (Government-furnished or Contractor-acquired), but only when approved by the Contracting Officer. If the Offeror requests that Government property be provided, other than that specified under "Government Furnished Property," below , the proposal shall include a comprehensive justification addressing the following items:
   A. State why the property is essential to contract performance and whether the property will be used exclusively for this contract.
   B. Describe other alternatives (e.g., purchase, lease, etc.) pursued and why they were not viable options.

2. Government Property
   The Offeror shall identify Government property in its possession which it proposes to use in the performance of the prospective contract as follows:
   A. A list or description of all Government property that the Offeror or its subcontractors propose to use on a rent-free basis. The list shall identify the accountable contract under which the property is held and the authorization for its use (from the Contracting Officer having cognizance of the property);
   B. The dates during which the property will be available for use (including the first, last, and all intervening months) and, for any property that will be used concurrently in performing two or

more contracts, the amounts of the respective uses in sufficient detail to support prorating the rent;

C. The amount of rent that would otherwise be charged in accordance with FAR 52.245-9, Use and Charges; and

D. A description of the Offeror's property management system, plan, and any customary commercial practices, voluntary consensus standards, or industry-leading practices and standards to be used in the Offeror in managing Government property.

NOTE: The Contracting Officer will consider any potentially unfair competitive advantage that may result from an Offeror or contractor possessing Government property. This will be done by adjusting the offers by applying, for evaluation purposes only, a rental equivalent evaluation factor, as specified in FAR 52.245-9.

3. Government-Furnished Property
   No Government Furnished Property is offered for this acquisition.

4. The management and control of any Government property shall be in accordance with the HHS Publication entitled, "HHS Contracting Guide for Contract of Government Property," which can be found at: http://hhs.gov/hhsmanuals/logisticsmanual/AppendixQ_HHS Contracting Guide.pdf .

b. Royalties

The Offeror shall furnish information concerning royalties which are anticipated to be paid in connection with performance of work under the proposed contract.

c. Submission of Electronic Funds Transfer Information with Offer, FAR Clause 52.232-38 (JULY 2013)

The Offeror shall provide, with its offer, the following information that is required to make payment by electronic funds transfer (EFT) under any contract that results from this solicitation. This submission satisfies the requirement to provide EFT information under paragraphs (b)(1) and (j) of the clause at 52.232 34, Payment by Electronic Funds Transfer Other than System for Award Management.

1. The solicitation number (or other procurement identification number).
2. The Offeror's name and remittance address, as stated in the offer.
3. The signature (manual or electronic, as appropriate), title, and telephone number of the Offeror's official authorized to provide this information.
4. The name, address, and 9 digit Routing Transit Number of the Offeror's financial agent.
5. The Offeror's account number and the type of account (checking, savings, or lockbox).
6. If applicable, the Fedwire Transfer System telegraphic abbreviation of the Offeror's financial agent.
7. If applicable, the Offeror shall also provide the name, address, telegraphic abbreviation, and 9 digit Routing Transit Number of the correspondent financial institution receiving the wire transfer payment if the Offeror's financial agent is not directly on line to the Fedwire and, therefore, not the receiver of the wire transfer payment.

(End of Provision)

d. Financial Capacity

The Offeror shall indicate if it has the necessary financial capacity, working capital, and other resources to perform the contract without assistance from any outside source. If not, indicate the amount required and the anticipated source.

e. Adequate Accounting System

FAR Part 16 sets forth the requirements and limitations for consideration of contract type. As stated in PART 3.2., General Instructions of this solicitation, the resultant contract will not be Firm-Fixed Price.

Therefore, the Offeror's/contractor's accounting system and practices shall be adequate and suitable for accumulating costs under government contracts.

To be considered for an award under this solicitation, the Offeror shall include, in the Business Proposal, the following Certification found in attachment 19:

“By submission of its signed offer, the Offeror certifies that it’s accounting system:

- Complies with generally accepted accounting principles (GAAP).
- Provides for:
    - Proper segregation of direct costs from indirect costs.
    - Identification and accumulation of direct costs by contract.
    - A logical and consistent method for the allocation of indirect costs to intermediate and final cost objectives.
    - Accumulation of costs under general ledger control.
    - A timekeeping system that identifies employees' labor by intermediate or final cost objectives.
    - A labor distribution system that charges direct and indirect labor to the appropriate cost objectives.
    - Interim (at least monthly) determination of costs charged to a contract through routine posting of books of account.
    - Exclusion from costs charged to government contracts of amounts that are not allowable in terms of FAR 31, "Contract Cost Principles and Procedures," or other contract provisions.
    - Identification of costs by contract line item and by units (as if each unit or line item were a separate contract) if required by the proposed contract.
    - Segregation of preproduction costs from production costs, if applicable.
- Accounting system provides financial information:
    - Required by contract clauses concerning limitation of cost (FAR 52.232-20 and21) or limitation on payments (FAR 52.216-16).
    - Required to support requests for progress payments.
- Accounting system was designed, and records are maintained in such a manner that adequate, reliable data are developed for use in pricing follow-on acquisitions.
- Accounting system is currently in full operation.

The Contracting Officer reserves the right to request, with the Final Proposal Revision (FPR), a current (within 18 months) CPA opinion confirming that the Offeror's accounting system is compliant as certified above.

11. **Qualifications of the Offeror**

The Offeror are requested to submit a summary of the Offeror's "General Experience, Organizational Experience Related to this RFP, Performance History and Pertinent Contracts."

a. General Experience

General experience is defined as general background, experience and qualifications of the Offeror. A discussion of proposed facilities which can be devoted to the project may be appropriate.

b. Organizational Experience Related to the RFP

Organizational experience is defined as the accomplishment of work, either past or on-going, which is comparable or related to the effort required by this RFP. This includes overall Offeror or corporate experience, **but not** the experience and/or past performance of individuals who are proposed as personnel involved with the Statement of Work in this RFP.

c. Performance History

Performance history is defined as meeting contract objectives within **delivery** and **cost schedules** on efforts, either past or on-going, which is comparable or related to the effort required by this RFP.

d. Pertinent Contracts

Pertinent contracts are defined as a listing of each related contract completed within the last three years or currently in process. The listing should include: 1) the contract number; 2) contracting agency; 3) contract dollar value; 4) dates contract began and ended (or ends); 5) description of contract work; 6) explanation of relevance of work to this RFP; 7) actual delivery and cost performance versus delivery and cost agreed to in the contract(s). For award fee contracts, separately state in dollars the base fee and award fee available and the award fee actually received. The same type of organizational experience and past performance data should be submitted.

e. Pertinent Grants

List grants supported by the Government that involved similar or related work to that called for in this RFP. Include the grant number, involved agency, names of the grant specialist and the Science Administrator, identification of the work, and when performed.

The Offeror are cautioned that omission or an inadequate or inaccurate response to this very important RFP requirement could have a negative effect on the overall selection process. Experience and past performance are factors which are relevant to the ability of the Offerors to perform and are considered in the source selection process.

12. **Subcontractors**

If subcontractors are proposed, please include a commitment letter from the subcontractor detailing:

a. Willingness to perform as a subcontractor for specific duties (list duties).
b. What priority the work will be given and how it will relate to other work.
c. The amount of time and facilities available to this project.
d. Information on their cognizant field audit offices.
e. How rights to publications and patents are to be handled.
f. A complete cost proposal in the same format as the Offeror's cost proposal.

Note: Organizations that plan to enter into a subcontract with an educational concern under a contract awarded under this RFP should refer to the following Web Site for a listing of clauses that are required to be incorporated in Research & Development (R&D) subcontracts with educational institutions: http://ocm.od.nih.gov/contracts/rfps/FDP/FDPclausecover.htm

13. **Proposer's Annual Financial Report**

A copy of the organization's most recent annual report shall be submitted as part of the business proposal.

14. **Travel Cost/Travel Policy**

a. Travel Costs – Commercial

Costs for lodging, meals, and incidental expenses incurred by Contractor personnel shall be considered to be reasonable and allowable to the extent they do not exceed on a daily basis the per diem rates set forth in the Federal Travel Regulations, General Services Administration (GSA). Therefore, if travel costs are applicable and proposed by Offerors, please be advised that they shall be calculated using the per diem rate schedule as established by GSA. Reimbursement of travel costs under any contract awarded from this RFP shall be in accordance with FAR 31.205-46.

b. Travel Policy

One copy of the Offeror's (and any proposed subcontractor's) written travel policy shall be included in the business proposal (original only). If an Offeror (or any proposed subcontractor) does not have a written travel policy, the Offeror shall so state.

3.7.5 Past Performance

A. Offerors shall submit the following information as part of their Business proposal.

A list of the all the contracts completed during the past Five years and ALL CONTRACTS currently being performed that are similar in nature to the solicitation work scope. Contracts listed may include those entered into by the Federal Government, agencies of state and local governments and commercial concerns. Offerors may also submit past performance information regarding predecessor companies, key personnel who have relevant experience or subcontractors that will perform major or critical aspects of the requirement when such information is relevant to the instant acquisition. For the purposes of this solicitation, a "major subcontract" is defined as having a value of $500,000.

Include the following information for each contract or subcontract listed:

1. Name of Contracting Organization
2. Contract Number (for subcontracts, provide the prime contract number and the subcontract number)
3. SBIR Topic Number and Phase I or II, if applicable.
4. Contract Type (i.e. Cost-reimbursement, fixed price, labor hour, time and materials)
5. Total Contract Value
6. Description of Requirement
7. Contracting Officer's Name and Telephone Number
8. Program Manager's Name and Telephone Number
9. North American Industry Classification System (NAICS) Code

10. Whether contract was an SBIR, STTR, or other. The Offeror may provide information on problems encountered on the identified contracts and the Offeror's corrective actions.

11. Negotiated Indirect Rates

B. The Government is not required to contact all references provided by the Offeror. Also, references other than those identified by the Offeror may be contacted by the Government to obtain additional information that will be used in the evaluation of the Offeror's past performance.

4 METHOD OF SELECTION AND EVALUATION CRITERIA

4.1 EVALUATION FACTORS FOR AWARD

4.1.1 General

Proposals passing this initial screening will be evaluated against four factors. The factors in order of importance are: technical, areas of high program relevance, program balance (i.e. balance among areas of research), and availability of funds. Cost is less important to the overall contract award decision. The Government intends to make an award(s) to that Offeror(s) whose proposal provides the best overall value to the Government.

The Agency is under no obligation to fund any proposal or any specific number of proposals in a given topic. It also may elect to fund several or none of the proposed approaches to the same topic or subtopic. The Government reserves the right to make award(s) without discussions.

The evaluation will be based on the demonstrated capabilities of the prospective Contractors in relation to the needs of the project as set forth in the SOLICITATION. The merits of each proposal will be evaluated carefully. Each proposal shall document the feasibility of successful implementation of the requirements of the SOLICITATION. Offerors shall submit information sufficient to evaluate their proposals based on the detailed factors listed below.

4.1.2 Cost/Price Evaluation

Offeror(s) cost/price proposal will be evaluated for reasonableness. For a price to be reasonable, it shall represent a price to the government that a prudent person would pay when consideration is given to prices in the market. Normally, price reasonableness is established through adequate price competition, but may also be determined through cost and price analysis techniques as described in FAR 15.404.

Cost Realism: The specific elements of each Offeror(s) proposed costs are realistic when the proposed cost elements are evaluated and found to: 1) be realistic for the work to be performed; 2) reflect a clear understanding of the requirements; and 3) be consistent with the unique methods of performance and materials described in the Offeror(s) technical proposal.

Cost Realism will be evaluated only on the Offeror(s) inputs which the Government will use to determine the most probable cost to perform the contract in a manner consistent with the Offeror's proposal. Cost realism analysis will be conducted in accordance with FAR 15.404-1(d). The result of the cost realism analysis will be considered in the making the best value tradeoff decision.

4.1.3 Technical Evaluation Factors

The evaluation factors are used by the external peer review committee when reviewing the technical proposals. The factors below are listed in the order of relative importance with weights assigned for evaluation purposes. Subfactors are listed in order of relative importance.

Technical Evaluation Factors for Phase II Proposal	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%
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 II from private sector or other non-SBIR funding sources, (c) any other indicators of commercial potential for the proposed research, and the existence of third phase follow-on commitments for the subject research.	30%
3. The qualifications of the proposed PDs/PIs, supporting staff and consultants. For proposal 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%

4.1.4 Past Performance Factor

Offerors' past performance information will be evaluated subsequent to the technical evaluation. However, this evaluation will not be conducted on any Offeror whose proposal is determined to be technically unacceptable.

The evaluation will be based on information obtained from references provided by the offeror, other relevant past performance information obtained from other sources known to the Government, and any information supplied by the offeror concerning problems encountered on the identified contracts and corrective action taken.

The government will assess the relative risks associated with each offeror. Performance risks are those associated with an offeror's likelihood of success in performing the acquisition requirements as indicated by that offeror's record of past performance.

When assessing performance risks, the Government, to the fullest extent practicable, will focus on the past performance of the offeror as it relates to all acquisition requirements, in terms of Quality, Schedule, Cost Control, Business Relations, Management, Small Business and Other factors as deemed appropriate.

The Government will consider the currency and relevance of the information, source of the information, context of the data, and general trends in the offeror's performance.

The lack of a relevant performance record may result in an unknown performance risk assessment, which will neither be used to the advantage nor disadvantage of the offeror.

4.2 OTHER AWARD CONSIDERATIONS

Offerors must have sufficiently addressed the following areas prior to award, if applicable:

4.2.1 Human Subject Evaluation

This research project involves human subjects. NIH Policy requires:

a. Protection of Human Subjects from Research Risks

The Offeror's proposal shall address the involvement of human subjects and protections from research risk relating to their participation, or provide sufficient information on the research subjects to allow a determination by NCI that a designated exemption is appropriate .If the Offeror claim that this research should be considered exempt from coverage by the Federal Regulations at 45 CFR 46, the proposal should address why the Offeror believe it is exempt, and under which exemption it applies. The reviewers will evaluate the proposal with regard to four issues: Risks to Human Subjects, Adequacy of Protection Against Risks, Potential Benefits of the Proposed Research to the Subjects and Others, and Importance of the Knowledge to be Gained. See PART 3 for a complete discussion of what is required to be addressed for each of these issues. Based on the response to this criterion, this section of the proposal may be rated "unacceptable" (i.e., concerns are identified as to the protections described against risk to human subjects or no discussion is found regarding protections against risk to human subjects) or "acceptable." If the reviewers find that this portion of the proposal is "unacceptable" they will provide a narrative supporting their finding.

If the Government includes the Offeror's proposal in the competitive range (for competitive proposals), or if the Government holds discussions with the selected source (for sole source acquisitions), the Offeror will be afforded the opportunity to address the concerns raised by the reviewers. The Offeror will be able to further discuss and/or clarify the Offeror's position until submission of the Offeror's Final Proposal Revision (FPR). Once discussions are closed with the submission of the Offeror's FPR, if the Offeror's proposed plan for the protection of human subjects from research risks is still found to be unacceptable, then the Offeror's proposal may not be considered further for award.

b. Women and Minorities

Women and members of minority groups and their subpopulations shall be included in the study population of research involving human subjects, unless a clear and compelling rationale and justification are provided indicating that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. In addition, for NIH-Defined Phase III clinical trials, all proposals and/or protocols shall provide a description of plans to conduct analyses, as appropriate, to detect significant differences in intervention effect (see NIH Guide http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm , Definitions - Significant Difference) by sex/gender, racial/ethnic groups, and relevant subpopulations, if applicable, unless the Government has specified that this solicitation involves a sex/gender specific study or a single or limited number of minority population groups. The proposal also shall include one of the following plans:

- Plans to conduct valid analysis 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/or racial/ethnic groups as subject selection criterion is not required; however, inclusion and analyses are 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 between subgroups.

Also, the proposal shall address the proposed outreach programs for recruiting women and minorities as participants. Reviewers will consider the areas covered here and in PART 3 of the solicitation in narrative form in their evaluation. Some of the issues they will evaluate include:

- whether the plan proposed includes minorities and both genders in adequate representation
- how the Offeror addresses the inclusion of women and members of minority groups and their subpopulations in the development of a proposal that is appropriate to the scientific objectives of the solicitation
- the description of the proposed study populations in terms of sex/gender and racial/ethnic groups and the rationale for selection of such subjects
- if exclusion is proposed, that the rationale is appropriate with respect to the health of the subjects and/or to the purpose of the research.
- In addition, for gender exclusion, the reviewers will examine the rationale to determine if it is because:
    - the purpose of the research constrains the Offeror's selection of study participants 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); or
    - gender representation of specimens or existing datasets cannot be accurately determined, and this does not compromise the scientific objectives of the research.
- For minority group exclusion, the reviewers will examine the rationale to determine if those minority groups are excluded because:
    - inclusion of those groups would be inappropriate with respect to their health; or
    - inclusion of those groups would be inappropriate with respect to the purpose of the research.
- For NIH-defined Phase III clinical trials, reviewers will also consider whether there is an adequate description of plans to conduct analyses to detect significant differences of clinical or public health importance in intervention effect(s) by sex/gender and/or racial ethnic subgroups when the intervention effect(s) is expected in the primary analyses, or if there is an adequate description of plans to conduct valid analyses of the intervention effect in subgroups when the intervention effect(s) is not expected in the primary analyses.

If the Offeror determines that inclusion of women and minority populations is not feasible, the Offeror shall submit a detailed rationale and justification for exclusion of one or both groups from the study population with the technical proposal. The Government will review the rationale to determine if it is appropriate with respect to the health of the subjects and/or the purpose of the research.

Based on the evaluation of the response to this criterion, this section of the proposal may be rated "unacceptable" (i.e., no discussion can be found regarding the proposed gender/minority inclusion plans, or concerns are identified as to the gender or minority representation, or the proposal does not adequately address limited representation of one gender or minority; or the plan is not in accordance with NIH policy

guidelines) or "acceptable." See PART 3 of the solicitation for the requirements of women/minorities inclusion. If the reviewers find that this portion of the proposal is "unacceptable" they will provide a narrative supporting their finding.

If the Government includes the Offeror's proposal in the competitive range (for competitive proposals), or if the Government holds discussions with the selected source (for sole source acquisitions), the Offeror will be afforded the opportunity to address the concerns raised by the reviewers. The Offeror will be able to further discuss and/or clarify the Offeror's position until submission of the Offeror's Final Proposal Revision (FPR).Once discussions are closed with the submission of the Offeror's FPR, if the Offeror's proposed plan for the inclusion/exclusion of women and minorities is still found to be unacceptable, then the Offeror's proposal may not be considered further for award.

c. Children

Children (i.e. individuals under the age of 21) shall be included in all human subject research unless there are clear and compelling reasons not to include them.

The Offeror's proposal shall include a description of plans for including children. If the Offeror plan to exclude children from the required research, the Offeror's proposal shall present an acceptable justification for the exclusion. If the Offeror determine that exclusion of a specific age range of child is appropriate, the Offeror's proposal shall also address the rationale for such exclusion. Also, the plan shall include a description of the expertise of the investigative team for dealing 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/objective of the solicitation. Also, see PART 3of the solicitation for further specific requirements on inclusion of children.

Based on the reviewers' evaluation of the Offeror's response, this section of the proposal may be rated "unacceptable" (i.e., no discussion can be found regarding the proposed inclusion plans for children; or concerns are identified as to the Offeror's response regarding the inclusion of children; or the plan is not in accordance with NIH policy guidelines) or "acceptable." If the reviewers find that this portion of the proposal is "unacceptable" they will provide a narrative supporting their finding.

If the Government includes the Offeror's proposal in the competitive range (for competitive proposals), or if the Government holds discussions with the selected source (for sole source acquisitions), the Offeror will be afforded the opportunity to address the concerns raised by the reviewers. The Offeror will be able to further discuss and/or clarify the Offeror's position until submission of the Offeror's Final Proposal Revision (FPR). Once discussions are closed with the submission of the Offeror's FPR, if the Offeror's proposed plan for the inclusion of children is still found to be unacceptable, then the Offeror's proposal may not be considered further for award.

d. Data and Safety Monitoring

The Offeror's proposal shall include a general description of the Data and Safety Monitoring Plan for all clinical trials. The principles of data and safety monitoring require that all biomedical and behavioral clinical trials be monitored to ensure the safe and effective conduct of human subjects research, and to recommend conclusion of the trial when significant benefits or risks are identified or if it is unlikely that the trial can be concluded successfully. Risks associated with participation in research shall be minimized to the extent practical and the method and degree of monitoring should be commensurate with risk. Additionally, all plans shall include procedures for adverse event reporting. Finally, generally, for Phase III clinical trials, the establishment of a Data and Safety Monitoring Board (DSMB) is required, whereas for Phase I and II clinical trials, the establishment of a DSMB is optional. The reviewers will rely on the Statement of Work and PART 3

in the solicitation, as well as any further technical evaluation factors in this PART 4.2, as applicable, for the solicitation's specific requirements for data and safety monitoring.

As a part of the evaluation for proposals, the reviewers will consider the acceptability of the proposed data and safety monitoring plan with respect to the potential risks to human participants, complexity of study design, and methods for data analysis. Based on the evaluation of the response to this criterion, this section of the proposal may be rated "unacceptable" (i.e., concerns are identified as to the adequacy of the monitoring plan or no discussion can be found regarding the proposed monitoring plans) or "acceptable." If the reviewers find that this portion of the proposal is "unacceptable" they will provide a narrative supporting their finding.

If the Government includes the Offeror's proposal in the competitive range (for competitive proposals), or if the Government holds discussions with the selected source (for sole source acquisitions), the Offeror will be afforded the opportunity to address the concerns raised by the reviewers. The Offeror will be able to further discuss and/or clarify the Offeror's position until submission of the Offeror's Final Proposal Revision (FPR). Once discussions are closed with the submission of the Offeror's FPR, if the Offeror's proposed plan for data and safety monitoring is still found to be unacceptable, then the Offeror's proposal may not be considered further for award.

4.2.2 Live Vertebrate Animals Evaluation

The Offerors proposal shall include, as a separate section of the Technical Proposal titled "Vertebrate Animal Section," (VAS) a complete, concise (no more than 1-2 pages) description addressing the following five points. (See NIH Guide Notice NOT-OD-10-049 at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-10-049.html):

a. Detailed description of the proposed use of the animals, including species, strains, ages, sex and number to be used.

b. Justification for the use of animals, choice of species, and numbers to be used.

c. Information on the veterinary care of the animals.

d. Description of procedures for minimizing discomfort, distress, pain and injury.

e. Method of euthanasia and the reasons for the selection.

As part of the overall technical evaluation of proposals, the reviewers will consider the acceptability of the Offeror's description in the VAS of the technical proposal. The discussion of all five points will be addressed and evaluated. Based on the evaluation of this Section, the VAS may be rated "unacceptable" (i.e., concerns are identified as to the adequacy of the description addressing each of the five points, or no discussion can be found regarding the VAS), or "acceptable." If the reviewers find that this Section of the technical proposal is "unacceptable" they will provide a narrative supporting their findings.

If the Government includes the Offeror's proposal in the competitive range (for competitive proposals), or if the Government holds discussions with the selected source (for sole source acquisitions), the Offeror will be afforded the opportunity to address the concerns raised by reviewers. The Offeror will be able to further discuss and/or clarify the Offeror's position until submission of the Offeror's Final Proposal Revision (FPR). Once discussions are closed with the submission of the Offeror's FPR, if the Offeror's proposed description under the VAS is still found to be unacceptable, then the Offeror's proposal may not be considered further for award.

If a subcontract is proposed, an Inter-Institutional Agreement shall be established with the Office of Laboratory Animal Welfare (OLAW) prior to award.

4.2.3 Evaluation of Data Sharing Plan

The Offeror's plan for the sharing of final research data shall be assessed for appropriateness and adequacy. If the Offeror's proposal does not include a plan or if the plan in the Offeror's proposal is considered "unacceptable," and the Government includes the Offeror's proposal in the competitive range (for competitive proposals), or if the Government holds discussions with the selected source (for sole source acquisitions), the Offeror will be afforded the opportunity to further discuss, clarify or modify the Offeror's data sharing plan during discussions and in the Offeror's Final Proposal Revision (FPR). If the Offeror's data sharing plan is still considered "unacceptable" by the Government after discussions, the Offeror's proposal may not be considered further for award.

4.2.4 Evaluation of Plan for Sharing Model Organisms for Biomedical Research

The Offeror's proposal shall address the plans for sharing model organisms, OR state appropriate reasons why such sharing is restricted or not possible. Offerors shall also address as part of the sharing plan if, or how, they will exercise their intellectual property rights while making model organisms and research resources available to the broader scientific community. The discussion areas regarding intellectual property outlined in PART 3 should be addressed.

If the Offeror's proposal does not include a plan, appropriate reasons for restricting sharing, or, if the plan in the Offeror's proposal is considered "unacceptable," and the Government includes the Offeror's proposal in the competitive range(for competitive proposals), or if the Government holds discussions with the selected source (for sole source acquisitions), the Offeror will be afforded the opportunity to further discuss, clarify or modify the Offeror's plan for sharing model organisms during discussions and in the Offeror's Final Proposal Revision (FPR). If the Offeror's plan for sharing model organisms is still considered "unacceptable," or the Offeror's justification for restricting sharing is still considered inappropriate by the Government after discussions, the Offeror's proposal may not be considered further for award.

4.2.5 Evaluation of Plan for Submission of Genome-Wide Association Study (GWAS) Data

The Offeror's plan for the submission of genome-wide association study (GWAS) data to the NIH-designated GWAS data repository will be assessed for appropriateness and adequacy. Proposals submitted for GWAS in which the data submission expectation cannot be met will be considered for award on a case-by-case basis.

5 CONSIDERATIONS

5.1 PHASE II AWARD CONSIDERATIONS

It is anticipated that all Phase II awards will be cost-plus-fixed-fee **contracts**.

Phase II contracts may not exceed the designated topic cost ceiling - including direct costs, indirect costs, and negotiated fixed fee. The designated topic ceilings are outlined in PART 8.

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.

The estimated number of awards and estimated dollar value of awards have been determined on a per topic basis as stated in PART 9.

Additional Phase II Considerations

1. The Contractor shall perform a minimum of one-half of the research and/or analytical effort (total contract price less profit/fee) conducted under this contract. Any deviation from this requirement shall be approved in writing by the Contracting Officer.

In accordance with the National Defense Authorization Act for FY 2013 (January 2013), the prime is prohibited from expending on subcontractors more than 50 percent of the amount paid under the contract. However, the Act excludes from the 50% limitation on any subcontracts with any similarly situated entities that have the same small business concern statues as the prime contractor. For example, if the business concern is an 8(a) entity, it could subcontract work to other 8(a) entities without that work counting toward the limitation. Other similarly situated entities includes mall business concerns, women-owned small business concerns, women-owned small disadvantaged business concerns, service-disabled veteran-owned small business concerns, and HUBZone small business concerns. The Contracting Officer shall approve deviations from these requirements in writing after consultation with the agency SBIR Program Manager/Coordinator.

2. The Principal Investigator shall be primarily employed with the Contractor. Primary employment means that more than on half (50%) of the employee's time is spent with the Contractor. Primary employment with the Contractor precludes full-time employment at another organization.

3. All research or research and development work shall be performed by the Contractor and its subcontractors in the United States.

5.2 REPORTING REQUIREMENTS

All reports required herein shall be submitted in electronic format. In addition, one hardcopy of each report shall be submitted to the Contracting Officer.

All electronic reports submitted shall be compliant with Section 508 of the Rehabilitation Act of 1973. Additional information about testing documents for Section 508 compliance, including guidance and specific checklists, by application, can be found at: http://www.hhs.gov/web/508/index.html under "Making Files Accessible."

All paper/hardcopy documents/reports submitted under this contract shall be printed or copied, double-sided, on at least 30 percent post-consumer fiber paper, whenever practicable, in accordance with FAR 4.302(b).

a. Technical Progress Reports

1. **Progress Reports**
   Contractors will be required to submit progress reports as stipulated in the terms and conditions of award, which at a minimum will consist of the below reports. In addition, specific deliverables may be required as outlined in the attachment titled ABSTRACT OF RESEARCH PLAN listed in PART 9.

2. **In addition** to the required reports set forth elsewhere in this Schedule, the preparation and submission of regularly recurring Technical Progress Reports will be required in any contract resulting from this solicitation. These reports will require descriptive information about the activities undertaken during the reporting period and will require information about planned activities for future reporting periods. The frequency and specific content of these reports will be determined prior to contract award. *[Note: Beginning May 25, 2008, the Contractor shall include the applicable PubMed Central or NIH Manuscript Submission reference number when citing publications that arise from its NIH funded research.]*

   [ ] Monthly
   [X] Quarterly
   [ ] Semi-Annually
   [X] Annually
   [ ] Annually (with a requirement for a Draft Annual Report)
   [ ] Final - Upon final completion of the contract

[X] Final - Upon final completion of the contract (with a requirement for a Draft Final Report)

A. Quarterly Progress Report

This report shall include a description of the activities during the reporting period and the activities planned for the ensuing reporting period the first reporting period consists of the first full three months of performance including any fractional part of the initial month. Thereafter, the reporting period shall consist of three full calendar months.

The first report shall be due TBD. Thereafter, reports shall be due on or before the 10th calendar day following each reporting period. A Quarterly Report shall not be required when an Annual Report is due.

B. Annual Progress Report

This report shall include a summation of the results of the entire contract work for the period covered.

The first report shall cover the period from award date through the anniversary date of this contract and shall be due on the 15th calendar day following the reporting period. An annual report will not be required for the period when the Final Report is due.

C. Draft and Final Report

This report is to include a summation of the work performed and results obtained for the entire contract period of performance. This report shall be in sufficient detail to describe comprehensively the results achieved.

The Contractor shall provide the Contracting Officer and Contracting Officer's Representative with an electronic copy of the Final Report in draft form. The Contracting Officer's Representative will review the draft report and provide the Contractor with comments with 15 calendar days after receipt. The Final Report shall be corrected by the Contractor, if necessary and the final version delivered as specified in the resulting contract.

3. Summary of Salient Results

Contractor will be required to prepare and submit, with the final report, a summary (not to exceed 200 words) of salient results achieved during the performance of the contract. This report will be required on or before the expiration date of the contract.

b. Other Reports/Deliverables

1. SBIR Lifecycle Certifications

The SBIR Lifecycle Certifications as provided in PART 9 of this solicitation are required both prior to invoicing 50% of the total award amount, and prior to the final invoice payment.

2. Reporting of Financial Conflict of Interest (FCOI)

All reports and documentation required by 45 CFR Part 94, Responsible Prospective Contractors including, but not limited to, the New FCOI Report, Annual FCOI Report, Revised FCOI Report, and the Mitigation Report, shall be submitted to the Contracting Officer in Electronic format. Thereafter, reports shall be due in accordance with the regulatory compliance requirements in 45 CFR Part 94.45 CFR Part 94 is available at: http://www.ecfr.gov/cgi-bin/text-idx?c=ecrf&SID=0af84ca649a74846f102aaf664da1623&rgn=div4&view=text&node=45:1.0.1.1.51&idno=45. See Part 94.5, Management and reporting of financial conflicts of interest for complete information on reporting requirements.

(Reference subparagraph g. of the INSTITUTIONAL RESPONSIBILITY REGARDING INVESTIGATOR FINANCIAL

CONFLICTS OF INTEREST Article in PART 5.6 of this contract.)

3. Section 508 Annual Report
The contractor shall submit an annual Section 508 report in accordance with the schedule set forth in the ELECTRONIC AND INFORMATION TECHNOLOGY ACCESSIBILITY Article in of any resulting contract. The Section 508 Report Template and Instructions for completing the report are available at: http://www.hhs.gov/web/508/contracting/technology/vendors.html under "Vendor Information and Documents."

4. Presentation of Progress
The Contractor shall prepare and submit a presentation which shall be due upon request of the Contracting Officer's Representative. Presentation of the slides shall occur through webinar, or teleconference. The presentation shall cover the following:

a. Discussion of the Contractor's project status.
b. The Contractor's achievements during the period of performance period (patents, publications, sales, regulatory approvals, partnerships, awards, etc.).
c. Detailed results of the performed research and development.
d. Discussion of proposed milestones and whether they were achieved during the contract performance to date.
e. Questions to the NCI.

5. Multiple Principal Investigators Leadership Plan
The Contractor shall submit a revised/updated Leadership Plan in the event of a change in any of the Principal Investigators named in the Key Personnel Article in SECTION G of any resulting contract. The revised plan is subject to review and approval by the Contracting Officer.

6. Invention Reporting Requirement
All reports and documentation required by FAR Clause 52.227-11, Patent Rights-Ownership by the Contractor including, but not limited to, the invention disclosure report, the confirmatory license, and the Government support certification, shall be directed to the Division of Extramural Inventions and Technology Resources(DEITR), OPERA, OER, NIH, 6705 Rockledge Drive, Suite 310, MSC 7980, Bethesda, Maryland 20892-7980(Telephone: 301-435-1986). In addition, one copy of an annual utilization report, and a copy of the final invention statement, shall be submitted to the Contracting Officer. The final invention statement (see FAR 27.303(b)(2)(ii)) shall be submitted to the Contracting Officer on the expiration date of the contract.

The annual utilization report shall be submitted in accordance with the DELIVERIES Article in any resultant contract. The final invention statement (see FAR 27.303(b)(2)(ii)) shall be submitted on the expiration date of the contract. All reports shall be sent to the following address:

Contracting Officer
National Institutes of Health
National Cancer Institute
Office of Acquisition
9609 Medical Center Drive
Building 9609, Room TBD
Bethesda, Maryland 20892

If no invention is disclosed or no activity has occurred on a previously disclosed invention during the applicable reporting period, a negative report shall be submitted to the Contracting Officer at the address listed above.

To assist contractors in complying with invention reporting requirements of the clause, the NIH has developed "Interagency Edison," an electronic invention reporting system. Use of Interagency Edison is encouraged as it streamlines the reporting process and greatly reduces paperwork. Access to the system is through a secure interactive Web site to ensure that all information submitted is protected. Interagency Edison and information relating to the capabilities of the system can be obtained from the Web (http://www.iedison.gov), or by contacting the Extramural Inventions and Technology Resources Branch, OPERA, NIH.

5.3 PAYMENT SCHEDULE

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 System for Award Management (SAM) located at www.sam.gov.

Invoices/financing requests submitted for costs incurred under cost reimbursement contracts will be on a monthly basis unless otherwise authorized by the Contracting Officer.

PROVISIONS APPLICABLE TO DIRECT COSTS

This article will prohibit or restrict the use of contract funds, unless otherwise approved by the Contracting Officer. The following is a list of items that may be included in the resultant contract as applicable. 1) Conferences & Meetings, 2)Food for Meals, Light Refreshments & Beverages, 3) Promotional Items, 4) Acquisition, by purchase or lease, of any interest in real property; 5) Special rearrangement or alteration of facilities; 6) Purchase or lease of any item of general purpose office furniture or office equipment regardless of dollar value; 7) Travel Costs including Foreign Travel; 8)Consultant Costs; 9) Subcontract Costs; 10) Patient Care Costs; 11) Accountable Government Property; 12) Printing costs; and 13) Research Funding.

5.4 INNOVATIONS, INVENTIONS, and PATENTIS

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 limited right to use such data for Government purposes only.

1. Each agency shall 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 shall 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 of 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. 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 shall 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 and 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 February 24, 2014. 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 Phase I and II SBIR awards. The data rights protection period lapses only: (1) Upon expiration of the protection period applicable to the SBIR award, or (2) by agreement between the awardee and the agency.

Proprietary Information

Information contained in unsuccessful proposals will remain the property of the applicant. The Government may, however, retain copies of all proposals. Public release of information in any proposal submitted will be subject to existing statutory and regulatory requirements. If proprietary information is provided by an applicant in a proposal, which constitutes a trade secret, proprietary commercial or financial information, confidential personal information or data affecting the national security, it will be treated in confidence, to the extent permitted by law. This information must be clearly marked by the applicant with the term "confidential proprietary information" and the following legend must appear on the title page of the proposal: "These data shall not be disclosed outside the Government and shall not be duplicated, used, or disclosed in whole or in part for any purpose other than evaluation of this proposal. If a funding agreement is awarded to this applicant as a result of or in connection with the submission of these data, the Government shall have the right to duplicate, use, or disclose the data to the extent provided in the funding agreement and pursuant to applicable law. This restriction does not limit the Government's right to use information contained in the data if it is obtained from another source without restriction. The data subject to this restriction are contained on pages _____of this proposal.

Invention Reporting

SBIR awardees shall report inventions to the awarding agency within 2 months of the inventor's report to the awardee. The reporting of inventions may be accomplished by submitting reports as described in the Reporting Requirement's subsection titled Invention Reporting.

Copyrights

With prior written permission of the Contracting Office, the awardee normally may 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 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 the National Cancer Institute," or "The project described was supported by contract number _____from the National Cancer Institute."

Patents

Small business concerns may normally retain the principal worldwide patent rights to any invention developed with Government support. In such circumstances, the Government receives a royalty-free license for Federal Government use, reserves the right to require patent holder to license others in certain circumstances, and may require that anyone exclusively licensed to sell the invention in the United States shall normally manufacture it domestically. 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 minimum 4-year period (that may be extended by subsequent SBIR funding agreements) to allow the awardee a reasonable time to pursue a patent.

5.5 COST-SHARING

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 the Offeror's proposal. Cost-sharing is an explicit arrangement under which the Contractor bears some of the burden of reasonable, allocable, and allowable contract costs. If cost-sharing is

proposed, it should be reflected in the Offeror's budget summary.

5.6 PROFIT OR FEE

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.

5.7 JOINT VENTURES OR LIMITED PARTNERSHIPS

Joint ventures and limited partnerships are eligible provided the entity created qualifies as a small business concern as defined in this program solicitation.

5.8 RESEARCH AND ANALYTICAL WORK

For Phase II a minimum of one-half of the research and/or analytical effort must be performed by the proposing small business concern unless otherwise approved in writing by the funding agreement officer after consultation with the agency SBIR Program Manager/Coordinator.

5.9 AWARDEE COMMITMENTS

Upon award of a contract/funding agreement, the awardee will be required to make a legal commitment through acceptance of numerous clauses in the Phase II contract. The outline that follows is illustrative of the types of clauses to which the contractor would be committed. This list is not a complete list of clauses to be included in a Phase II contract, and is not the specific wording of such clauses. Copies of complete terms and conditions are available upon request.

The following are illustrative of the type of clauses that may be found in any resultant contract:

1. Standards of Work. Work performed under the funding agreement shall conform to high professional standards.
2. Inspection. Work performed under the funding agreement is subject to Government inspection and evaluation at all times.
3. Examination of Records. The Comptroller General (or a duly authorized representative) shall have the right to examine any pertinent records of the awardee involving transactions related to this funding agreement.
4. Default. The Government may terminate the funding agreement if the contractor fails to perform the work contracted.
5. Termination for Convenience. The funding agreement may be terminated at any time by the Government if it deems termination to be in its best interest, in which case the awardee will be compensated for work performed and for reasonable termination costs.
6. Disputes. Any dispute concerning the funding agreement that cannot be resolved by agreement shall be decided by the contracting officer with right of appeal.
7. Contract Work Hours. The awardee may not require an employee to work more than 8 hours a day or 40 hours a week unless the employee is compensated accordingly.
8. Equal Opportunity. The awardee will not discriminate against any employee or offeror for employment because of race, color, religion, sex, or national origin.
9. Affirmative Action for Veterans. The awardee will not discriminate against any employee or application for employment because he or she is a disabled veteran or veteran of the Vietnam era.
10. Affirmative Action for Handicapped. The awardee will not discriminate against any employee or offeror for employment because he or she is physically or mentally handicapped.
11. Officials Not To Benefit. No Government official shall benefit personally from the SBIR funding agreement.

12. Covenant Against Contingent Fees. No person or agency has been employed to solicit or secure the funding agreement upon an understanding for compensation except bona fide employees or commercial agencies maintained by the awardee for the purpose of securing business.
13. Gratuities. The funding agreement may be terminated by the Government if any gratuities have been offered to any representative of the Government to secure the award.
14. Patent Infringement. The awardee shall report each notice or claim of patent infringement based on the performance of the funding agreement.
15. American Made Equipment and Products. When purchasing equipment or a product under the SBIR funding agreement, purchase only American-made items whenever possible.

The complete listing of the SBIR Phase II contract clauses may be accessed at: http://oamp.od.nih.gov/dgs/general-clauses .

5.10 LIMITATIONS ON THE USE OF APPROPRIATED FUNDS

NIH POLICY ON ENHANCING PUBLIC ACCESS TO ARCHIVED PUBLICATIONS RESULTING FROM NIH-FUNDED RESEARCH

NIH-funded investigators shall submit to the NIH National Library of Medicine's (NLM) PubMed Central (PMC) an electronic version of the author's final manuscript, upon acceptance for publication, resulting from research supported in whole or in part with direct costs from NIH. NIH defines the author's final manuscript as the final version accepted for journal publication, and includes all modifications from the publishing peer review process. The PMC archive will preserve permanently these manuscripts for use by the public, health care providers, educators, scientists, and NIH. The Policy directs electronic submissions to the NIH/NLM/PMC: http://www.pubmedcentral.nih.gov.

Additional information is available at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-033.html.

NEEDLE DISTRIBUTION

The Contractor shall not use contract funds to carry out any program of distributing sterile needles or syringes for the hypodermic injection of any illegal drug.

ACKNOWLEDGEMENT OF FEDERAL FUNDING

The Contractor shall clearly state, 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: (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) the percentage and dollar amount of the total costs of the project or program that will be financed by nongovernmental sources.

RESTRICTION ON ABORTIONS

The Contractor shall not use contract funds for any abortion.

CONTINUED BAN ON FUNDING OF HUMAN EMBRYO RESEARCH

The Contractor shall not use contract funds 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)). 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. Additionally, in accordance with a March 4, 1997 Presidential Memorandum, Federal funds may not be used for cloning of human beings.

LIMITATION ON USE OF FUNDS FOR PROMOTION OF LEGALIZATION OFCONTROLLED SUBSTANCES
The Contractor shall not use contract funds to support activities that promote the legalization of any drug or other substance included in schedule I of the schedules of controlled substances established under section 202 of the Controlled Substances Act, except for normal and recognized executive-congressional communications. This limitation shall not apply when the Government determines that 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.

DISSEMINATION OF FALSE OR DELIBERATELY MISLEADING INFORMATION
The Contractor shall not use contract funds to disseminate information that is deliberately false or misleading.

INSTITUTIONAL RESPONSIBILITY REGARDING INVESTIGATOR FINANCIALCONFLICTS OF INTEREST
The Institution (includes any contractor, public or private, excluding a Federal agency) shall comply with the requirements of 45 CFR Part 94, Responsible Prospective Contractors, which promotes objectivity in research by establishing standards to ensure that Investigators (defined as the project director or principal Investigator and any other person, regardless of title or position, who is responsible for the design, conduct, or reporting of research funded under NIH contracts, or proposed for such funding, which may include, for example, collaborators or consultants) will not be biased by any Investigator financial conflicts of interest. 45 CFR Part 94 is available at the following Web site: http://www.ecfr.gov/cgi-bin/text-idx?c=ecfr&SID=0af84ca649a74846f102aaf664da1623&rgn=div5&view=text&node=45:1.0.1.1.51&idno=45

As required by 45 CFR Part 94, the Institution shall, at a minimum:

a. Maintain an up-to-date, written, enforceable policy on financial conflicts of interest that complies with 45 CFR Part 94, inform each Investigator of the policy, the Investigator's reporting responsibilities regarding disclosure of significant financial interests, and the applicable regulation, and make such policy available via a publicly accessible Web site, or if none currently exist, available to any requestor within five business days of a request. A significant financial interest means a financial interest consisting of one or more of the following interests of the Investigator (and those of the Investigator's spouse and dependent children) that reasonably appears to be related to the Investigator's institutional responsibilities:

    1. With regard to any publicly traded entity, a significant financial interest exists if the value of any remuneration received from the entity in the twelve months preceding the disclosure and the value of any equity interest in the entity as of the date of disclosure, when aggregated, exceeds $5,000. Included are payments and equity interests;

    2. With regard to any non-publicly traded entity, a significant financial interest exists if the value of any remuneration received from the entity in the twelve months preceding the disclosure, when aggregated, exceeds $5,000, or when the Investigator (or the Investigator's spouse or dependent children) holds any equity interest; or

    3. Intellectual property rights and interests, upon receipt of income related to such rights and interest. b.

Require each Investigator to complete training regarding the Institution's financial conflicts of interest policy prior to engaging in research related to any NIH-funded contract and at least every four years. The Institution shall take reasonable steps [see Part 94.4(c)] to ensure that investigators working as collaborators, consultants or subcontractors comply with the regulations.

c. Designate an official(s) to solicit and review disclosures of significant financial interests from each Investigator who is planning to participate in, or is participating in, the NIH-funded research.

d. Require that each Investigator who is planning to participate in the NIH-funded research disclose to the Institution's designated official(s) the Investigator's significant financial interest (and those of the Investigator's spouse and dependent children) no later than the date of submission of the Institution's proposal for NIH-funded research. Require that each Investigator who is participating in the NIH-funded research to submit an updated disclosure of significant financial interests at least annually, in accordance with the specific time period prescribed by the Institution during the period of the award as well as within thirty days of discovering or acquiring a new significant financial interest.

e. Provide guidelines consistent with the regulations for the designated official(s) to determine whether an Investigator's significant financial interest is related to NIH-funded research and, if so related, whether the significant financial interest is a financial conflict of interest. An Investigator's significant financial interest is related to NIH-funded research when the Institution, thorough its designated official(s), reasonably determines that the significant financial interest: Could be affected by the NIH-funded research; or is in an entity whose financial interest could be affected by the research. A financial conflict of interest exists when the Institution, through its designated official(s), reasonably determines that the significant financial interest could directly and significantly affect the design, conduct, or reporting of the NIH-funded research.

f. Take such actions as necessary to manage financial conflicts of interest, including any financial conflicts of a subcontractor Investigator. Management of an identified financial conflict of interest requires development and implementation of a management plan and, if necessary, a retrospective review and mitigation report pursuant to Part 94.5(a).

g. Provide initial and ongoing FCOI reports to the Contracting Officer pursuant to Part 94.5(b).

h. Maintain records relating to all Investigator disclosures of financial interests and the Institution's review of, and response to, such disclosures, and all actions under the Institution's policy or retrospective review, if applicable, for at least 3 years from the date of final payment or, where applicable, for the other time periods specified in 48CFR Part 4, subpart 4.7, Contract Records Retention.

i. Establish adequate enforcement mechanisms and provide for employee sanctions or other administrative actions to ensure Investigator compliance as appropriate.

j. Complete the certification in PART 9 entitled, Representations, Certifications, and Other Statements of Offerors titled.

If the failure of an Institution to comply with an Institution's financial conflicts of interest policy or a financial conflict of interest management plan appears to have biased the design, conduct, or reporting of the NIH-funded research, the Institution shall promptly notify the Contracting Officer of the corrective action taken or to be taken. The Contracting Officer will consider the situation and, as necessary, take appropriate action or refer the matter to the Institution for further action, which may include directions to the Institution on how to maintain appropriate objectivity in the NIH-funded research project.

The Contracting Officer and/or HHS may inquire at any time before, during, or after award into any Investigator disclosure of financial interests, and the Institution's review of, and response to, such disclosure, regardless of whether the disclosure resulted in the Institution's determination of a financial conflict of interests. The Contracting Officer may require submission of the records or review them on site. On the basis of this review of records or other information that may be available, the Contracting Officer may decide that a particular financial conflict of interest will bias the objectivity of the NIH-funded research to such an extent that further corrective action is needed or that the Institution has not managed the financial conflict of interest in accordance with Part 94.6(b). The issuance of a Stop Work Order by the Contracting Officer may be necessary until the matter is resolved.

If the Contracting Officer determines that NIH-funded clinical research, whose purpose is to evaluate the safety or effectiveness of a drug, medical device, or treatment, has been designed, conducted, or reported by an Investigator with a financial conflict of interest that was not managed or reported by the Institution, the Institution shall require the Investigator involved to disclose the financial conflict of interest in each public presentation of the results of their search and to request an addendum to previously published presentations.

5.11 ADDITIONAL INFORMATION

This program 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.

Before award of an SBIR contract, the Government may request the offeror to submit certain organizational, management, personnel, and financial information (not otherwise requested in the proposal instructions) to assure responsibility of the offeror.

The Government is not responsible for any monies expended by the offeror before award of any contract.

This program solicitation is not an offer by the Government and does not obligate the Government to make any specific number of awards. Also, awards under the SBIR Program are contingent upon the availability of funds.

The SBIR Program is not a substitute for existing unsolicited proposal mechanisms. Unsolicited proposals will not be accepted under the SBIR Program.

If an award is made pursuant to a proposal submitted under this SBIR Program solicitation, a representative of the contractor will be required to certify that the concern has not previously been, nor is currently being paid for essentially equivalent work by any federal agency.

6 SUBMISSION OF PROPOSALS

The Offeror's proposal shall be organized as specified in PART 3.2 General Instructions. Shipment and marking shall be as indicated below.

a. PROPOSALS DUE DATE AND TIME

Proposals will be received at the below addresses, and in the number of copies specified below, before 4:30 PM EST on February 3, 2015

b. EXTERNAL PACKAGE MARKING

In addition to the addresses cited below, mark each package as follows:

"**BAA N44CM47014-11** TO BE OPENED BY AUTHORIZED GOVERNMENT PERSONNEL ONLY"

c. NUMBER OF COPIES

TECHNICAL PROPSAL: ORIGINAL* AND **FIVE (5)** COPIES TO:
BUSINESS PROPOSAL: ORIGINAL* AND **THREE (3)** COPIES TO:
TWO (2) CD ROM WITH THE TECHNICAL PROPOSALS TO:
TWO (2) CD ROM WITH THE BUSINESS PROPOSALS TO:

d. SUBMISSION ADDRESSES

If hand-delivered or using courier service
Rosemary Hamill
Contracting Officer
Office of Acquisitions
National Cancer Institute
9609 Medical Center Drive
Room 1E560
Rockville, Maryland 20850

If using U.S. Postal Service
Rosemary Hamill
Contracting Officer
Office of Acquisitions
National Cancer Institute
9609 Medical Center Drive, Room 1E560
MSC 9704
Bethesda, Maryland 20892-9704

***THE ORIGINALS SHALL BE READILY ACCESSIBLE FOR DATE STAMPING PURPOSES.**

NOTE: Please be aware that the U.S. Postal Service's "Express Mail" **DOES NOT** deliver to the Rockville, Maryland address **AND** delivery to the Bethesda, Maryland address will result in a delayed delivery to our office in Rockville, Maryland (up to 3 – 5 days). If a proposal is not received at the place, date, and time specified herein, it will be considered a "late proposal."

7 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 Library in the Offeror's 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

8 RESEARCH TOPICS

Topic 277 Development of Companion Diagnostics
Budget (total costs): $1,500,000 for two (2) years

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
Recently, the demand for companion diagnostics has greatly increased with the recognition that matching the right

patient to the right drug can improve patient care and may decrease health care costs. More than a dozen companion diagnostic tests have been approved by the FDA to guide the prescription of products in oncology, cardiovascular disease, and infectious disease. Among them, tests of Philadelphia chromosome, tumor-associated EGFR overexpression, and HER2 protein overexpression have been identified by the FDA as "required" for the identification of candidate cancer patients for receiving Gleevec, Erbitux (cetuximab) and Herceptin (trastuzumab), respectively, in certain indications.

Despite initial success, many therapies in the cancer area are still lacking prediction and guidance from companion diagnostics. This is true for both primary as well as adjuvant treatments. In particular, many patients die from recurrence and metastasis as a result of unpredicted resistance to drugs and/or radiation therapy. Guidance towards effective and safe therapy is therefore much in need. Companion diagnostics include tests that are developed after a drug has come to market, tests that are being developed in conjunction with the development of a drug and tests to predict the interaction of novel agents with existing standard of care therapies such as radiation or cytotoxic chemotherapy. This contract topic seeks to stimulate research, development, and commercialization of innovative tests and technology platforms for all these types of companion diagnostic applications. Companies with advanced biomarkers are particularly encouraged to apply.

Project Goals:
The goal of this contract topic is to develop companion diagnostics for selecting patients for which a particular therapeutic regimen, including existing drugs and those in clinical development and radiation, will be safe and effective. Although the example companion diagnostic tests mentioned above are for targeted therapies, tests may also encompass therapeutics outside of this class. These tests include, but are not limited to tumor RNA/protein expression or overexpression, gene mutation or deletion/insertion, allelic variation, and enzymatic deficiency. Noninvasive and minimally invasive sampling methods (e.g., body fluids and mouth swab) are preferred. Other sampling methods are also acceptable if they provide significantly improved predictive value, accuracy, and clinical applicability. This topic is not intended to support the development of assays unless they provide predictive/prognostic information for a therapy. For example, development of an assay for the sole purpose of measuring whether the drug hits its target would not be considered responsive.

Phase II Activities and Expected Deliverables:

- Demonstrate clinical utility and value by testing sufficient numbers of patients to unequivocally prove statistical significance with regards to patient selection for the therapy.
- If the phase I conclusions are mainly based on animal experiment or ex vivo modeling, then a correlation study between these models and treatment in human subjects may be expected.
- Establish marketing partner or alliance with pharmaceutical companies that are developing the therapy unless the therapy is already on the open market.
- Deliver the final SOP to NCI for evaluation.

Topc 309 Development of Low Cost, Small Multi-Analyte Technologies for Cancer Diagnosis, Prognosis and Early Detection

Budget (total costs): 1,000,000 for two (2) years

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:
Cancer is recognized as a multistep process involving multiple genomic and epigenomic alterations that occur in multiple phases. The complexity of cancer requires multivariate assays for accurate diagnosis, prognosis and treatment monitoring. Recently, two multivariate gene-expression assays, Oncotype DX and MammaPrint, have been developed for determining whether chemotherapy is necessary for breast cancer. The Oncotype DX analyzes the expression of a 21-gene signature by TaqMan RT-PCR. The MammaPrint microarray which measures the expression of 70 breast cancer genes as a signature, provides information about the likelihood of tumor recurrence and guides treatment.

Given the multivariate and heterogeneous nature of the disease, it is likely that the early detection and diagnosis of cancer will be based on multiple analytes. However, the currently available clinical multi-analyte technology platforms have many limitations, including the requirement of multiple biopsies and special specimen collection/storage process. Additionally, their processes are often slow, complex, labor intensive and with sup-optimal sensitivity. These factors contribute to the added cost which also limits their broad applicability. For example the current list price of both Oncotype DX and MammaPrint are over $4000 per sample.

While the various NIH and other Government (DOD, DARPA, NSF, NASA, USDA etc) programs are developing new cutting edge technologies, their focuses are not on commercialization, and these novel technologies have not penetrated into clinical use. This contract topic seeks to promote the development of such innovations in early detection and diagnostic technology to facilitate the commercialization of low cost, efficient multi-analyte technologies with optimal sensitivity for cancer early detection, diagnosis and prognosis. In particular, this topic requests the development of technologies that can obtain multi-analyte molecular information from small volume clinical specimens (e.g. core biopsy, fine needle aspiration, circulating tumor cells or FFPE sections). In addition, this contract topic encourages proposals based on improving both early detection and diagnosis of cancer from easily accessible samples (e.g. blood, sputum, urine, fecal) with low abundant cancer markers.

Project Goals:
The short-term goal for the project is to develop working prototypes of low cost devices or methodologies for multi-analyte analysis of small samples or easily accessible samples with low abundant cancer biomarkers. Long-term goals are to improve cancer early detection, diagnosis, prognosis and treatment monitoring by developing low cost, more efficient, and more sensitive devices or methodologies for multi-analyte detection and analysis. Additionally, this topic requests the development of technologies that can be used with small volume, small numbers of cells or low cancer biomarker abundant clinical specimens obtained through regular biopsy procedures (e.g. core biopsy, FNA), surgery (e.g. FFER sections) or minimally invasive methods (e.g. blood, sputum, urine, and fecal). The technology should be innovative and make use of recent advances in areas such as microfluidics, nanotechnology, multichannel imaging, and transducer technologies for biosensors including optical, electrochemical, piezoelectric, Field Effect Transistor, cantilevers or any other rapid multi-analytes transducers. These devices and methodologies should be more cost efficient than current ones (>5x cost reduction), have significantly improved sensitivity/specificity (>10x) and can be used with samples obtained from single core biopsy or FNA. Acceptable devices and methodologies should be able to analyze at least 30 markers (DNA, RNA, RNAi, or proteins) simultaneously within four hours. If the innovation includes an integrated device, the cost of the market ready device should be less than $15,000. Ideally, the input for the device should be core biopsy, FNA or any small clinical biopsy specimen and the output should be the profile of the markers. This solicitation also encourages developing non-invasive biomarker based technologies and available multi-analyte technologies and assays for cancer early detection.

Accepted devices or methodologies include, but are not limited to:

- Rapid sample preparation and multi-analyte concentration technologies for high quality DNA/RNA RNAi/protein/cell.
- Multi-analyte amplification technologies for DNA,RNA, ncRNAs, RNAi, proteins, and glycoproteins.
- Low-frequency mutation analysis (e.g. for multiple relevant genetic markers/mutations).

- Rapid DNA sequencing (e.g. for multiple relevant genetic markers/mutations).
- Advanced PCR techniques.
- New protein or DNA/RNA/RNAi labeling and label free technologies. Preference will be given to label free technologies.
- Point of Care DNA, RNA or antibody microarrays.
- Automated integrated system.

Phase II Activities and Expected Deliverables:

- Develop a prototype of the device or analytical tool incorporating the technology demonstrated in Phase I including automation, software and data analysis.
- Test the device with clinically relevant cancer biomarkers.
- Test with a sufficient number of patient samples in several laboratories to demonstrate concordance, clinical utility and advantages, with an appropriate consideration of statistical significance.

Topic 313 RNAi Cancer Therapeutics using Nanotechnology

Budget (total costs): $1,000,000 for two (2) years

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:
In 2011, the SBIR Development Center hosted an industry roundtable to solicit inputs from life science industry professionals on emerging areas that are ripe for technology development by the small business community. Participants at this meeting expressed strong interest in using the SBIR mechanism to foster and encourage the development of novel RNA interference (RNAi) delivery platforms, particularly as a strategy for addressing therapeutic targets previously deemed "undruggable" by small molecules. Such therapeutics are gaining prominence due to their versatility and efficiency in treating cancer, as well as a variety of other genetic diseases; however, treating patients with RNAi has proven challenging, as it is difficult to achieve intracellular delivery to specific tissues and organs expressing the target gene. In particular, cellular uptake of naked RNAi is extremely inefficient owing to its polyanionic nature. The majority of intravenously administered RNAi is removed from circulation by hepatic and renal clearance, and the remaining RNAi is subject to degradation by nonspecific nucleases in the blood. Moreover, injecting large quantities of RNAi may elicit an immune response, and other "off-target" effects may result in toxicity. While RNAi delivery to tumor cells poses these and other challenges, the ability to overcome these challenges is expected to facilitate the development of new and highly efficacious anti-cancer agents. Nanoparticle-based delivery systems are especially attractive as such strategies afford the opportunity to target specific cell, tissue, and organ types, while also increasing circulation half-life and shielding RNAi from degradation. Importantly, ongoing clinical trials are successfully utilizing nanoparticle-based delivery systems for cancer-related RNAi therapeutics, indicating that nanotechnology-based approaches hold great promise. To accelerate such efforts, the National Cancer Institute (NCI) requests proposals for the development of novel, commercially viable nanotechnology-based platforms for the delivery of RNAi cancer therapeutics.

Project Goals:
Proposals submitted under this contract topic should involve the design, fabrication, characterization, and preclinical evaluation of novel nanoparticle-based drug formulations capable of delivering candidate RNAi therapeutics for the treatment of cancer. Of particular interest are delivery systems that can achieve targeted delivery of RNAi to tumor cells, favorable pharmacokinetics and circulation times, and efficient uptake of RNAi by tumor cells. Nanotechnologies which minimize immune responses and/or off-target effects of RNAi are also desirable.

Nanotechnology-based RNAi therapeutic agents acceptable under this contract topic include siRNA, shRNA, miRNA, other ncRNA(s) and combinations thereof. Antisense oligonucleotides are also acceptable. This contract topic is not intended to fund basic research to identify molecular targets for RNAi therapy, conduct exhaustive comparative studies of multiple nanoparticle delivery systems, or establish new animal models. Concepts delivering DNA, messenger RNA, and/or proteins are also not acceptable candidates for this topic, nor are viral delivery platforms for RNAi.

The RNAi-nanoparticle constructs under development may incorporate additional functionalities to supplement or enhance the therapeutic RNAi. Such functionalities may include, but are not necessarily limited to, the following:

- Novel nanoparticle delivery vehicles
- Constructs involving novel tumor targeting
- Novel RNAi loading and releasing schemes
- Nanoparticle constructs capable of crossing the blood-brain barrier, penetrating pancreatic stroma, overcoming multi-drug resistance, or treating metastatic cancer
- Combination therapies utilizing multiple RNAi payloads (e.g., RNAi-based Logic Circuits)
- Other combination therapies utilizing at least one RNAi therapeutic and one conventional chemotherapeutic agent (i.e., non-nucleic acid agent)

Phase II Activities and Expected Deliverables (include at least three of the following):

- Provide a plan and timeline to complete preclinical development for the RNAi/nanotherapeutic, culminating in the filing of an IND with the FDA
- Demonstrate *in vivo* preclinical efficacy (properly powered studies)
- Demonstrate acceptable safety (i.e., toxicity in rodents and/or large animals)
- Demonstrate acceptable pharmacokinetics and pharmacodynamics
- Conduct process development to support clinical manufacturing (e.g., scale-up feasibility)
- Conduct other R&D activities needed to complete an IND application, carried out in a suitable pre-clinical environment

Topic 314 Development of Human Tissue Culture Systems that Mimic the Tumor Microenvironment

Budget (total costs): $2,000,000 for two (2) years

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:
There is a critical need to improve the accuracy of preclinical drug efficacy screening and testing through the development of *in vitro* culture systems that more effectively mimic the *in vivo* environment. Currently, two-dimensional (2D) *in vitro* culture systems or *in vivo* animal models are the primary tools used to test cancer cell responses to drugs. However, drug sensitivity data obtained via 2D culture systems can be misrepresentative, while animal models are expensive, time-consuming, and not always predictive of the effects on human tumors in their native environment. Three-dimensional (3D) culture systems that mimic the tumor microenvironment using human tissue could be a better tool for drug screening by providing a more accurate, *in vivo*-like structure and organization than 2D culture systems, without the cost and time associated with using animal models. In addition, culture systems using human tissue may produce responses more predictive of humans than animal models. Advances in bioengineering and 3D cell culture models have led to *in vitro* systems that better replicate the structure, physiology,

and function of tissues seen *in vivo*. 3D models more accurately mimic the *in vivo* milieu than current 2D *in vitro* culture systems by recreating the morphology and arrangement of individual cells, concentration gradients of signaling molecules and therapeutic agents, and the composition, structure, and mechanical forces of extracellular matrix around cells. The use of 3D systems that recreate the human tumor microenvironment could improve drug development in at least two ways: 1) speed decision-making for whether a particular therapeutic agent is worth pursuing in an animal model, reducing the time and cost of development; 2) lead to fewer clinical trial failures because of earlier, more relevant results from human tissue.

Properly representing the tumor microenvironment is particularly critical for testing the effectiveness of anti-cancer therapeutic agents. For example, extravascular transport in solid tumors is a fundamental determinant of the efficacy of both locally and systemically administered cancer agents. Large diffusion distances in tumor tissues, elevated interstitial fluid pressure, and interactions between anti-cancer drugs, tumor tissue, and normal tissue are factors that significantly limit drug diffusion in the extravascular compartment. Additionally, due to rapid proliferation and poor blood supply to tumor cells, the tumor microenvironment is often acidic and hypoxic, which can lead to the resistance of tumor cells to both drug and radiation therapy. Thus, systems to properly recreate the tumor microenvironment are essential to advance the discovery and development of effective anti-cancer agents.

Project Goals:
The focus of this topic is the development of 3D human tissue model culture systems that accurately mimic the tumor microenvironment, including factors affecting tumor cell responses such as vascularization and interactions with heterogeneous cell types. The project goal is to produce a system that is validated against known effective anti-cancer agents to demonstrate the system's utility as a predictive tool and screening assay. It is anticipated that the development of 3D systems representative of human tumor microenvironments will lead to an increase in the quality of and reduction in the timelines and costs associated with screening drugs, and enhancement in efficacy information for regulatory decisions.

Essential characteristics of an *in vitro* tumor microsystem should include all or some of the following features: 1) multicellular architecture that represents physiologically relevant characteristics of the tumor and tissue of origin; 2) reproducible and viable operation with simple and clear protocols; 3) ability to examine multiple aspects of cancer, such as tumor growth, angiogenesis, cell proliferation, migration, and/or invasion; and 4) compatibility with high content screening platforms that include multiple molecular read-outs, such as genomic, proteomic, metabolomic, or epigenomic analyses. System development should permit scale-up production such that the system can be reliably reproduced at a cost with reasonable expectation for market success. An eventual goal for such systems may include the ability to incorporate individual patient tumor biopsies to test patient-specific responses to available agents.

It is important to note that full 3D tumor microenvironment systems will consist of more than just an extracellular matrix containing tumor cells and will facilitate the inclusion of various cell types to mimic tumor cell interaction with surrounding normal cells and their effects on cancer aggressiveness and response to anti-cancer drugs. Examples include stromal cells that can induce chemoresistance and encourage metastasis, as well as endothelial cells that can carry therapeutics to the cancer. This topic is not intended to fund microphysiological organ systems for the study of toxicity, though tumor culture systems developed under this topic may be combined as a module with systems such as those being developed through the collaborative program between NIH, FDA, and DARPA:
http://www.ncats.nih.gov/research/reengineering/tissue-chip/tissue-chip.html

Phase II Activities and Expected Deliverables:

- Benchmark performance in developed system against applicable *in vivo* animal model(s) and known clinical performance
  - Test multiple agents with known clinical profiles in the developed prototype
    - Test at least one agent that has proven efficacious in animal trials but not in clinical trials

- Assess genomic, proteomic, metabolomic, and epigenomic profile of the tumor system
  - Use validated markers and/or evaluative criteria from *in vivo* histologic analysis
  - Genomic data may be compared to The Cancer Genome Atlas
- Compare dose-response relationships of known anti-cancer agents
  - Demonstrate the ability to scale-up the system for use in high-throughput therapeutic agent screening assays
- Demonstrate the ability to perform high-throughput quantitative analysis on samples, such as simple harvesting and/or automated imaging

Topic 315 Development of Companion Diagnostics: Enabling Precision Medicine in Cancer Therapy

Budget (total costs): $1,500,000 for two (2) years.

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:
The demand for companion diagnostics has greatly increased with the recognition that matching the right patient to the right drug at the right time can improve patient care and may decrease health care costs. More than a dozen companion diagnostic tests have been approved by the FDA to guide the prescription of products in oncology, cardiovascular disease, and infectious disease. Among them, tests of the Philadelphia chromosome, tumor-associated EGFR overexpression, and HER2 protein overexpression have been identified by the FDA as "required" for the identification of candidate cancer patients to receive Gleevec, Erbitux (cetuximab), and Herceptin (trastuzumab), respectively, for certain indications. In 2011, the FDA approved two pairs of new oncology drugs and their companion diagnostic tests simultaneously. These decisions suggest that the era of companion diagnostics has arrived.

Despite initial success, many therapies in the cancer arena (both primary and adjuvant treatments) still lack prediction and guidance from companion diagnostics. Many patients die from recurrence and metastasis as a result of unpredicted resistance to drugs or radiation developed during therapy, or due to pre-existing tumor insensitivity to the drugs or radiation therapy. Guidance towards effective and safe therapy is greatly needed and can be provided by companion diagnostics, which include tests developed after a drug has come to market, tests developed in conjunction with the development of a therapeutic agent, and tests to predict the interaction of novel agents with existing standard of care therapies, such as radiation or cytotoxic chemotherapy. This topic seeks to stimulate research, development, and commercialization of innovative tests and technology platforms for all types of companion diagnostic applications. Companies with advanced biomarkers are particularly encouraged to apply.

Project Goals:
The goal of this contract topic is to develop companion diagnostic assays that identify patients for which a particular therapeutic regimen, including radiation therapy, existing drugs, and drugs in clinical development will be safe and effective.

Tests for monitoring the response to treatment for the purpose of adjusting treatment (e.g. schedule, dose, discontinuation) to achieve improved safety or effectiveness are also acceptable under this contract topic. Though the examples mentioned above are for targeted therapies, tests may also encompass therapeutics outside of this class. These tests include, but are not limited to, tumor RNA/protein expression or overexpression, gene mutation or deletion/insertion, allelic variation, and enzymatic deficiency. Noninvasive and minimally invasive sampling methods (e.g., body fluids and mouth swab) are preferred. Other sampling methods are also acceptable if they provide significantly improved predictive value, accuracy, and clinical applicability.

This topic is not intended to support the development of assays that do not provide predictive/prognostic information for a therapy. For example, the development of an assay for the sole purpose of measuring whether the drug hits its intended target (e.g., pharmacodynamic assay) would not be considered responsive under this contract topic. A novel test/device providing information that is useful in cancer diagnostics or prognostics, but not a determining factor for the safe and effective use of a therapeutic product, would also not be considered responsive.

Phase II Activities and Expected Deliverables:

- Demonstrate clinical utility and value by testing sufficient numbers of patients from multiple sites to unequivocally prove statistical significance with regards to patient selection for the therapy
- If the primary conclusions reached during the Phase I studies were based on animal experiments or *ex vivo* modeling, then a correlation study between these models and treatment in human subjects is expected
- Establish marketing partnership or alliance with the company developing the therapy, unless the therapy is already approved for marketing
- It is preferred that the test be performed in at least one independent CLIA-certified laboratory
- Deliver the final SOP to NCI for evaluation

Topic 316 Development of CYC Isolation Technologies Enabling Downstream Single Cell Molecular Analysis

Budget (total costs): $1,500,000 for two (2) years.

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:
Circulating tumor cells (CTCs) are cancer cells shed from either the primary tumor or its metastases and are circulating in the peripheral blood. While metastases are directly responsible for the majority of cancer deaths, CTCs may constitute seeds for metastases and may be instrumental for the spread of the disease. Many studies have shown that the presence of CTCs in peripheral blood or bone marrow is of prognostic significance in different types of solid tumors, and that the number and molecular changes of CTCs may help predict or monitor response to treatment. An increasing number of studies have shown large molecular and cellular heterogeneity of CTCs from the same types of cancer and even from CTCs from the same patient. This phenomenon has made the interpretation of cancer status very difficult. Current FDA-approved CTC analysis is based on immunological capture of CTCs by magnetic beads. This method does not capture all types of CTCs, and the recovery of the captured cells for subsequent molecular or cellular analysis is limited; hence, it is important to develop improved methodologies for CTC isolation that enable subsequent genomic, proteomic, or metabolomic analysis at the single cell level in order to understand the origin and role of these subpopulations of CTCs in cancer progression and treatment response. Enabling CTC analysis at the single-cell level will significantly contribute to cancer research and the selection of treatment options for patients based on changes in CTC numbers and molecular characteristics before and during treatment.

Project Goals:
The long-term goal of the project is to integrate new or established technologies to enable molecular characterization and analysis of individual CTCs isolated from blood or bone marrow. An ideal system will be a modular platform combining a CTC capture and separation module with several other modules for downstream molecular analysis such as genomic, metabolomic, proteomic and mutation analysis at the individual cell level. Non-modular systems will also be acceptable. The short-term goal is to demonstrate the technical viability of the proposed technology to isolate and analyze CTCs at the single-cell level in an experimental setting. If molecular analysis is not performed with the proposed device, a detailed description about compatible downstream analysis technology(/ies), including manufacturers and model numbers, is required.

Acceptable studies include but are not limited to:

- CTC isolation and enrichment technologies such as magnetic separation, microfluidics, size separation, and negative or positive selection
- Integrated CTC devices which combine CTC capture and molecular analysis
- Viable CTC cell isolation and/or culturing for treatment assessment
- Low-cost multichannel scanning, imaging, flow cytometry, spectral analysis or equivalent technologies for CTC molecular analysis with the potential to combine with innovative single-cell isolation (e.g. micro dissection)
- Non-separation-based technologies for CTCs that enable molecular analysis

Phase II Activities and Expected Deliverables:

- Develop a prototype of the device incorporating the technology demonstrated in Phase I with at least two of the applications below or other applications with significant clinical utility:
    - Single CTC whole genome sequencing
    - Single CTC molecular phenotyping
    - Single CTC proteomic analysis
    - Single CTC metabolomic analysis
    - Single CTC targeted multiplex gene expression analysis
    - Single CTC targeted multiplex mutation analysis
    - Single CTC targeted multiplex epigenetic analysis
    - Culture of individual CTCs with sufficient percent of viable cells for *ex vivo* analysis (e.g. drug treatment)
- Test the device with a sufficient number of patient samples to demonstrate clinical utility and advantages, with appropriate consideration of statistical significance
- Establish a marketing partnership or alliance with an established diagnostic or device company

Topic 317 Wound Healing Preparations Incorporating Nitric Oxide-releasing Materials (NIH Technology Transfer)

Budget (total costs): $1,500,000 for two (2) years.

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.

For frequently asked questions on this contract topic see: http://sbir.cancer.gov/funding/contracts/fy2013_faq.asp

Summary:
Non-healing wounds can pose significant problems for cancer patients (e.g., in cases where multiple operations are required for local recurrence, when large wounds are slow to close, and especially when patients receive radiation at sites requiring surgery). In addition, the effects of chemotherapy, nutritional deficits along with co-morbidities (e.g., diabetes), and infections can complicate wound healing. Therefore, the cancer patient population has the potential for non-healing wounds due to the nature and effects of the oncologic disease process and its treatments (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2206003/). Improved methods are thus needed for treating non-healing wounds that often result in lengthy hospital stays, application of multiple types of dressings and ointments, and hyperbaric methods.

Nitric oxide (NO) is an important bio-signaling molecule whose role has been extensively recognized in the body's endogenous immune, inflammatory, and tissue regenerative responses. Therapeutic application of exogenous topical NO-generating agents has been shown to provide powerful, broad-spectrum antimicrobial action, and NO is capable of providing numerous wound-healing benefits if delivered at the proper concentrations. However, since NO is an easily oxidized gas, controlled topical delivery of NO to a desired area is difficult. The National Cancer Institute (NCI)

has developed a family of polymers based on poly(acrylonitrile) that are capable of storing NO bound in a stable chemical functionality, called a diazeniumdiolate group, and releasing NO under aqueous conditions. The next logical step in the utilization of these materials for biomedical applications is the incorporation of these NO-releasing poly(acrylonitrile)-based compositions into suitable, biocompatible dressings for application to wounds to fight infection, modulate inflammation, and promote angiogenesis and collagen synthesis in order to accelerate wound closure and/or otherwise improve functional outcomes.

This invention is the subject of issued patents US 7,968,664 and US 8,093,343, and HHS Reference Number E-188-2004.

Project Goals:
The ultimate goal of this effort is to develop a commercially viable wound-healing dressing, utilizing this NCI-developed technology, to alleviate the suffering and costs caused by non-healing wounds, thereby establishing a precedent for supportive care for cancer while quickly creating a product of merit. The short-term goal of this project is to develop a prototype of such a dressing and to provide data that clearly demonstrate the potential of this stable NO-releasing material/formulation. The work scope may include design and fabrication of the material with *in vitro* evaluation (e.g., product stability testing) and preliminary *in vivo* assessment of its efficacy and final prototype development. These data will support the continued development of the experimental medical device to the point of filing an Investigational Device Exemption (IDE). The long-term goal of this topic is to enable a small business to bring a fully developed product incorporating NCI's NO-releasing polymer technology to the clinic and the market.

The dressing to be developed under this contract should demonstrate the ability to maintain the stability of the diazeniumdiolate group during storage and sterilization, and to release NO when triggered by any mechanism related to wound contact (e.g., thermal or aqueous stimuli, biochemical interaction, etc.), or triggered by the health care provider (e.g., light source, chemical mixing, etc.). Since one of the major potential benefits of sustained and controlled release of therapeutic NO is the reduced frequency with which the care provider must contact the wounded skin to apply therapeutics and change the dressing, any stable, NO-releasing formulation will be considered including, but not limited to, fabric-based "traditional" dressings incorporating poly(acrylonitrile) as one of the textile components, hydrogels, creams, gels, nanomaterials, meshes, films, coatings, etc.

This is an NIH TT (Technology Transfer) contract topic from the NCI. This is a program whereby inventions from the NCI Intramural Research Program (Center for Cancer Research, CCR) 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 contract topic shall work closely with the NCI CCR inventors of this technology. The inventors will provide assistance in a collaborative manner with reagents 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 NCI CCR inventors. However, a pre-submission public briefing and/or webinar will be given by NCI staff to explain in greater detail the technical and licensing aspects of this program (for further information, see http://sbir.cancer.gov/news/upcoming/). In addition, a list of relevant technical, invention, and licensing-related questions and answers (including those from the public briefing) will be posted, maintained, and updated online (http://sbir.cancer.gov/news/upcoming/) during this time period.

The awarded contractor will automatically be granted a royalty-free, non-exclusive license to use NIH-owned and patented background inventions 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. Offerors submitting an SBIR contract proposal in response to this topic are strongly encouraged to submit concurrently an application for a commercialization license to such background inventions. Under the NIH NCI 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 this NIH invention, an SBIR offeror or contractor must submit a license application to the NIH Licensing and Patenting Manager: Betty Tong Ph.D., tongb@mail.nih.gov or 301-594-6565. Please click to download a license application (for PDF download), or, (for Word Doc. download), and view model license agreements here.

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/information-licensees. 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 NIH TT contract period of performance will be owned by the contractor subject to the terms of Section 8.5.

Phase II Activities and Expected Deliverables:

- All studies in Phase II shall be conducted with the ultimate aim of producing a product acceptable to the FDA, and shall thus follow the recommendations contained in the FDA document "Guidance for Industry: Chronic Cutaneous Ulcer and Burn Wounds-Developing Products for Treatment" published June 2006 and available for download from the FDA website.
- Conduct appropriate stability studies, including thermal stability at sterilization temperatures and shelf life characterization
- Provide quantitative evidence of improved wound healing over the current standard-of-care
- Demonstrate capability for commercial production of the product
- Demonstrate capability to manufacture and sterilize the lead candidate in an industrial setting
- Prototype should demonstrate the ability to provide medical benefit, robust stability, and commercial potential

Topic 318 Test to predict Effectiveness of Docetaxel Treatment for Prostate Cancer (NIH Technology Transfer)

Budget (total costs): $2,000,000 for two (2) years.

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.

For frequently asked questions on this contract topic see: http://sbir.cancer.gov/funding/contracts/fy2013_faq.asp

Summary:
Over the past two years, medical oncologists have added three new therapies to the therapeutic arsenal against Castration-Resistant Prostate Cancer (CRPC): abiraterone, Sipleucel-T, and cabazitaxel. Before approval of these agents, docetaxel was the only life-extending therapeutic option for men with CRPC, and docetaxel remains the standard of care for men who can tolerate chemotherapy. Moreover, there are several promising agents that are likely to be FDA-approved for CRPC in coming years (i.e., MDV-3100, EPI-001, and TOK-001). Therefore, the commercial availability of a method to determine which CRPC patients will have a superior response to docetaxel therapy (and which CRPC patients will not respond), will allow medical oncologists to consider other approved options in certain patients, thereby "personalizing" CRPC therapy.

The National Cancer Institute (NCI) has developed a genotype test that can indicate the duration of survival following docetaxel therapy in men with CRPC. The test detects a genetic variant in cytochrome P450 1B1 (*CYP1B1*3; 4326C>G*) that encodes a leucine-to-valine amino acid substitution, L432V, in the translated protein. This genetic polymorphism

causes *P450 1B1* *3 to synthesize higher than normal concentrations of a reactive estrogen species (e.g., estradiol-3,4-quinone [E2-3,4Q]) that reduces docetaxel activity via two distinct mechanisms. Firstly, E2-3,4Q binds directly to docetaxel at biological pH, thereby reducing docetaxel potency. Secondly, E2-3,4Q antagonizes the mechanism of action of docetaxel (i.e., microtubule stabilization), by destabilizing the interaction between tubulin thiol groups that are required to form microtubules. Therefore, a simple genotypic test can determine whether or not a patient will respond to docetaxel, or whether treatment with other newly-approved anticancer agents is warranted. The genetic marker *CYP1B1*3* could be used as a prognostic tool to predict survival rate and propensity to respond to docetaxel treatment.

This invention is the subject of filed patent applications US20100280084A1 and EP1943358, and HHS Reference Number E-307-2005/0.

Project Goals:
The focus of this topic is to advance development of this genetic test which would provide rapid and useful *a priori* predictions of the clinical outcome of docetaxel patients and guide the therapeutic strategy for each patient. The short-term goals of this project are to: (i) develop a rapid and reproducible assay for the CYP1B1*3 variant; (ii) provide additional preclinical evidence necessary for carrying the CYP1B1*3 genotype test into the clinical setting; and (iii) determine if cabazitaxel activity is related to the CYP1B1*3 allele and reactive estrogen species. The long-term goal of this project is obtain FDA approval for the test, to establish broader utility for the CYP1B1*3 test in treatment of other cancer types, implement the test in conjunction with alternate therapeutics that act via modulation of this estrogen responsive pathway, and to further translate the utility of the genotype test to wider clinical use. This technology, once demonstrated in the field of prostate cancer, could be applied to breast and lung cancer genetic markers that have clinical application in defining the chemotherapeutic treatment schedules for individual patients.

Phase I deliverables included technique development, further demonstration of the mechanism of CYP1B1*3 interference, validation that genotype is related to survival using retrospective CRPC patient samples, and identification of the percentage of samples with the variant. A future Phase II SBIR award would include a genotype-directed prospective clinical trial with docetaxel and/or cabazitaxel to demonstrate improved taxane outcomes in genotyped patients.

This is an NIH TT (Technology Transfer) contract topic from the NCI. This is a program whereby inventions from the NCI Intramural Research Program (Center for Cancer Research, CCR) 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 contract topic shall work closely with the NCI CCR inventor of this technology. The inventor will provide assistance in a collaborative manner with reagents 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 NCI CCR inventor. However, a pre-submission public briefing and/or webinar will be given by NCI staff to explain in greater detail the technical and licensing aspects of this program (for further information, see http://sbir.cancer.gov/news/upcoming/). In addition, a list of relevant technical, invention, and licensing-related questions and answers (including those from the public briefing) will be posted, maintained, and updated online (http://sbir.cancer.gov/news/upcoming/) during this time period.

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background inventions. Under the NIH NCI 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.

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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/information-licensees. 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 NIH TT contract period of performance will be owned by the contractor subject to the terms of Section 8.5.

Phase II Activities and Expected Deliverables:

- Conduct a genotype-directed prospective clinical trial with docetaxel and/or cabazitaxel to demonstrate improved taxane outcomes in genotyped patients (The NCI may provide samples from retrospective studies and assist with getting more samples)
- Identify the percentage of patients with the *CYP1B1*3* variant
- Translate the test to the commercial clinical setting in a manner sufficient to pass CLIA certification
- Develop a commercially-viable prototype

Topic 319 Technology to Generate Anti-Peptide Capture Reagents for Affinity-Enriched Protemic Studies

Budget (total costs): $1,000,000 for two (2) years.

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:
Anti-peptide capture reagents can be used to identify and quantify proteins containing a target peptide sequence with a number of applications in biological research and bioassay development. For instance, they are used routinely in techniques such as immunoprecipitation, Western blot, and immunohistological identification and protein localization. A recently-developed application of such reagents is Stable Isotope Standards and Capture by Anti-Peptide Antibodies (SISCAPA), which utilizes antibodies to enrich peptides from complex matrices for quantitation of proteins by stable isotope dilution mass spectrometry. SISCAPA has the potential for simultaneous quantification of multiple targets from a given sample. There is growing interest in the development of such multiplex protein assays, including large-scale biomarker candidate verification studies and analyses of targeted biological pathways. Concurrent quantification of multiple protein analytes is highly desirable in these applications to minimize sample requirements, handling, and assay costs per analyte, while maximizing throughput.

Project Goals:
The goal of this project is to develop new technologies that generate reproducible, well-characterized anti-peptide capture reagents for use in affinity-enriched proteomic studies for the cancer research community. An important characteristic of the desired reagents is the ability to immunoprecipitate their target peptide with high affinity. These

reagents should be comparable or superior to ELISA-based antibody technologies in terms of specificity, affinity, and sensitivity and be reproducibly generated in a cost-effective and efficient (e.g. renewable) manner. Currently, mice are often used to generate monoclonal antibodies or alternative capture reagents, but peptides do not always elicit a potent immune response, which can result in low yield of antibodies to effectively immunoprecipitate the target peptides. The desired technology will likely be one that produces a strong immune response to peptide antigens, and may include the use of species other than mice for the generation of antibodies, since other species may have more diverse epitope recognition and improved immune response to small-size epitopes.

The development of these affinity capture reagents will be done in coordination with NCI's Clinical Proteomic Technologies for Cancer (CPTC) group. A list of proteins or proteotypic peptides derived from cancer biomarker candidates may be requested from CPTC. Furthermore, these capture reagents must be made available as a resource to the scientific community. The suggested choices of performance platforms that the affinity reagents must be compared to include mass spectrometry-based quantitative assays, immunoprecipitation, ELISA-based assays, Western blot, and immunohistochemistry. In addition, other considerations should include sensitivity/specificity/affinity information for the reagents, and method comparison with gold standard practices, precision, and LOD/LOQ.

Phase II Activities and Expected Deliverables:

- Implement the new fully functional anti-peptide capture reagent development strategies/technologies and project plan for development of at least 100 anti-peptide capture reagents capable of immunoprecipitation in coordination with CPTC program staff
    - Reagents should be able to capture the target peptides of interest from complex biological mixtures such as blood, plasma, or tissue
- Demonstrate whether the antibodies can immunoprecipitate full-length proteins
- Test performance criteria against affinity, specificity, immunoprecipitation and affinity-enriched SRM-MS (Selected Reaction Monitoring-Mass Spectrometry) platforms or clinical-grade ELISA tests if available
- Work with CPTC to integrate capture reagents into proteomic research platforms

Topic 320 High Quality Cancer-Related Standards for Metabolomics Research

Budget (total costs): $1,000,000 for two (2) years.

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:
The metabolome is a measure of the output of biological pathways and, as such, is often considered more representative of the functional state of a cell than other 'omics measures such as genomics or proteomics. In addition, metabolites are conserved across various animal species, facilitating the extrapolation of research findings in laboratory animals to humans. Despite early promise, challenges remain before the full potential of metabolomics can be realized – including the limited availability of high quality metabolite standards and of companies/core facilities that provide metabolomics services. The NIH Common Fund is currently developing a multi-component program to help increase metabolomics research capacity. SBIR contracts that focus on identifying and synthesizing reliable metabolite standards will complement this effort by attracting current and emerging small businesses to develop these much needed tools – which in turn will contribute towards achieving an important NIH Common Fund goal of increasing the repertoire of high quality and authentic standards for identification, characterization and quantization of metabolites. Entities that wish to compete for such contracts must be cognizant of the current cost and intellectual property rights challenges that have restricted the use of said tools in basic, pre-clinical, and translational research

alike and consequently make reasonable efforts to make said standards and corresponding product sheets widely accessible to the metabolomics community at large.

Project Goals:
The short and long-term project goals involve the development of both isotopically labeled (i.e., ^{15}N, ^{13}C or ^{2}H) and unlabeled metabolite standards for use with mass spectrometry (MS) and/or nuclear magnetic resonance spectroscopy (NMR), respectively. Compounds need to be synthesized in GLP labs with ISO 9000 certification, and purified by either chromatographic methods or crystallization to >95% purity.

Classes of metabolites that require standards for metabolite identification include, but are not limited to:

1. Glycolytic and other energy intermediates
2. Amino acid metabolism
3. Lipids (phospholipids, glycerolipids, sphingolipids, glycolipids, oxylipins)
4. Acylcarnitines and acylglycines
5. Secondary drug metabolites
6. Secondary food metabolites
7. Fatty acids

Offerors should focus their proposals on developing at least one set of metabolite standards, where all compounds in the set are linked to one cancer-related metabolic pathway.

Phase II Activities and Expected Deliverables:

- Scale up of synthesis, purification, and formulation/packaging/chemical stability of Phase I deliverables to allow for more extensive product validation
- Validate the metabolite standards set for reproducible performance in MS or NMR as appropriate
- Provide letters of interest from potential customers, and later letters of commitment from customers to purchase the product developed under this contract

Topic 321 Chemically Defined Glycan Libraries for Reference Standards and Clycomics Research (Joint NCI-NIGMS Program)

Budget (total costs): $1,000,000 for two (2) years.

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:
Glycans play important roles in cell recognition, motility, signaling processes, cell differentiation, cell adhesion, microbial pathogenesis, and immune recognition. Carbohydrate-based high throughput assays (e.g. glycan microarrays, nanoparticles) hold great promise for the rapid analysis of carbohydrate binding proteins (CBPs), elucidation of CBP biology, and the development of diagnostics, vaccines, and therapeutics for a number of diseases, including cancer. However, the utility of these high throughput assays is limited by the paucity of robust biologically relevant glycan libraries available for screening. Glycan standards are also needed to perform structural analysis, especially for monitoring changes in glycosylation that can significantly affect protein function and the safety and efficacy of bio-therapeutics.

NCI participates in trans-NIH initiatives to further glycomics research as part of the Alliance of Glycobiologists for Detection of Cancer, which partners with NCI's Early Detection Research Network, as well as the Glycomics and Glycotechnology Biomedical Technology Research Centers and the Consortium for Functional Glycomics which are funded by NIGMS. Small businesses that develop new glycan libraries for defining the specificities of CBPs, probing the immune response, screening for cancer-associated glycan biomarkers, and enabling glycan structural analysis will more rapidly advance the field of glycomics.

Contract offerors must be cognizant of the current cost and intellectual property rights challenges that have restricted the use of chemical libraries in basic, preclinical, and translational research, and be willing to abide by NIH policies pertaining to the sharing and dissemination of unique research resources developed with NIH funding. Abiding by the NIH *Principles and Guidelines for Recipients of NIH Research Grants and Contracts on Obtaining and Disseminating Biomedical Research Resources* will ensure that libraries and data generated from them will be deposited into existing repositories and databases that will serve as resources for the entire glycobiology community for non-commercial research purposes.

Project Goals:
The goals of this program are to support the synthesis and commercial distribution of robust, well-characterized new carbohydrate libraries that are amenable to being functionalized/linkered for use in high throughput assays, are useful as standards in mass spectrometry (MS) and nuclear magnetic resonance (NMR) applications, and can be used to expand existing screening platforms, structural assays, and additional tool development. These libraries would need to be made with appropriate quality control documentation, and at reasonable cost.

The *Expanding the Chemical Space for Carbohydrates: Roadmap to Automated Synthesis* workshop report, presented to the NIGMS National Advisory Council in 2011, highlights the critical need for comprehensive chemically-defined glycan libraries for: development of screening platforms with sufficient numbers of structures and diversity to cover the major sectors of mammalian glycomes, use as analytical standards, use as substrates for enzymology, and use as building blocks to increase the glycan chemical space with newly identified enzymes. For analytical standards, biologically relevant groups of related structures with emphasis on isomers will be most useful. Compound collections that provide a basis for development of MS or NMR-based experimental conditions for differentiation of closely related structures are highly desirable. Based on current literature, a 10k-12k glycan collection is needed to represent the functional human glycome, and populate a comprehensive glycan array in a manner that would significantly move the field of glycomics forward. Presently, estimates suggest that only 1000 or so glycans have been synthesized for research purposes, and of these, only a few hundred are commercially available.

A number of NIH institutes (NIGMS, NCI, NIAID, NHLBI) support specific efforts in glycomics and several others (NIDDK, NIDCR, NICHD, NIAMS) also have interests in glycobiology. Discovery labs in The Alliance of Glycobiologists for Detection of Cancer, supported by NCI have a current need for libraries of glycans to facilitate structural studies and high-throughput analysis of carbohydrates derived from biological sources. SBIR contracts focused on synthesis of chemically defined glycan libraries that represent important subsets of the human glycome including representative N- and O- linked glycan libraries, glycan structures found on glycosphingolipids, and libraries of glycosaminoglycan oligomers, would speed progress towards a comprehensive mammalian glycan library. Ready access to these reagents is expected to speed progress in the emerging field of glycomics. Compounds must be synthesized and purified utilizing best practices to >98% purity as established by NMR.

It is recommended that offerors focus their proposals on developing at least one robust glycan library of significant complexity. Libraries of free, reducing-end glycans required include, but are not limited to:

Hybrid-type and complex N-glycan core structures with various multiples of antennae

- Hybrid-type N-glycans with all combinations of mannose cores

- Complex-type N-glycans with basic structures of bi-, tri- tetra-antennary, and bisected versions of those, terminating in either sialic acid, galactose, or N-acetylglucosamine. Further elaboration of antennae might include lactosamine extensions, fucosylation, or sulfation. Variability of these features in the antennae is also required to distinguish topological isomers.
- High mannose-type glycans and isomers.

O-glycans

- O-glycan Cores 1 and 2, as well as O-glycans bearing fucosylated and sialylated lactosamines of various lengths and degrees of internal fucosylation.

Human Blood Group Antigens

- ABO blood group (N-Acetylgalactosamine, galactose) antigens (ABO(H) and their variations - A1, A2, H-type 1, H-type 2, H-type 3, H-type 4, etc.).
- Lewis blood group (human fucose-containing) antigens (sLex, Lex , Lea, sLea, repeating Lex, etc., on glycolipid, N- and O-glycan backbones, etc.).

Glycosphingolipid head groups

- Ganglioside-, globoside-, lactosamine-, and neo-lactosamine-based core structures

Phosphorylated mannose glycans

- P-Man-R and GlcNAc-P-Man-R

Glycosaminoglycans (GAGs)

- Glycosaminoglycan fragments (especially heparan sulfate oligosaccharides) of 4 to 8 saccharides with/without defined sulfation.

Glycopeptides

- O-linked core structures on building blocks (such as Fmoc, Ser, or Thr) that can be utilized in peptide synthesis.

Phase II Activities and Expected Deliverables:

- Expand the reducing glycan libraries representative of a sector(s) of the mammalian glycome and not presently commercially available to at least 100 compounds
- Verify structures of the synthesized compounds by NMR
- Scale up the synthesis, purification, structural verification, and packaging of all compounds in the libraries
- Provide the spectra used to confirm each glycan's structure as part of product information
- In collaboration with an NIGMS-designated screening center: provide ~50 µg of each of the newly synthesized compounds made to expand the libraries for printing on glycan arrays, appropriate validation testing, and subsequent use in NIGMS-funded screening assays
- Provide letters of interest from potential customers to purchase the product developed under this contract

Topic 322 Real-Time Integration of Sensor and Self-Report Data for Clinical and Research Applications

Budget (total costs): $1,000,000 for two (2) years.

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:
Wireless sensors, and mobile devices and applications are increasingly marketed for health monitoring or interventions in consumer and clinical settings for prevention or management of chronic disease. A rapidly expanding market segment of technologies are focused on objective measures of health related behaviors (e.g., physical activity, sleep, diet, medication adherence, etc.). These mobile health technologies offer the capability to collect tremendous volumes of high quality health data, with continuous monitoring or event recording functions, in near real time. The expanding use of behavioral monitoring technologies, applications and mobile messaging provides new opportunities within consumer health, clinical care, and research. However, meaningful interpretation of the high volume of data generated from monitoring technologies is a challenge for the patient, care team and the researcher. Further, health monitoring technologies are often criticized for lacking additional contextual data to facilitate their interpretation.

Added to data from sensors and monitoring technology, self-reported measures can provide invaluable psychosocial, contextual, and environmental health-related information. Patient-reported outcomes in physical, mental or social health domains include physical abilities, fatigue, pain, depression, and social interactions. The expanded use of smartphone technologies lends itself to private, convenient, real-time data collection of self-reported measures. However, development or optimization of cross-platform mobile applications and scalable, efficient, cloud-based server platforms for rapid and real-time self-reporting and monitoring of these measures is needed.

Real-time integration of objective and patient-reported data could improve understanding and clinical management of acute and time-varying symptoms such as fatigue, pain, or depression experienced by cancer and other chronic disease patients. The integrated collection of objective and self-reported data can stimulate innovation within clinical and research settings, including clinical trials, clinical care, case-management, interventions, surveillance, and epidemiologic studies. For example, temporal integration of medication monitoring technologies, such as smart pill cases and sensor-based activity and sleep data, with patient-reported measures of depression, fatigue, or pain could enhance pharmaceutical clinical trial results. However, efficient systems and platforms for the capture, storage, integration, visualization, and reporting of these data streams are extremely limited or non-existent.

Project Goals:
This topic's short-term goal is the development of innovative, secure, privacy-compliant mobile applications and paired analytic systems to control the collection, transfer, integration, analysis and reporting of objective and self-reported health-related measures. Longer term goals include the integration of these data systems and layers in health care and research settings to support customized monitoring and feedback loops, alerts, or alarms for consumers, patients, or members of the health care team.

Responses to this topic are expected to address the development of efficient methods and platforms to:

1. Collect data from behavioral health monitoring technologies and self-reported behavioral, psychosocial, environmental, and contextual measures.
2. Demonstrate integration with various wireless sensors.
3. Appropriately secure data at each stage of collection, transfer, and storage.
4. Temporally integrate information from multiple data sources.
5. Visualize data using customizable tools.
6. Analyze and report on (patient identified or de-identified) individual or group level data using customizable tools and reporting systems.

7. Maintain compliance with HIPAA, privacy, and consent management protocols as required for platform specific applications.

The resulting platform's utility extends from consumer health to clinical care and research settings for behavioral monitoring and prevention or management of disease. This topic encourages development of innovative, secure, privacy compliant mobile applications and 2-way mobile messaging techniques to facilitate and control the collection and transport of temporal data inputs from behavioral health monitoring technologies, self-reported measures, and associated metadata. The data acquisition systems described above must be paired with efficient, scalable back-end systems for data importation, storage, integration, visualization, analyses, and output reporting. Data elements may include (but are not limited to) wireless physical activity or sleep sensors/monitors, physiologic sensors, adherence monitors, sensor-based measures of stress or fatigue, dietary intake measures, geospatial location tags or linkages, images, text based annotations, speech recording and recognition; and self-reports of behavioral, psychosocial, environmental, and contextual data.

An essential task for each proposal is the development of transparent and customizable analytic tools for temporal data integration, visualization, and summary reporting of individual or group level measures. Recommended short term targets for system outputs are to provide reports to patients/participants, clinicians/researchers, and health systems; with longer term targets to provide reports directly to electronic medical records and public health surveillance systems. Recommended reports are consistent with current health outcomes policy priorities and objectives in the Meaningful Use Matrix for electronic health records established by the Health Information Technology Policy Committee (see http://healthit.hhs.gov/portal/server.pt).

Phase II Activities and Expected Deliverables:

- Beta-test and finalize front-end mobile applications developed in Phase I
- Beta-test and finalize automated file transfer, screening, and database importation protocols and systems
- Develop, beta-test, and finalize data integration and visualization tools developed in Phase I
- Develop, beta-test, and finalize care team/researcher user-interface systems
- Develop and beta-test output reporting systems capabilities for multiple system output targets listed above
- Demonstrate system compatibility with sensor(s), mobile platform(s), and mobile device(s), included in the Phase I compatibility matrix
- Perform regression testing for both front-end and back-end system functions
- Conduct usability testing of consumer/patient-facing mobile applications and any associated web portals and care team/researcher-facing user interface features including system management, analyses, and reporting applications
- Develop systems documentation where applicable
- In the first year of the contract, provide the program and contract officers with a letter(s) of commercial interest
- In the second year of the contract, provide the program and contract officers with a letter(s) of commercial commitment

Topic 323 Development of Radiation Modulators for Use During Radiotherapy

Budget (total costs): $1,500,000 for two (2) years.

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:
Radiotherapy is employed in the treatment of over half of all cancer patients. Many of those patients suffer adverse effects during and/or after treatment. Additionally, tumors recur in approximately half the patients treated with curative intent. Enhancing specific tumor killing and minimizing normal tissue damage from radiotherapy would

improve tumor control and patient quality of life. An ideal intervention would both enhance radiation effects in tumors and protect the normal tissues.

Radiosensitizers are agents that are intended to enhance tumor cell killing while having a minimal effect on normal tissues. Recently, two new radiation sensitization drugs have proven clinically effective: Temozolomide treatment with radiotherapy for glioblastoma and Cetuximab treatment combined with radiation for head and neck squamous cell cancers. There is significant potential for further development of novel radiosensitizing agents.

Conventionally, *radioprotectors* are defined as agents given before radiation exposure to prevent or reduce damage to normal tissues, while *mitigators* refer to those agents given during or after a patient's prescribed course of radiation therapy to prevent or reduce imminent damage to normal tissues. Both radioprotectors and mitigators are also being developed as potential countermeasures against radiological terrorism and several have shown promise in pre-clinical testing. In order for these to be developed and useful in clinical radiation therapy applications, it is imperative to demonstrate that they do not protect cancer cells.

The importance of developing agents that sensitize tumor cells, protect or mitigate radiation-induced damage in normal tissue, improve survival, quality of life, and palliative care in cancer patients was emphasized in a recent NCI workshop on *Advanced Radiation Therapeutics – Radiation Injury Mitigation* held on January 25th 2010 (Movsas B, et al. Decreasing the adverse effects of cancer therapy: National Cancer Institute guidance for the clinical development of radiation injury mitigators. Clin Cancer Res. 2011 Jan 15;17(2):222-8. Epub 2010 Nov 3. PMID: 21047979), and in a workshop on *Radiation Resistance in Cancer Therapy: Its Molecular Bases and Role of the Microenvironment on its Expression* held Sept 1–3, 2010. Prior workshops have dealt with sensitization, protection, or radiation effects assessment (Colevas AD, et al. Radiation Modifier Working Group of the National Cancer Institute. Development of investigational radiation modifiers. J Natl Cancer Inst. 2003 May 7;95(9):646-51. Review. PMID:12734315; Stone HB, et al. Models for evaluating agents intended for the prophylaxis, mitigation and treatment of radiation injuries. Report of an NCI Workshop, December 3–4, 2003. Radiat Res. 2004 Dec;162(6):711-28. PMID: 1554812.)

This contract topic encourages the development of innovative and promising radioprotectants, mitigators, or sensitizers that either selectively protect normal tissues (but not tumors) against ionizing radiation or selectively sensitize tumors, thereby increasing the therapeutic ratio of radiation. Proposals for radiation modulators are solicited that include preclinical and/or early phase clinical studies demonstrating safety, efficacy, dose, schedule, pharmacokinetics (PK), pharmacodynamics (PD), and metabolism. Proposals should also demonstrate a clear understanding of regulatory requirements, and should include a regulatory plan including key steps such as a pre-IND meeting with FDA, submission of an investigational new drug (IND) application, approval of clinical trial design, and ultimately drug registration.

Project Goals:
The goal is to stimulate collaborations among academic institutions, small businesses, and contract research organizations in order to promote the rapid development of innovative radioresponse modifiers that will decrease normal tissue injury and/or enhance tumor killing thereby improving radiotherapy outcomes. The long-term goal is to enable small businesses to fully develop, license, and/or market radio response modifiers for clinical use.

The contract proposal must describe:

Phase II:

- The approach to early-phase human trials designed to take into account relevant molecular pathways and targets, and aim to gather pharmacodynamic and pharmacokinetic data to confirm the compound's observed behavior in animal studies.

- The approach and experiments to assess the safety and efficacy of the compound(s) in early-phase human trials employing, as appropriate, physician-reported endpoints as well as patient-reported outcomes.

Deliverables:
Phase II proposals must contain a section entitled "Regulatory Plan" detailing plans for early involvement of the FDA. There should be a description of how the applicant plans on meeting the requirements to: 1) define suitable biomarkers and endpoints, 2) file IND and 3) design and perform phase 0-2 clinical trials in preparation for product transition to phase 3 clinical trials by groups such as the Radiation Therapy Oncology Group.

Where cooperation of other partners is critical for implementation of the proposed methodology, the applicant should provide evidence of such cooperation (through partnering arrangement, letters of support, etc.).

The following deliverables may be required depending on a compound's maturity in the developmental pipeline:

Phase II:

For advanced pre-clinical work:

- Design of NCI and Institutional Animal Care and Use Committee (IACUC)-approved *in vivo* experimentation plan including statistical validation of experimental design, and sample size determination including power calculations
- Selection and approval of tumor cell panel and normal tissues for *in vitro* testing
- Demonstration of bioavailability PK and PD in rodent model
- For radiation protectors/mitigators: demonstration by physiologic testing and histological assessment that irradiated normal tissues are spared over a 6-month period
- Demonstration of effects (sensitization or lack of protection as appropriate) on tumors using *in vivo* radiation regrowth delay assays
- Collection of data validating lack of drug toxicity, efficacy, and specificity for normal cells over tumor cells in the case of radiation protectors/mitigators
- Documentation of the testing protocol and testing results should be provided to NCI as part of the Phase II progress report for pre-clinical studies

For proposals advancing to early phase human trials:

- Identify GMP drug source
- Obtain IND approval
- Provide evidence of established clinical collaboration
- Submit protocol for IRB approval
- Define suitable clinical endpoints and patient-oriented outcomes

Topic 324 Novel Imaging Agents to Expand the Clinical Toolkit for Cancer Diagnosis, Staging, and Treatment

Budget (total costs): $1,500,000 for two (2) years.

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:
Medical imaging plays a key role in clinical management of cancer patients. Cancer imaging agents are used in

conjunction with medical imaging equipment, and, by highlighting the contrast between normal and malignant tissues, they allow the collection of information on cancer presence, spread, and metabolism.

Recent scientific advances in nanotechnology, radiochemistry, reporter gene imaging, cancer stem cell imaging, and other fields now enable the development of novel imaging agents for:

- Early detection and diagnosis of cancer.
- Differentiation of benign disease from malignancy.
- Stratification of patients for the purpose of selecting a cancer therapy.
- Surgical planning.
- Evaluation of tumor response to chemotherapy and radiation therapy.
- Detection of cancer recurrence.

Despite significant preclinical scientific progress, very few cancer imaging agents are available in the clinic. This SBIR contract topic seeks to stimulate the commercialization of novel imaging agents, including but not limited to: nanotechnology-based imaging agents, radiopharmaceuticals for positron emission tomography (PET) and single photon emission computed tomography (SPECT), targeted contrast agents for X-ray, computed tomography (CT), and magnetic resonance imaging (MRI), optical contrast agents, and reporter gene imaging technologies.

One specific area of interest under this topic is the development of single-domain antibody fragments used to target radionuclides for imaging and targeted radiotherapy of cancer. Single-domain antibody fragments are comprised of the single variable region of naturally-occurring antibodies that lack a light chain or engineered antibody fragments. This type of small protein or peptide has advantages over conventional antibodies and antibody fragments in terms of favorable and tunable clearance kinetics, ability to recognize hidden or uncommon epitopes, agent format flexibility, and ease of manufacture. Therefore, developing an imaging technology for early diagnosis of cancer at the molecular level based on single domain antibody fragments will be encouraged.

Project Goals:
The short-term goal of this SBIR contract topic is to support research and development activity at small businesses that are developing cancer imaging agents. The imaging agent should be novel and, when appropriate, have high affinity and specificity against tumor targets. It should also display fast *in vivo* clearance, rapid tumor accumulation, sufficient *in vivo* stability and good bioavailability, and low immunogenicity and toxicity. The work scope may include animal testing, formulation, GMP production, pharmacokinetic studies, pharmacodynamic studies, and toxicological studies. These data will support the rationale for continued development of the experimental medical imaging agent to the point of filing an Investigational New Drug application (IND).

The long-term goal of this contract topic is to enable small businesses to bring novel classes of fully developed cancer imaging agents to the clinic and the market. Therefore, businesses are encouraged to submit applications for development of lead compounds representing novel technology platforms.

Phase II Activities and Expected Deliverables:
Phase II should follow the development plan laid out in the Phase I, and should further support commercialization of proposed cancer imaging agents. The Phase II research plan must contain specific, quantifiable, and testable feasibility milestones.

Expected activities may include:

- Complete of all pre-clinical experiments according to the development plan
- Demonstrate fast *in vivo* clearance, rapid tumor accumulation, sufficient *in vivo* stability, good bioavailability, and low immunogenicity/toxicity of the imaging agent

- Demonstrate high reproducibility and accuracy of the imaging technology in several animal models
- When appropriate, demonstrate similar or higher specificity and sensitivity of the technology when compared to other imaging technologies
- When appropriate, demonstrate capabilities to monitor efficacy of drugs in tumor cell lines and/or animals
- Produce sufficient amount of clinical grade material suitable for an early clinical trial
- If warranted, file an IND or an exploratory IND for the candidate imaging agent
- Complete small-scale clinical study

Topic 325 Innovative Radiation Sources for Advanced Radiotherapy Equipment.

Budget (total costs): $2,000,000 for two (2) years.

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:
Radiation therapy is an important tool in the cancer treatment arsenal. Conventional radiotherapy with photons is currently used to treat 50% of all cancer patients. The success of radiation therapy and the risk of side effects depend heavily on the ability to concentrate radiation in the tumor while not injuring adjacent normal tissues. Recent developments in radiation therapy instrumentation have increased the ability to direct radiation energy, thereby improving the clinical utility of this treatment.

Although significant progress has been made, one of the limiting factors in the development of novel radiotherapy approaches is the size and cost of radiation sources. For many types of modern advanced radiotherapy, the equipment needed to produce such radiation is bulky and extremely expensive. At the same time, continuing advances in particle acceleration approaches enable breakthrough innovations in this field. An example of such advancement is the development of technologies for charged particle acceleration using high-power lasers (laser-plasma acceleration). New technologies enable the construction of compact, cost-efficient external beam accelerators, and facilitate new applications of radiotherapy. Another potential class of applications is the development of fiber-optics-based systems for endoscopic delivery of gamma or electron beams. These and other technologies present key opportunities in enabling next-generation radiation therapy instruments.

Project Goals:
This contract topic seeks to stimulate research, development, and commercialization of innovative radiation sources that could be used to reduce the cost and footprint of radiation treatment systems, and thus enable novel routes for radiotherapy delivery.

It is expected that the proposed innovation be driven by clinical practice. Therefore, in addition to standard proposal components, the contract proposal must contain specific discussion of:

1. Evidence of an existing clinical problem that is addressed by the proposed radiation source
2. Analysis of competitive methods to address the same problem and explanation of competitive advantages of proposed system.

The short-term goal of the project is to perform proof-of-principle technical feasibility demonstration of innovative radiation source or source components. The long-term goal of the project is to develop a robust, reliable radiation source and to incorporate it into a radiotherapy system.

Phase II Activities and Expected Deliverables:
Phase II activities should support development of a full-scale prototype of a radiation source with beam parameters appropriate for the clinical application.

- Design and develop a prototype radiation source with parameters (e.g., beam energy, flux, stability, etc.) that are acceptable for clinical radiation oncology application
- Demonstrate that the system is capable of delivering a treatment dose in a clinically acceptable period of time in an anthropomorphic phantom
- Provide a data sheet detailing performance of the developed system to NCI as part of the Phase II progress report

Where cooperation with other equipment manufacturers is critical for implementation of proposed technology, company should provide evidence of such cooperation (through partnering arrangement, collaboration, or letters of intent) as part of the Phase II proposal.

9 SUBMISSION FORMS AND CERTIFICATIONS

9.1 SOLICITATION ATTACHMENTS

1. Proposal Intent Sheet: http://oamp.od.nih.gov/sites/default/files/DGS/contracting-forms/intent.pdf

2. Section K – Representations, Certifications, and other Statements: http://oamp.od.nih.gov/sites/default/files/DGS/contracting-forms/sectionk_508_0.pdf

9.2 TECHNICAL PROPOSAL ATTACHMENTS

3. SBIR Proposal Cover Sheet: http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixA.pdf

4. Sample Statement of Work: http://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixE.docx

5. Abstract of Research Plan: http://www.grants.nih.gov/grants/funding/SBIRContract/ContractAppendixB.pdf

6. Planned Enrollment Report, PHS-389/2590 (Rev. 08/12): http://grants.nih.gov/grants/funding/phs398/CumulativeInclusionEnrollmentReport.pdf

7. Technical Proposal Cost Summary: http://oamp.od.nih.gov/sites/default/files/DGS/contracting-forms/Tech-Prop-Cost-Summ.pdf

8. Summary of Related Activities: http://oamp.od.nih.gov/sites/default/files/DGS/contracting-forms/summary-related-activities.pdf

9. Protection of Human Subject Assurance Identification/IRB Certification/Declaration of Exemption, OMB Form No. 0990-0263 (Formerly Optional Form 310): http://www.hhs.gov/ohrp/assurances/forms/of310.pdf

10. Contract Proposal Vertebrate Animal Section (VAS) Worksheet: http://grants.nih.gov/grants/OLAW/VAScontracts.pdf

9.3 BUSINESS PROPOSAL ATTACHMENTS

11. Certification for Applicants that are Majority-Owned by Multiple Capital Operating Companies, Hedge Fund or Private Equity Firms:

http://grants.nih.gov/grants/funding/sbir_forms/SBIR%20Application%20VCOC%20Certification.docx

12. SBIR Funding Certification: http://grants.nih.gov/grants/funding/sbir_forms/SBIR%20Funding%20Agreement%20Certification.docx

13. NIH form 2043, Proposal Summary and Data Record: http://oamp.od.nih.gov/sites/default/files/DGS/contracting-forms/NIH2043.pdf

14. Breakdown of Proposed Estimated Costs (plus fee) w/excel Spreadsheet: http://oamp.od.nih.gov/sites/default/files/DGS/contracting-forms/spshexcl_dec2012.xlsx

15. Offeror's Points of Contact: http://oamp.od.nih.gov/sites/default/files/DGS/contracting-forms/point-of-contact.pdf

16. Certificate of Current Cost or Pricing Data: http://oamp.od.nih.gov/sites/default/files/DGS/contracting-forms/cert-current-cost.pdf

17. Small Business Certification Form:

18. Disclosure of Lobbying Activities, OMB Form SF-LLL: http://www.gsa.gov/portal/forms/download/116430

19. Adequate Accounting System Certification:

9.4 INFORMATIONAL ATTACHMENTS

20. IDC Two Tier Example: http://oamp.od.nih.gov/sites/default/files/DFAS/IDCTwoTierExample_508.xlsx

21. SBIR Funding Agreement Certification – Life Cycle Certification: http://grants.nih.gov/grants/funding/sbir_forms/SBIR%20Life%20Cycle%20Certification.docx

22. Invoice/Financing Request and Contract Financial Reporting Instructions—Cost Reimbursement, NIH(RC)-4: http://oamp.od.nih.gov/sites/default/files/DGS/contracting-forms/rc4_508.pdf

23. Safety and Health, HHSAR Clause 352.223-70: http://oamp.od.nih.gov/sites/default/files/DGS/contracting-forms/Safety-Health-hhsar-1-06.pdf

24. Research Patient Care Costs, NIH(RC)-11: http://oamp.od.nih.gov/sites/default/files/DGS/contracting-forms/rc11.pdf

25. Cumulative Inclusion Enrollment Report: http://grants.nih.gov/grants/funding/phs398/CumulativeInclusionEnrollmentReport.pdf

26. Disclosure of Lobbying Activities, OMB Form SF-LLL: http://www.gsa.gov/portal/forms/download/116430