

Solicitation S16-001: NCI Experimental Therapeutics (NExT) Program Chemical Biology Consortium Volume 1: Technical and Cost Proposal Requirements

This Solicitation is divided into two documents for ease of Offeror response: this one, which is referred to as Volume 1: Technical and Cost Proposal Requirements, and another, which is referred to as Volume 2: Compliance Document Requirements. Volume 1 must be submitted by 5:00 PM ET on Thursday, November 5, 2015. Volume 2 is due by 5:00 PM ET on Thursday, January 14, 2016.

Introduction

This solicitation requests proposals from academic, non-profit or private institutions as well as small biotech companies or Contract Research Organizations (CROs) with expertise in small molecule drug discovery to participate in a Chemical Biology Consortium (CBC). The CBC is a highly collaborative drug discovery consortium designed to integrate all aspects of early stage drug discovery from target validation through candidate selection, leading to the discovery of new molecular entities that the National Cancer Institute (NCI) can sponsor in clinical development. The CBC Centers will provide project teams with the technical expertise and the scientific personnel that are needed to navigate scientific roadblocks and advance projects through the NExT pipeline (<http://next.cancer.gov/discoveryResources/cbc.htm>). As participants on multidisciplinary drug discovery teams, the CBC will enable translation of research findings from leading academic institutions and progression of early stage hit compounds into potent and selective drug candidates for the benefit of patients with cancer.

The organization and management structure of the Consortium is designed to conduct drug discovery research in an efficient and collaborative manner while minimizing the administrative workload associated with funding and oversight of the projects. Several key features of the CBC are:

- 1) The Consortium will be composed of two types of Centers, Dedicated CBC Centers and Specialized CBC Centers.
 - a) Dedicated CBC Centers are Centers that will be awarded Master Service Agreements with committed funding. Agreements will include funding for a broad work scope in chemical-biology. These Dedicated CBC Centers may also contribute specialized expertise to the projects.
 - b) Specialized CBC Centers are those with specialized technology or expertise that is required to advance individual projects. These Centers will be awarded different types of agreements based upon the technical proposal and the areas of programmatic need.

- c) Offerors may propose to be considered for either classification of CBC Center. The selection of each Center and determination of Center type will be made following review and evaluation of all proposals, and if necessary after visiting the potential CBC Center location.
- 2) Collaborative Project Teams will be composed of scientists from CBC Centers, the NCI, and the Frederick National Lab for Cancer Research (FNLCR). NCI administers the Consortium through a contract to Leidos Biomedical Research, Inc., the operations and technical support contractor for FNLCR. Co-Leaders for projects will be selected from the NCI and from one of the participating CBC Centers to lead the team in the planning and execution of the project, and in making key decisions. Project teams will meet monthly, and CBC Centers will submit scientific reports quarterly.
- 3) Intellectual property—NCI has created a framework that establishes a standard for collaboration among all participants and encourages the commercialization of breakthrough research findings. These guiding principles are described in the CBC Participants Agreement, and acceptance of these terms is required for participation in the CBC (http://dctd.cancer.gov/CurrentResearch/CBC_Agreement.pdf).

Key Solicitation Dates

- Written questions about the Solicitation and requests for clarifications must be submitted to cbcproposals@mail.nih.gov by 5:00 PM ET Wednesday, September 16, 2015. Answers will be provided to these questions, and new questions can be asked at Bidders Teleconference 1.
- Bidders Teleconference 1: 2:00 PM ET Thursday, September 24, 2015.
- Bidders Teleconference 2: 2:00 PM ET Thursday, October 15, 2015.
- Offeror's wishing to participate in these teleconferences should dial (U.S. and Canada) 855-462-5367 and enter passcode 3250774 when prompted. International callers wishing to participate in these teleconferences should dial 804-451-4138 and enter passcode 3250774 when prompted.
- Responses to Solicitation S16-001 Volume 1: Technical and Cost Proposals with Offeror Signature page, and Questionnaires from references (submitted to cbcproposals@mail.nih.gov) are due by 5:00 PM ET Thursday, November 5, 2015.
- Responses to Solicitation S16-001 Volume 2: Compliance Documents (submitted to cbcproposals@mail.nih.gov) are due by 5:00 PM ET, Thursday, January 14, 2016.

Statement of Objectives

A. Introduction

A.1. *CBC within the NCI Experimental Therapeutics Program*

The National Cancer Institute (NCI) established the Chemical Biology Consortium in 2009 as the drug discovery engine of the NCI Experimental Therapeutics (NExT) Program (<http://next.cancer.gov> and <http://next.cancer.gov/discoveryResources/cbc.htm>). The CBC consolidated activities of the earlier NCI RAID program and the NIH Molecular Libraries program (Figure 1) within NExT. However, unlike the MLPCN Program whose stated goal was to produce tool compounds (chemical probes), the NExT mission is to produce agents that move along a milestone-based path to become anticancer therapeutics. The consortium is composed of members from academic, government and private institutions that provide the essential scientific knowledge, skills and technical capabilities required to discover hit compounds and advance them into chemical leads and clinical candidates. Successful candidate compounds can quickly transition to evaluation in the clinic. For applicant PIs whose drug discovery projects are admitted into the NExT pipeline, the CBC provides technologies (e.g., HTS) and skill sets (e.g., experienced medicinal chemistry) often inaccessible to academic researchers and rarely found within a single institution. Thus, the CBC bridges the translational gap between scientifically-based therapeutic hypotheses and the creation of a novel chemical entity with potential to provide clinical benefit to cancer patients.

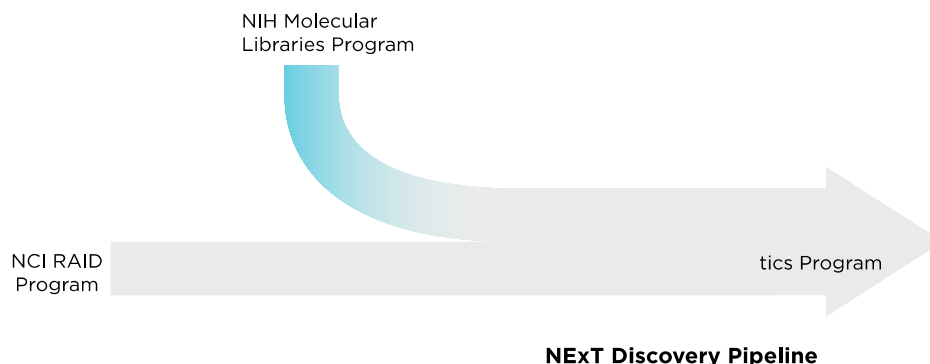


Figure 1. Creation of the CBC for discovery research at the front end of the NExT pipeline

Project Team Approach

NExT projects are undertaken by teams of scientists that bring together the varied expertise and skill sets required to advance the project from one milestone to the next. Members of the project team include scientists from participating CBC Centers, the Applicant PI, an NCI Project Co-Leader, a Contracting Officer's Scientific Representative from Leidos Biomed and various other participants depending upon the expertise required at that stage of the project. The team selects a CBC Co-Leader from one of the participating centers to work with the NCI Project Co-

Leader. The composition of the team may change as the project advances through the discovery stages of the NExT Pipeline (Figure 2) and different expertise is required.

NCI and Leidos Biomed staff provide project management support for the project teams. All team members have access to a Project Team SharePoint Site that houses data, reports, presentations and other supporting documentation specific to that individual project. Additionally, the NCI has a relational database for centralized storage of project team data. A data surfacing interface (D360 from Certara, <http://www.certara.com/products/sci-info/d360>) enables all team members to run queries against their project's data or to examine results of previously posted datasets. Access to these data is restricted based on an individual participant's membership on specific project teams, in accordance with the Confidentiality Terms of the CBC Participants Agreement.

CBC Steering Committee

The heads of the individual CBC Centers comprise the CBC Steering Committee. This body meets quarterly to discuss the progress on existing projects as well as to provide suggestions about how best to address the scientific needs of incoming early discovery projects. Additionally, this group provides feedback to NCI and Leidos Biomed management regarding operation of the consortium.

A.2. Governance and Contracting Mechanism

CBC Participants Agreement Overview



The NCI CBC Participants Agreement is structured to support the development and commercialization of therapeutic inventions that are essential for achieving the program's ultimate goal of bringing novel and effective therapeutics to cancer patients. (http://dctd.cancer.gov/CurrentResearch/CBC_Agreement.pdf). Within the Agreement, Intellectual Property (IP) protections are delineated that ensure IP ownership for inventor(s), while terms describing confidentiality and controlled data access encourage innovation and collaboration. Recognizing that protection of IP rights is a critical factor in the success of the CBC, acceptance of the Terms and Conditions under the IP and data-sharing plan in the Agreement is required for participation in the CBC.

Management of IP and shared inventions: Each participant will retain ownership of inventions made by its employees. Ownership of joint inventions made by two or more participants will be determined by applicable patent law. It is expected that participants with joint ownership of an invention will establish an appropriate agreement between them that establishes the rights and

responsibilities of each participant and reflects cooperation to efficiently develop such an invention to an appropriate commercial endpoint. Furthermore, it is expected that groups of participants, who own individual inventions that collectively may produce a beneficial commercial product(s), will similarly cooperate to reach an appropriate commercial endpoint.

Data and reagent sharing and confidentiality: NCI manages a centralized database for housing project team data, with access limited to participants on that project team. Timely entry of deliverable data into this database promotes collaboration among team members and ensures confidential access to data to protect IP rights. Sharing of materials generated within the CBC is encouraged and is governed by the terms within a straightforward NIH Material Transfer Agreement. The Agreement also documents how resources developed by the CBC may benefit the broader research community.

Publications and presentations: Publication of results and discoveries made by CBC Centers and project teams is encouraged within the bounds of the confidentiality terms set forth in the Agreement, and as subject to approval by NCI.

The NCI CBC Participants Agreement is administered directly by the NCI Technology Transfer Center (TTC). All Offerors should contact the TTC for a copy of and all matters pertaining to the Agreement:

Melissa Maderia, Ph.D., M.B.A.
Technology Transfer Specialist,
Technology Transfer Center
National Cancer Institute
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CBC administration through a contractual mechanism: The NCI operates the CBC through a set of contractual agreements with the participating CBC Centers. These agreements are made between the CBC Center and Leidos Biomed, which has the operations and technical contract from NCI for running FNLCR. As such, Leidos Biomed is a contractor for NCI and the agreements with the CBC Centers are subcontracts.

The nature of this contractual mechanism is described in detail in Volume 2 of this solicitation and is substantially different from a grant process. Whereas a grant provides funding to organizations to support research activities benefiting the recipient, a contract is a method to procure research support and services. The content of the subcontracted work is usually determined with considerable input from the sponsoring agency (NCI) and is established specifically to benefit the sponsor (NCI) by achieving an expected outcome or providing a specific product (including data, materials or results). Changes to the scope of work, the deliverables (and due dates) or budget must be mutually agreed upon by both parties to the agreement, and final approval must be issued by the Leidos Biomed Contracting Officer. Fulfilling obligations under a contract, as compared with a grant, requires knowledge of

different business practices and requires more flexibility on the part of the CBC site to manage staffing and personnel commitments.

A.3. *Selection of CBC Centers*

All proposals received in complete and proper format will be evaluated by a panel of subject matter expert reviewers and scored according to a uniform set of criteria. The four (4) major components of the evaluation are:

- (1) the technical capabilities and expertise present at the Center,
- (2) the demonstration of successful past performance and experiences using these capabilities and expertise,
- (3) the quality of scientific leadership and technical personnel who would participate in CBC projects, and
- (4) the availability of the necessary equipment, facilities and IT infrastructure to effectively carry out the proposed drug discovery activities.

In addition to scoring each Center's technical proficiency, the ability to function effectively in a project team environment that requires clear communication and sharing of data and reagents will be evaluated, as will the management practices in place to handle staffing, budget and contractual responsibilities. The Cost Proposal will be assessed to determine if costs are reasonable for the skill level of personnel proposed.

The determination of which Centers will be designated Dedicated CBC Centers and which will be designated Specialized CBC Centers will be based on the scoring of the proposals and the anticipated capacity and capabilities needed to support the portfolio of discovery projects within the NExT pipeline. Between the evaluation period and when awards are made, site visits to prospective CBC Centers may be conducted.

B. Statement of Objectives

The NExT program seeks to identify CBC Centers that can provide deep scientific expertise, highly skilled technical capabilities and resources to fulfill the essential activities necessary to advance early stage drug discovery projects through the Candidate Selection phase (see pipeline, Figure 2). Many areas of expertise are required in almost all early discovery projects. However, some projects either require, or benefit greatly from the application of specialized technologies. To support the variety of NExT discovery projects in an optimal fashion, the CBC will be composed of several Dedicated CBC Centers that will be staffed with experienced personnel and a commensurate level of financial support so as to provide the fundamental discovery competencies to project teams. Additionally, a variety of Centers, termed Specialized CBC Centers, will be selected that can provide alternative or cutting edge technical approaches for projects which would benefit from such methodology. Some Centers may be qualified and selected to provide both fundamental expertise as well as some specialized approaches.

In addition to having strong scientific and technological capabilities, CBC Centers also must have personnel who can work effectively in collaboration with other scientists on a multidisciplinary project team. Senior staff, or the PI from the Center, are expected to participate actively as members of the CBC Steering Committee and to contribute insightful perspectives that benefit the Consortium as a whole.

Lastly, CBC Centers will need to provide appropriate management oversight to effectively support their scientific contributions to NExT projects and the Consortium. Such responsibilities include handling personnel and staffing requirements to appropriately support project teams, to accurately process contractual and financial/budgetary/accounting documents in accordance with guidelines provided by the Leidos Biomed Contracting Office, and to manage and track spending on project team activities so as to stay within budget.

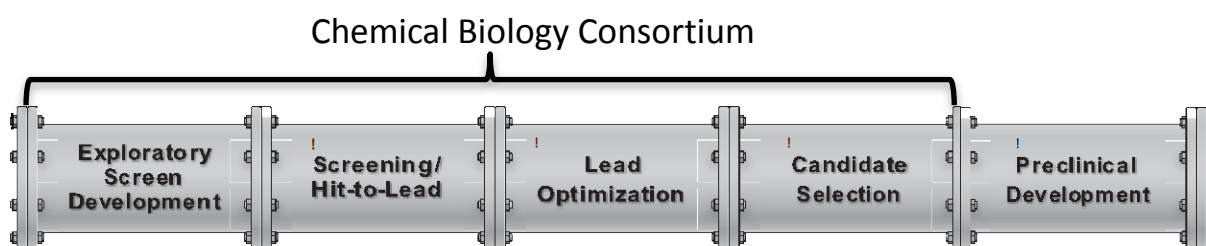


Figure 2. The 4 stages of drug discovery, prior to IND enabling studies, to be carried out by the CBC.

B.1. Scientific and technical capabilities to support drug discovery

Once assembled, the CBC will possess a broad range of fundamental and specialized expertise that can be deployed effectively to tackle each drug discovery project. The technologies and skills listed in the table below, and elaborated upon in the following paragraphs, indicate the categories of skills and expertise essential for supporting NExT projects through the Candidate Selection phase. Within these categories, there are many commonly used techniques and approaches to accomplish the goals, and the CBC will establish Dedicated Centers that are well versed in these methods to provide adequate coverage for the portfolio of projects. However, within each of these categories there also exist specialized techniques or methods that can provide a unique advantage for targets not well-suited or amenable to more traditional methods or techniques. Because of NExT's mission, its discovery projects often tackle novel targets and nontraditional mechanisms of action that benefit from these approaches. Thus, it is essential that this solicitation identify Centers with such specialized methods or innovative technologies.

Categories of Technologies and Skills Essential for Early Discovery

1. Protein production and purification for HTS, SAR assays and structural biology studies
2. Development of biochemical and cellular assays, including optimization and miniaturization for HTS
3. HTS capabilities—enzymatic, ligand binding, and cellular assays (HCS and fragment based screening as specialized technologies)
4. Cancer cell biology expertise—cell-based assays of target engagement and efficacy, target validation, mechanism of action studies (including drug sensitivity or resistance), biomarker development, gene expression and epigenetic profiling techniques (e.g. qPCR, ChIP-seq), cell line phenotyping and engineering (e.g. CRISPR)
5. Structural biology (X-ray crystallography, NMR, cryo-EM) and biophysical characterization methods (surface plasmon resonance (SPR), isothermal titration calorimetry (ITC))
6. Chemistry—medicinal and synthetic organic (library enrichment, fragment library enrichment as specialized technologies)
7. Compound profiling—enzyme or receptor panels, P450 inhibition, cellular panels, hERG
8. *In vivo* studies—PK, PD assays, MTD and efficacy (xenograft or genetically engineered mouse models), ADMET, metabolite ID
9. Scale-up synthesis and formulation to support *in vivo* studies

1. Protein Production

A critical first step for many drug discovery projects is the production and purification of active target protein, typically on milligram scale. In most cases, but not all, this material is derived from a recombinant expression system. The CBC needs Centers with expertise in a variety of recombinant expression vector systems and hosts. Expression in *E. coli* and in baculovirus infected insect cells are expected capabilities. Experience with yeast (e.g. *Saccharomyces cerevisiae*, *Pichia pastoris*) or transient expression in HEK293 cells or with recombinant vaccinia virus expression should be described as potential specialized technologies.

Purification of functional proteins and active enzymes is an essential step. The CBC seeks Centers with extensive knowledge of column chromatography, and other methods for purifying proteins. Expertise with a variety of methods for characterizing proteins is also desired, minimally including SDS-PAGE to determine purity, and gel filtration for apparent molecular size determination. Specialized capabilities such as whole protein ESI (electrospray ionization) MS to accurately determine the molecular weight of the purified protein (mass accuracy better than 0.01 % or 5 Da per 50 kDa protein) are also being sought for the Consortium, and would be particularly valuable methodology when covalent modifications of proteins are anticipated.

Once purified, proteins and enzymes need appropriate assessment of function to ensure their properties are suitable for their intended purpose. For example, enzymes should be assayed to quantify turnover and K_m values, which if possible to ascertain, should be consistent with or surpass previously published values. Proteins isolated for their ligand binding properties should have the K_D for the ligand determined. The CBC is seeking experts in analysis of biomolecular interactions and enzymatic processes who have substantial experience with direct measurements such as SPR or ITC as well as indirect approaches such as competition assays with labeled probes.

Proteins for structural biology

Proteins to be used for biophysical or structural biology studies are typically required in greater quantities and with a higher degree of purity and thoroughness of characterization. Centers with expertise in this area are being sought. For example, for X-ray crystallography the ability to isolate > 50 mg of protein of >98% purity is often required. Characterization of purified proteins for structural biology or biophysical studies can require other methods to assess homogeneity, such as differential scanning fluorimetry (thermal melting analysis) or dynamic light scattering. Furthermore, the ability to make a variety of different expression constructs with small modifications to affinity tags or the N- or C-terminus of the protein is often essential for obtaining suitable quantities of soluble and conformationally homogeneous protein. Offerors that are capable of providing specialized techniques such as production of uniformly ^{15}N -labeled protein for NMR studies would be valuable additions to the Consortium.

2. Assay development, optimization and miniaturization—biochemical and cellular

For successful identification of screening hits and assessment of potency of compounds during SAR campaigns, a reproducibly quantitative assay is essential. Core capabilities in assay development are being solicited for the Consortium.

Biochemical assays with purified proteins or enzymes will be established for measurement of ligand binding or enzymatic activity. CBC Centers selected for their expertise in this category will be facile with a variety of assay technologies for quantification of binding or activity, and have a detailed understanding of the

requirements for establishing a sensitive, yet robust assay. The Assay Guidance Manual (<http://www.ncbi.nlm.nih.gov/books/NBK53196/>) provides a thorough discussion of the numerous parameters that need to be considered when developing assays suitable for drug discovery. Centers with this core expertise should be skilled at optimizing biochemical assays resistant to common artifactual mechanisms of inhibition (e.g., adherence of protein to plates or denaturation). Miniaturization to 1536-well format is expected, whereas for SAR determinations, assays at this plate density may not be required. Centers that propose to offer specialized technologies, such as SPR binding assays, are expected to adhere to the same principles of reproducibility and standards of quantification, and would be expected to produce results at a more moderate throughput.

For certain projects, a cellular assay will be the basis for initial hit identification and validation, as well as subsequent SAR studies. Core expertise in developing sensitive, reproducible, quantitative cell-based assays including both target-based mechanistic assays and cell phenotypic assays is being sought. Experience measuring a variety of different cellular responses such as protein modification or translocation, cell viability or apoptosis induction (caspase activity), gene expression or epigenetic alterations is required. In addition to development of quantitative cellular assays, Centers should have expertise in optimizing and miniaturizing these assays so that they can be effectively developed for HTS.

3. HTS capabilities

NExT drug discovery projects will require the CBC to provide the capacity and core capabilities for high throughput screening of novel targets. Dedicated CBC Centers will have substantial experience using a variety of different assay technology platforms in high density screening formats. For optimal throughput and conservation of reagents in a typical high throughput screen, 1536 well format will be considered the standard. For more specialized assays that are not amenable to this degree of miniaturization, lower densities may be justified.

Specialized screening technologies also will be a valuable part of the CBC to enable NExT to address targets that are not amenable to standardized HTS assay formats. For example, specialized technologies will enable fragment screening approaches, whether by NMR, SPR, DSF or other methodologies. Specialized cell-based assay technologies are also being sought, such as high content screening, for projects in which common assay methodologies are not suitable.

Screening Libraries: NCI has assembled a screening collection of ~120K compounds that is available to all selected CBC screening centers. However, it is expected that Dedicated CBC Centers selected for their HTS capabilities will have their own collection of least 200,000 chemically diverse compounds, in addition to the CBC library, that would be

included in any HTS campaign. Additional sets of screening compounds, which are directed toward specific target classes or encompass novel chemistry, would add value to the CBC. Other specialized libraries, such as for fragment-based screening, should be present at centers with this screening capability.

4. Cancer cell biology expertise and mechanism of action elucidation

In addition to capabilities in common cell-based assay measurements, e.g., cell viability, the CBC is seeking centers of excellence in cancer cell biology. Personnel at these centers should have a deep understanding of the genetic basis for cellular transformation, of the properties and behaviors of transformed cells, and of steps involved in tumor progression. A Dedicated CBC Center with this capability should have experience successfully translating this understanding into assays useful for probing the mechanism of action of compounds. Assays that accurately reflect target engagement by compounds and assess downstream effects of that engagement are essential for guiding hit-to-lead SAR and lead optimization phases of a project.

Methodologies for manipulation of cellular phenotypes through approaches such as genome editing, RNA interference, antisense technology or virally mediated transgene expression to produce clones with new, desired properties will be standard tools for a Dedicated CBC center with cell biology expertise. Outputs to be measured include levels of gene and protein expression, the intracellular localization of proteins of interest, and markers of changes in post-translational modifications such as phosphorylation and methylation. It is expected that cell biology centers will demonstrate a high level of expertise in key cell biology assay techniques including cell transfection, qPCR, immunofluorescence, multiparameter cell analysis (such as bead-based and flow cytometry approaches), western blotting, ELISA and other immunoassays, immunoprecipitation, microarray analysis and fluorescent protein and reporter gene assays.

Experience in conducting mechanism of action studies (including mechanisms of sensitivity and resistance) to better elucidate the cellular consequences of compound action is also sought. Such studies should encompass the ability to profile key intracellular signaling networks, to measure changes in gene expression (including those linked to modification of epigenetic pathways) with techniques such as ChIP-seq and qPCR, and to assess cell phenotype changes linked to key survival and cell cycle pathways. Proficiencies in leading edge techniques in cell and molecular biology, which are not mentioned specifically in this solicitation, also should be included in the proposal.

5. Structural biology and biophysical characterization methods

The ability to visualize hit compounds bound to their target protein provides a significant advantage to the medicinal chemist working on a hit-to-lead optimization

campaign. Not only does the information provide guidance to identify areas for potential improvement in binding, but it also can suggest areas in which selectivity can be built into a compound so as to avoid off-target binding or interaction with other members within the same gene family. Centers selected for their expertise in structural biology will have all the skills required to determine crystal structures of protein targets with compounds bound. Typically these abilities include purification of proteins on a large scale and in high purity, the ability to characterize the proteins for stability and homogeneity, intimate familiarity with crystallization screening methodologies and the ability to optimize growth of small crystals once screening hits are found. Experience with ligand soaking and co-crystallization techniques is essential. Ready access to synchrotron facilities for rapid collection and processing of diffraction data is expected. Finally, the ability to solve structures rapidly by molecular replacement as well as to perform de novo structure determination, if needed, is essential.

In addition to expertise in X-ray crystallography, the CBC also is seeking centers that have less common, but complementary, expertise in structural biology. For example, excellence in protein 2D-NMR with ¹⁵N-labeled proteins is a particularly valuable methodology for studying small proteins, or independently folding domains of larger proteins. Fragment screening approaches with such methods have shown repeated success in identifying hit compounds of low molecular weight, and with a well-defined binding orientation. The ability to elaborate these small fragments or to link them to nearby fragments identified in the same screen have been the basis for numerous success stories when standard HTS campaigns failed to identify useful chemical starting points for optimization.

The use of cryoEM is becoming increasingly common for determining structures of very large proteins, or protein complexes, at near atomic resolution. Adding this specialized expertise to the CBC would provide valuable access to target structures that might otherwise be inaccessible with X-ray crystallography or with NMR.

In addition to the ability to visualize protein structures at atomic resolution, the use of methods for the biophysical characterization of proteins is an asset sought in the CBC. Such methods of characterizing proteins may include dynamic light scattering, analytical ultracentrifugation, differential scanning calorimetry, Raman spectroscopy, circular dichroism, XAFS spectroscopy, or spin-labeled methods. Centers with expertise in these techniques, or others such as saturation transfer difference NMR, are sought to provide the Consortium with a diversity of approaches to characterizing specific interactions of ligands or inhibitors with the target protein.

6. Synthetic and medicinal chemistry

An essential, core expertise for any small molecule drug discovery program is the ability to identify hit compounds and to elaborate those molecules into potent and selective

lead compounds, with the appropriate physical properties that will enable them to elicit a pharmacological effect *in vivo*. To be successful in this endeavor requires not only excellent synthetic organic chemistry skills, but also the medicinal chemistry knowledge that comes from years spent working in a pharmaceutical discovery environment. Thus the CBC is seeking Centers with superior capabilities in each of these categories.

Dedicated CBC Centers selected for their chemistry expertise should be well versed in traditional small molecule synthesis and isolation methodologies as well as spectroscopic and analytical techniques for characterizing the identity and purity of compounds. Experience with synthesis of chiral molecules and isolation of diastereomers is expected. Centers should have capabilities in parallel synthesis, optimization of reaction conditions, and completing syntheses on gram scale. Centers that have experience with more specialized methods such as ionic solvent mediated or fluorous phase chemistry, peptidomimetics, macrocycle, stapled or cross-linked peptide technologies, nucleoside or nucleoside mimetics, biosynthesis, chemoenzymatic transformations, glycosyltransferase-catalyzed synthesis or combinatorial sugar nucleotide synthesis are also sought to support projects that would benefit from such specialized chemistry expertise. Additional capabilities in other areas of specialization, such as multigram scale synthesis, reaction automation, metal catalysis, microwave, ultrasound or flow-assisted chemistry also would add value to the Consortium.

Isolation of pure compounds is one essential component of building a reliable SAR profile for a series of analogs. In addition to standard precipitation or extraction methods, and normal phase or reverse phase chromatography, expertise is being sought for technologies that expand this repertoire of purification techniques. Examples could include high-throughput purification with automated mass-detection, or access to supercritical fluid chromatography (SFC).

The choice of which molecules to synthesize is a critical decision point, prior to the practical steps of making and isolating the selected compounds. Numerous parameters factor into this decision. If the goal is exploration of a new scaffold then the ability to design a diverse set of analogs, which could be rapidly synthesized and easily elaborated, is needed. If the X-ray structure is available for the target with a bound compound, then the ability to capitalize on that structural information to guide the synthesis of new analogs that test specific binding hypotheses would be required. These capabilities are essential skill sets that the NExT program is soliciting to incorporate into the CBC. Centers that can leverage computational abilities such as virtual library design, principal components analysis, QSAR, and virtual docking and modeling with energy minimization scoring also would be an asset to the Consortium and be of benefit to projects in hit-to-lead and lead optimization.

7. Compound profiling

As SAR is being developed around a hit series, a project team often seeks a broader depth of selectivity profiling. To fill this need, the CBC is seeking Centers that can provide a suite of screening assays, for instance to profile activity of compounds against a large collection of enzymes from the same target class or gene family (e.g., kinases, proteases, methyl transferases or esterases, GPCRs). Frequently these assays are *in vitro*, biochemical assays. However, profiling compounds through a panel of cell-based assays with a diversity of ligands to which they respond also can be useful for predicting, or understanding the selectivity of analogs and subsequent *in vivo* pharmacological responses.

The NCI60 is a publicly available NCI resource that tests a compound's effect on the growth of 60 different cancer cell lines. Whereas this resource is an asset that CBC projects utilize, sometimes a project team wishes to profile lead compounds against a more molecularly diverse set of cell lines, particularly when the therapeutic indication is not clearly defined, or when susceptibility to the inhibitor may depend on an as yet undetermined genetic lesion. Thus, proposals are being solicited from offerors who can provide access to panels of primary human cells and to genetically diverse cancer cell line models, including Conditionally Reprogrammed Cells. Extensive genetic characterization of the cancer cell lines is expected, along with the software tools that allow correlations to be drawn between effects of the compound on cells and genotype.

In later stages of hit-to-lead, and particularly during lead optimization, knowledge of whether lead compounds inhibit any of the cytochrome P450 enzymes is factored into the medicinal chemistry plan and the selection of compounds for pharmacology experiments. Thus, the CBC seeks access to a suite of CYP assays for projects at this stage. Furthermore, if efficacious analogs exhibit microsomal instability, the identity of the particular CYP450 that metabolizes the compound may be investigated. Thus, availability of metabolism assays with individual CYP isozymes is a specialized capability that the CBC would like to have available for projects working on metabolically sensitive scaffolds.

Another common assessment made during lead optimization is the ability of compounds to affect the hERG potassium ion channel. This assay should be provided as a functional channel blocking assay. Assays which measure binding of the compound to the hERG protein are less definitive than the functional assay. But if a compound series has a significant problem with inhibiting hERG channel function, and many analogs therefore need to be screened to find a path away from hERG liability, then the relatively high throughput binding assay would be a useful specialized method.

8. In vivo studies

For successful completion of Lead Optimization and Candidate Selection phases of its projects, the CBC intends to identify sites at which *in vivo* studies can be completed. Such studies include pharmacokinetic (PK) assessment of a compound's bioavailability, distribution, serum half-life and clearance. Routes of administration in rodents or dogs should include IV, IP, SC and PO. In addition to completing the in-life phase, such facilities should also be capable of the subsequent bioanalytical studies to quantify concentrations of compound in plasma or tissues, and to complete the PK analysis. Ideally, these sites will provide some formulation expertise to support dosing of compounds without a known formulation or with suboptimal physical properties.

In addition to core expertise in standard PK studies, expertise is also being sought in more specialized drug metabolism and pharmacokinetic (DMPK) studies of advanced compounds. Capabilities should include identification and measurement of metabolites derived from the dosed compound. Expertise with determination of routes of excretion of the dosed compound and its metabolites is sought.

For efficacy studies in oncology, core expertise is required in conducting mouse xenograft studies. A large variety of human cancer cell lines should be available for implantation into immunocompromised mice. Expert knowledge of take rates and typical growth rates for the different tumor types is required, as well as knowledge of "standard of care" agents that can be compared in well-established xenograft models. Prior to initiation of full scale efficacy studies, analysis of MTD will be assessed with dosing through the intended route of administration. Tumor growth will be assessed by traditional caliper measurements or via quantitative imaging analysis using luciferase or similar noninvasive methods.

The ability to take plasma, tissue and tumor samples from mice during efficacy studies to enable measurement of pharmacodynamic (PD) markers appropriate for the target is essential. Centers with demonstrated proficiency in the development of PD assays, design of PK/PD experiments and analysis of samples to assess PD endpoints are sought. Expert capabilities in quantitative gene expression analysis (such as qPCR), immunohistochemistry and immunofluorescence, ELISA or western blotting and flow cytometry are required. Expertise in multi-parameter approaches such as bead-based technologies (e.g., Luminex), mass spectroscopy, high throughput sequencing, magnetic resonance spectroscopy or positron emission tomography (PET) is also sought.

9. Scale-up synthesis and/or formulation

During Lead Optimization or the Candidate Selection phase, an improved or optimized synthetic scheme will likely be needed to support *in vivo* studies. These changes also will provide the foundation for the larger scale syntheses that will be required later for preclinical development and IND enabling toxicology studies, and cGMP manufacturing

of the API. Although these later IND-enabling and manufacturing steps lie outside the scope of this Solicitation, Centers that are selected for their capabilities in scale-up synthesis will have expertise and capacity for the synthesis and analytical characterization of multigram quantities of intermediates and final compounds, and knowledge of optimizing synthetic routes amenable to subsequent cGMP manufacturing.

Studies to identify a stable, robust formulation that provides good bioavailability and reproducible absorption of the API may be needed during Lead Optimization or Candidate Selection. Centers are sought with the ability to optimize formulation based upon compound class and structure, physicochemical properties, desired administration route, total dose, dose volume and stability. Expertise in analytical characterization of the drug substance within complex formulations should be part of the core capabilities in this area.

Types of formulations for late lead optimization *in vivo* studies may include liquids, suspensions, emulsions, lyophilized products, nanoparticles, and liposomes. The solubility and stability constraints of different small molecules may require specialized excipients to confer increased solubility and/or stability. Such approaches could include pH modification, co-solvents, surfactants, complexation agents and emulsions. In addition to physical and chemical stability of the formulation, expertise with sterilization, storage, stability monitoring and administration equipment may be necessary for specialized applications.

Oral dosing of the drug product is often the preferred route of administration, particularly when chronic therapy is anticipated. Thus, the NCI is seeking expertise in development of simple, effective oral formulations, with an option to resort to increasingly complex mixtures, if needed. The ability to conduct proof-of-concept PK studies using the prototype formulations is required. The design of proper formulation assessments should consider pharmaceutical and biopharmaceutical factors such as: aqueous, organic and lipid solubility, crystallinity, pKa, logP, food effects, permeability and efflux, non-enzymatic degradation in the GI tract, and metabolism.

The CBC is NOT responsible for carrying out steps required during Preclinical Development such as API manufacturing and stability testing or IND enabling GLP toxicology studies. Thus, this solicitation does not seek proposals that describe expertise in these areas.

B.2. Effective project team participation—communication, data sharing and compound management

High performing multidisciplinary project teams require personnel with not only extensive scientific expertise, but also the ability to communicate clearly, to critically analyze data, to engage effectively in discussion of results and to participate in team-based decision making and implementation. Discussion of strategy or alternative approaches to solve challenges the project encounters is a significant responsibility of all senior team members. Formal leadership on NExT drug discovery project teams is shared between two project co-leaders, one from NCI and one selected by the team from a participating CBC Center.

To facilitate team-wide sharing of project team data, which enables the discussions and decision-making described above, the NCI has created a secure, central, relational database and uses the D360 software package for searching, retrieving, tabulating and graphing the results. Access to each project's data is restricted to those participating on that project team. The progress of a project relies upon participating Centers to provide the assay data and results, which are generated at their site, in a format and structure that is able to be uploaded to this centralized NCI database. Thus, CBC Centers need to have robust capabilities for processing and sharing data in a variety of useable formats. In addition to disseminating data and results in a timely fashion, the CBC Participants also are responsible for ensuring the accuracy and completeness of the data set.

At project team meetings, typically held monthly, CBC participants will present their experimental results and indicate what conclusions they have drawn and how these results affect the progress or direction of the project. Team meetings often have a dozen or more participants, with a variety of scientific backgrounds, so clear, concise communication by scientists with full understanding of what they are presenting is essential for the team to effectively assimilate the new information. Furthermore, distribution of the presenter's slides prior to the team meeting provides the other team members with an opportunity to become familiar with the new results prior to the actual meeting. The CBC is seeking Centers whose scientists have excellent communication skills to fulfill these responsibilities.

Whereas distribution of information (data and results) to fellow team members is critical for effective team decision making, a standardized and streamlined approach for distributing physical compound samples to be assayed is essential for timely generation of the data. To meet this goal, the NCI has established a process for registration of compound structures, assignment of an NSC ID to each compound and subsequent deposition of a solid sample at the NCI/DTP Repository. Participating CBC Centers will be responsible for registration of the compounds synthesized at their site and for shipping solid samples to the Repository for storage. The Repository will then distribute samples to other Centers working on that NExT drug discovery project, upon request from the project team. CBC Centers are being sought that will be fully capable of meeting these requirements for sample tracking, processing and compound submission.

B.3. Contractual obligations, including management of personnel, staffing, and budget

The CBC is operated through a contracting mechanism, detailed in Volume 2 of the Solicitation. Successful Offerors will be awarded a subcontract by Leidos Bioimmedical Research, Inc. As such, successful participation in the CBC requires knowledge of business practices different from those used to secure grant funding. Also, to maintain the proposed commitment of expertise to the CBC and of personnel to CBC projects will require flexibility in staffing arrangements by the CBC site's management. One important component of staffing and personnel management at the CBC Center will be to have a succession plan for any key scientific staff.

Under a contractual agreement, sites will be required to submit an invoice for the work that has been accomplished, and will be reimbursed upon approval of the invoice. Thus, the appropriate accounting and budget tracking procedures need to be available to provide the required invoices and staffing reports. Responses in Volume 2 of the Solicitation will be evaluated to ensure sites have the required accounting and budget tracking procedures in place.

CBC Centers are being sought that have experience with this funding mechanism or have well-established procedures that will enable them to manage these obligations effectively.

C. Deliverables

Participation in the CBC will require a major commitment of scientific effort to successfully move NExT drug discovery projects forward. It also will entail a moderate amount of reporting and documentation to track scientific contributions to, and progress by, the Project Team, as well as to justify the submitted invoices.

Each CBC Center participating on a Project Team will submit, each quarter, a scientific report that summarizes the progress made, the accomplishments, and any significant challenges encountered, during the last 3 months of working on the project. A report will be submitted for each project to which the CBC Center is contributing. The length of the report will vary with the number of personnel committed to the project, and other factors, but should not exceed 5 pages.

A Level of Effort (LOE) report is to be submitted monthly. This document should be in a simple table format and itemize which personnel were working on which project(s) and the number of hours (or % effort) that each individual worked on each project.

C.1. Detail and Schedule of Deliverables

Deliverable	Due Date
Scientific report summarizing accomplishments on different projects	Quarterly
Level of effort (LOE) report indicating hours worked on CBC projects	Monthly
Invoices commensurate with LOE report	Monthly
Participation at project team meetings (and occasional subteam or planning sessions)	Monthly (as needed)
Participation by CBC Center's leader(s) at CBC Steering Committee Meetings	Quarterly
Participation at NCI project reviews, as requested	Semiannually (estimated)
Final reports: Scientific	At close of a project

Proposal Evaluation Criteria

Proposals will be evaluated based on the criteria below. Awardees may be selected based on a high composite evaluation score or for obtaining high scores in individual technical categories within the proposal.

Between the time of evaluating the proposals and making an award, an evaluation team may visit the site at which the Offeror intends to conduct the proposed work.

The most important factor in the evaluation will be the overall strength of the proposal in describing the Offeror's expertise and capabilities in the technical objectives described in Section B.1. Scores will be derived from ratings in each of the four parameters listed below. Responses in the proposal to objectives in Section B.2 and B.3 and the determination of Cost Reasonableness will factor into decisions to select awardees, but will carry less weight.

Section B.1. Scientific and Technical Capabilities

The four parameters for evaluation of Section B.1 of the proposal are:

1. Technical Capabilities and Approach

The Offeror demonstrates a clear understanding of the scope, objectives, and challenges of carrying out small molecule drug discovery research as part of a multi-center team funded by a contractual mechanism.

The proposed approach and capabilities describe the required level of excellence that will be needed in each category proposed.

Novel or specialized technologies that would benefit the Consortium, but were not specifically mentioned in the SOO are thoroughly described.

2. Experience and Past Performance

The proposed center has demonstrated previous expert level experience in the technologies and procedures required to perform effectively and complete small molecule drug discovery projects.

Examples of past performance and accomplishments of the center are provided for projects of relevant size, scope, difficulty and technical objectives.

The Past Performance Questionnaires, completed by collaborators who were selected by the Offeror, indicate a track record of being a successful and productive collaborator or fellow project team participant.

3. Team: Key Personnel and Scientific Staff

Level of staffing, in numbers and qualifications, is appropriate for the Offeror's proposed role in the defined scientific categories in Section B.1.

Key Personnel have documented expertise in the scientific role(s) ascribed to them in the proposal. Evidence of qualified past performance is provided.

The proposed succession plan for the PI and Key Staff demonstrates a clear ability for the project to successfully continue if Key Staff leave the project or the CBC Center.

4. Equipment and facilities

The Offeror has the appropriate scientific equipment and facilities to carry out the activities described in the proposal.

The Offeror has an appropriate service, preventative maintenance and replacement plan for essential equipment and facilities so as to maintain the proposed operations for 5 years. Evidence of an Institutional commitment to this plan is provided.

The necessary information technology infrastructure is present to support modern day drug discovery activities, process and share data and results with team members, supply data and results

Section B.2. Project team participation

The proposal describes operating procedures by which scientists at the Offeror's site effectively participate in multi-center project teams, including mechanisms:

- for communication between team members,
- for sharing data and results with team members and for uploading data to the NCI database,
- for distribution of compounds to team members and to the NCI/DTP Repository

Past performance and information in the completed Questionnaires from references indicates a track record of high quality participation on project teams.

Section B.3. Management

The organizational structure at the Center allows for the CBC Center PI to effectively manage personnel and staffing on projects.

Project management capabilities exist to ensure effective participation on project teams, and adequate budget and financial control mechanisms are outlined.

Evidence that local management and the institution's business office can effectively handle the contractual mechanisms by which the CBC administers projects, including tracking staffing effort on projects and supplying timely invoices.

Cost Reasonableness

Overall costs are reasonable for the proposed participation in the CBC, considering the level of expertise of the scientific staff, and the anticipated costs of supplies, equipment and facilities to effectively participate on CBC projects.

Technical Proposal Requirements

Proposals should be written in no smaller than size 10 font, and formatted with 1" margins and 1.1 line spacing.

Executive Summary (1 page limit)

The executive summary shall contain a high level overview of why your institution or organization is qualified to be a CBC Center of excellence in drug discovery for small molecule, anti-cancer therapeutics. The summary should briefly describe your response to the three (3) Objectives being solicited in the SOO and indicate the breadth and depth of your Center's experience that demonstrates your Center is highly qualified. Succinctly address each of the three (3) Objectives from the SOO listed below:

- (1) The categories of essential/core or specialized skills you are proposing to make available for this CBC initiative that will enable small molecule drug discovery project teams in the NExT program to be successful.
- (2) The demonstrated ability of your Center to function productively in a collaborative, project team environment.
- (3) The capabilities and available resources of your institution to effectively manage scientific personnel, budgets and contractual interactions.

In addition to addressing these fundamental requirements of the proposal, you should also describe any other features, abilities, properties or operational approaches at your organization that distinguishes your institution from others working in this field.

The summary shall be on separate page or include a section break before the rest of the proposal.

Technical Approach (not to exceed 20 pages)

Offerors should submit a detailed proposal that clearly identifies the Technical Categories in Section B.1 for which they wish to be considered. Information provided for Sections B.2 and B.3 should pertain to your Center's overall approach to working on drug discovery project teams, and should not be described in relation to specific technical categories.

Section B. 1, Scientific Expertise and Technical Capabilities: Clearly identify which technical categories in Section B.1 you are addressing in your proposal. Provide a thorough description of the expertise your institution and personnel can contribute to meet the needs of the CBC in each selected category.

The categories listed in Section B.1 are quite broad and each one lists a variety of methods that can be applied to this aspect of small molecule drug discovery. If your institution possesses additional capabilities or skill sets that fit these categories, but are not specifically mentioned within a category, describe them and indicate how they would be of significant benefit to the CBC and its projects. Furthermore, describe any unique aspects of your approach or expertise, and why your approach could more efficiently and effectively accomplish the objectives.

Section B.2, Project team participation, communication, data sharing and compound management:

Describe your Center's approach to interactions on multi-centered project teams.

Describe the principles you follow to ensure good communication and collaboration among multiple contributing centers on a project team.

Describe your anticipated project management commitment to track progress on projects and to ensure that agreed-upon timelines will be met.

Describe your data management capabilities and the mechanisms available to enable sharing results with project team members at other centers. Describe your IT support for data handling that will enable efficient transfer of data and results to the NCI database, for access by all project team members.

Section B.3: Contractual obligations, including management of personnel, staffing and budget.

Describe the methods, procedures and processes you use to manage personnel and staffing on projects, to monitor budget and to track expenses. Describe any specific mechanisms that are currently employed by your Organization to ensure compliance with contractual obligations, such as tracking personnel effort on projects and converting that effort into invoiced amounts.

Describe your overall risk mitigation strategy to avoid pitfalls in advancing drug discovery projects, working on multi-center teams, or managing staffing and budgets.

Experience and Past Performance (3 page limit)

For Section B.1. describe your Center's range and depth of past experience and demonstrated capabilities with small molecule drug discovery. Indicate how the expertise described in your Technical Proposal was instrumental in moving previous projects forward. Illustrative examples from current or recently completed projects should be included.

For **Section B.2** provide examples from recent projects where the approach your Center has utilized to foster effective communication and collaboration has been successful, or where you have seen alternatives fail.

For **Section B.3**, describe past experience working on projects that were supported through a contractual mechanism, and indicate how your organization effectively managed staff and budgets.

Send out and track the completion of the Past Performance Questionnaires (Attachment 1) to points of contact (References) of at least three teaming partners, subcontractors or collaborators on relevant projects. The responsibility to send out and track the completion of the Past Performance Questionnaires and for the submittal of those completed Questionnaires by the References to Leidos Biomed at cbcp proposals@mail.nih.gov rests solely with the offeror. Provide the names of the institutions and of the point of contact (the Reference) who will be supplying the completed Questionnaires.

Team and Key Personnel (5 page limit)

Provide a brief summary of the management structure and general organizational arrangement of your Center. Indicate which layer or level of personnel will contribute as technical staff on projects and who else would actively participate in the CBC.

Introduce the members of your team who will be instrumental in meeting the Objectives and who will be critical for making your organization a high performing CBC Center. Give an overview of the expertise they provide and how their skills will be integrated into project teams and the Consortium so as to obtain maximum benefit from their abilities.

For named individuals, describe each person's role and the anticipated percentage of their time that would be invested in the CBC. All Key Personnel shall be clearly indicated. Résumés should be included in NIH Biosketch format (<http://grants.nih.gov/grants/funding/424/index.htm>) in this section. The proposed time commitment for each Key Person should be indicated here.

Include a succession plan that describes the process by which new leadership will be selected in the event that the PI or other Key Staff is no longer willing or able to lead the proposed commitment to the CBC. Describe the mechanism for ensuring stable staffing of projects with high quality scientific personnel.

Provide two or three specific examples of significant contributions which members of your team made to the performance of that team. Clearly indicate who on your team performed, what role each played on the project, and the criteria that were used to judge their performance.

Facilities and Equipment (2 page limit)

Describe the scientific equipment that you have available to you to accomplish the proposed technical work. Indicate whether your use of this equipment is under your control, or is shared with other scientists at your institution, which might limit your access to it. For any unique pieces of critical equipment or instrumentation, indicate the plan to maintain access to this technology in the event of breakdown or malfunction.

Describe the facilities in which the proposed experimental studies will be conducted.

Cost Proposal Requirements

A formal cost proposal is not required; however, Offerors should provide at a minimum a listing of the labor categories, which will be required to support their proposed effort along with the associated annual salary, indirect rate and other direct costs. A cost estimate worksheet is included as Attachment 2 to this document in order to aid in preparing the requested cost proposal.

Information requested is considered to be minimal and further information may be required prior to award of any Agreement.

ATTACHMENT 1 – PAST PERFORMANCE QUESTIONNAIRE

In addition to submitting technical proposals, Offerors are to forward the following questionnaire to at least (three) 3 references. The completed questionnaires will be sent from the reference directly to cbcproposals@mail.nih.gov; the offeror will NOT receive a copy of the completed form.

The Offeror should include in their technical proposal a list of the institutions or individuals asked to be references and inform the reference that a member of the proposal evaluation group may be in contact with them regarding their response should it become necessary. Instruct your references to clearly indicate in the filename of the submitted questionnaire both the name of their institution (the reference) and for whom the reference has been submitted (your institution's name) so the documents can be correctly routed to the reviewers of your proposal.

The NCI Experimental Therapeutics (NExT) Program, Chemical Biology Consortium is soliciting proposals from Centers wanting to participate in the second version of this program (for more information see <http://next.cancer.gov/>). Your assistance is requested in providing a complete and honest reference to aid in the evaluation of the Offeror that has submitted a proposal in response to this solicitation.

Submit the completed questionnaire in PDF file format to cbcproposals@mail.nih.gov. The filename for the submitted document should include both the name of your institution (the reference) and the Center for whom the reference is being submitted (the requester), to ensure the documents are correctly routed to the reviewers.

This questionnaire, when filled in, shall be treated as Source Selection Sensitive in accordance with FAR 3.104-3 and shall not be disclosed to anyone outside of the Proposal Evaluation Group for Solicitation S16-001.

PLEASE PROVIDE THE FOLLOWING INFORMATION

Name of respondent and contact information:

REFERENCE'S NAME: _____

REFERENCE'S INSTITUTION: _____

REFERENCE'S PHONE NUMBER: _____

REFERENCE'S EMAIL: _____

The name of the institution that has requested you serve as a reference:

REQUESTING INSTITUTION: _____

1. DESCRIBE THE COLLABORATIONS OR PROJECTS ON WHICH YOU WORKED WITH THE OFFEROR, AND WHICH ARE THE BASIS FOR THESE COMMENTS. INDICATE THE LENGTH OF TIME YOU WORKED WITH THE OFFEROR ON THIS/THESE PROJECTS.

INDIVIDUAL RATINGS EVALUATION:

Please indicate your satisfaction with the Requester's performance by placing an "X" in the appropriate block using the scale provided to the right of each question. This scale is defined as follows:

CODE PERFORMANCE LEVEL

- E** EXCEPTIONAL - Quality of performance exceeded all requirements and expectations. The completion and delivery of results or materials was accomplished with only minor problems for which corrective actions were highly effective. The Requester was pro-active in identifying any problems, providing alternatives and recommending solutions.
- VG** VERY GOOD - Quality of performance met requirements and exceeded many expectations. The scope of work was accomplished with only minor problems for which corrective actions were highly effective.
- S** SATISFACTORY – Quality of performance met requirements. The scope of work was accomplished with some problems, but corrective actions were satisfactory.
- M** MARGINAL – Quality of performance did not meet some requirements. Serious problems were encountered completing the scope of work, and they were not resolved satisfactorily. The proposed corrective actions appeared to be only marginally effective or were not fully implemented.
- U** UNSATISFACTORY – Quality of performance failed to meet most requirements and satisfactory completion of the work was not accomplished in a timely manner. Corrective actions were not attempted or were ineffective.
- NA** NOT APPLICABLE - Unable to provide a score as the question does not apply.

Technical Approach	E	VG	S	M	U	NA
Extent to which the Requester exhibited the knowledge and skills necessary to understand and perform all technical functions						
Extent to which the Requester had an adequate number of dedicated resources to support the program						
Your satisfaction with the Requester's responsiveness to unexpected or unscheduled changes in the project						
Ability of Requester to respond innovatively to technical challenges or other unanticipated findings						
The quality of the work completed by the Requester						
Extent to which the Requester delivered adequate reports (for example, testing results) and made comprehensible presentations of results to the team						
Ability of Requester to work collaboratively with other members of the project team.						
Timeliness of delivery of reports or communication of new results						
Team and Key Personnel	E	VG	S	M	U	NA
Contribution of scientific leadership to critical analysis and interpretation of results that enables high quality team decision making and strategic thinking						
Appropriately qualified scientific, technical staff who can correctly analyze, interpret and communicate experimental results.						

Management Approach	E	VG	S	M	U	NA
Overall effectiveness in management of personnel, including the ability to accommodate required changes in staffing levels and to successfully replace any scientific staff when needed						
Ability to manage timely delivery of results and reports to the team						
Effective management of interactions between different team members, with timely and effective resolution of any conflicts						
Understanding of contractual funding mechanisms and effectiveness in working with Requester's institution's business office to comply with these financial and reporting requirements						
Cost Performance	E	VG	S	M	U	NA
Accuracy in forecasting costs						
Demonstrated ability to accomplish the work within forecasted costs						
Demonstrated ability to anticipate unforeseen costs before they are incurred						
Sufficiency and timeliness of cost reporting						

What were the Requester's greatest strengths when working with you on this project or collaboration?

In what areas do you think the Requester's performance as a team member or scientific collaborator could be improved?

Have there been any disputes or strong disagreements between you and the Requestor? If yes, please explain the circumstances and resolution.

If your interaction or collaboration with the Requester is not ongoing, what was the cause for termination of the project?

Would you have any reservations about working with this collaborator in the future or having them participate in one of your critical and demanding programs?

Yes____ No ____

If yes, please explain (e.g., inability to meet cost, performance, or delivery schedules, etc).

Please provide a statement describing your overall experience with the Requester being reviewed. Include any information you feel may be helpful in accurately evaluating this Requester's past and/or present performance.

Additional Remarks

OVERALL EVALUATION RATING (circle one):

Overall Assessment: (a) EXCEPTIONAL (b) VERY GOOD (c) SATISFACTORY (d) MARGINAL (e) UNSATISFACTORY

I, the undersigned evaluator, hereby attest that to the best of my knowledge all the statements recorded above are true.

Evaluator Name (typed)	Evaluator Signature	Date

ATTACHMENT 2 – COST ESTIMATE WORKSHEET

Direct Labor

Labor Category	Annual Salary	% of Effort	Total Salary	Fringe %*	Fringe Amount*	Total Direct Labor
A. SUBTOTAL DIRECT LABOR						

Other Direct Costs

OTHER DIRECT COSTS (Provide itemized list with prices)	
B. SUBTOTAL OTHER DIRECT COSTS	
TOTAL DIRECT COSTS (Subtotal Direct Labor + Other Direct Costs)	
INDIRECT COSTS OR OVERHEAD (%)*	
TOTAL COSTS (Subtotal Direct Labor + Subtotal Other Direct Costs + Indirect Costs)	

***NOT APPLICABLE FOR T&M TYPE AGREEMENTS**

ATTACHMENT 3 – OFFEROR SIGNATURES

1. Offeror Principal Investigator Signature

On behalf of the Offeror's submission of the Technical and Cost Proposal (hereinafter referred to as Offer), Principal Investigator certifies by signing this Offer that all information contained therein is current, accurate, complete, and applicable to this Offer.

Signature

Name

Title

Organization

Address

City, State, and ZIP Code

Phone:

Email:

2. Offeror Authorized Signature

In consideration of the Offeror's Principal Investigator noted above, the following individual is duly authorized to make an Offer on behalf of the Offeror.

Offeror certifies by signing this Offer that all information contained herein is current, accurate, complete, and applicable to this Offer and shall be hereby incorporated into any resulting Agreement that may result from this Offer.

Further, by submission of this Offer, Offeror certifies that Offeror has the financial capacity, working capital, experience, and other necessary resources as well as fiscal management procedures in place to properly administer any resultant award from submission of this Offer.

Signature

Name

Title

Organization

Address

City, State, and ZIP Code

Phone:

Email:



Leidos Biomedical Research, Inc.

Solicitation S16-001: NCI Experimental Therapeutics (NExT) Program Chemical Biology Consortium Volume 2: Compliance (Business Office) Document Requirements

This Solicitation is divided into two documents: this one, which is referred to as Volume 2: Compliance Document Requirements, and another, which is referred to as Volume 1: Technical and Cost Proposal Requirements. Volume 1 must be submitted by 5:00 PM ET on Thursday, November 5, 2015. Volume 2 is due by 5:00 PM ET on Thursday, January 14, 2016.

A. Key Solicitation Dates

- Written questions about the Solicitation and requests for clarifications must be submitted to cbcproposals@mail.nih.gov by 5:00 PM ET Wednesday, September 16, 2015. Answers will be provided to these questions, and new questions can be asked at Bidders Teleconference 1.
- Bidders Teleconference 1: 2:00 PM ET Thursday, September 24, 2015.
- Bidders Teleconference 2: 2:00 PM ET Thursday, October 15, 2015.
- Offerors wishing to participate in these teleconferences should dial (U.S. and Canada) 855-462-5367 and enter passcode 3250774 when prompted. International callers wishing to participate in these teleconferences should dial 804-451-4138 and enter passcode 3250774 when prompted.
- Responses to Solicitation S16-001 Volume 1: Technical and Cost Proposals (submitted to cbcproposals@mail.nih.gov) are due by 5:00 PM ET Thursday, November 5, 2015.
- Responses to Solicitation S16-001 Volume 2: Compliance Documents (submitted to cbcproposals@mail.nih.gov) are due by 5:00 PM ET, Thursday, January 14, 2016.

B. Solicitation Administration

This solicitation is issued by Leidos Biomedical Research, Inc. (Leidos Biomed), a wholly owned subsidiary of Leidos Corporation under its prime contract with the National Cancer Institute (NCI) at Frederick. The provisions and clauses contained herein and attached are influenced by and reflect the relationship of the parties in that Agreement, which was awarded and is administered under the provision of the Federal Acquisition Regulation (FAR).

C. Agreement Type

Given the breadth of possible proposals and the variety of sources from which they may originate, this Agreement does not prescribe a particular Agreement type or other specifics that will be established

during discussions that will occur between Leidos Biomed and Offerors. It is anticipated that the resulting Agreement will be issued using one of the contract types described in FAR Part 16 as agreed to through final negotiations. Prior to award, the appropriate Agreement type will be established and reflected in the awarded Agreement.

D. Instructions to Offerors

D.1. General Information

Participants will have an unparalleled opportunity to participate in a highly collaborative drug discovery partnership with the NCI. Using state-of-the-art communication, data-sharing and project management tools, the Chemical Biology Consortium (CBC) will effect a paradigm shift in the use of public-private partnerships to translate knowledge from leading academic institutions into ground-breaking new drug candidates for patients with cancer.

- Proposals must be submitted electronically in Searchable Adobe Acrobat, Microsoft Word or Microsoft Excel formats, as applicable.
- Individual files submitted must not exceed 15 MB in size; this may require that a document be broken down into multiple files prior to submission.
- All submissions must be clearly identified to include the Offeror's name, Principal Investigator's name and Solicitation Number S16-001.
- Late offers will not be considered for award.

D.2. Offeror Site Visit

A SITE VISIT MAY BE REQUIRED BEFORE AGREEMENT AWARD MAY OCCUR. By submitting an offer in response to this Solicitation, the Offeror is agreeing to make its facilities and associated personnel available for a site visit to occur prior to subcontract award.

D.3. Proposal Instructions to Offeror

To be considered responsive to this Solicitation, the Offeror must provide and/or complete the following requirements:

- Complete Section E. Representations and Certifications of this document.
- Complete Section F.2. E-Verify Compliance.
- Complete Section F.3. Office of Laboratory Animals Welfare (OLAW) – if the work proposed involves animals.
- Complete Sections G.1 and G.2 Offeror Representatives .

- Complete Attachment 1 – Certificate of Accounting and Billing System Adequacy (For Cost Reimbursement Agreements)
- Complete Attachment 2 – Worksheet for Review of the Vertebrate Animal Section (VAS) – if the work proposed involves animals.
- Review Attachment 3 - Leidos Biomed Terms and Conditions. It is requested that the Offeror exercises due diligence in reviewing the Terms and Conditions prior to submitting a formal proposal in response to this Solicitation and in the context of the proposed Statement of Objectives. Any requested exceptions or risk areas identified shall be part of the proposal submission as redlined changes in the Attachment. Negotiations in good faith are expected and excessive exceptions requested may result in significant delays of award.
- For Cost Reimbursable Type Agreements, include with response, a copy of organization's negotiated indirect cost (IDC) rate agreement. If no current IDC rate agreement is in effect, provide a detailed explanation that details the methodology used for determining the proposed IDC costs including a description of the cost components for both base and pool costs.
- Complete and submit with the offer an IRS Form W-9. All Offerors MUST be registered with the System for Award Management (SAM) -- formerly the Central Contractor's Registration (CCR). Offerors may register with SAM at <http://www.sam.gov>. The address included on the W-9 MUST match the address registered at SAM, and/or included with the Representations, Certifications, and Other Statements of Offerors. **FOR INTERNATIONAL, ALL OFFERORS MUST COMPLETE W-8BEN-E IN PLACE OF W-9. LINK MAY BE FOUND AT <http://www.irs.gov/pub/irs-pdf/fw8bene.pdf>**

D.4. Solicitation Volume 2 Attachments

Attachment	Document Description
1	Certificate of Accounting and Billing System Adequacy (For Cost Reimbursement or Time and Material Type Agreements)
2	Vertebrate Animal Section (VAS) Worksheet (Only if the work proposed includes animals)
3	Leidos Biomed Terms and Conditions

E. Representations and Certifications

In order to be considered responsive, all Offers must provide the following information:

- ☐ Our organization's System for Award Management (SAM) record is current and Representations and Certifications listed under the record are accurate for submission of this proposal to Leidos Biomed as of Insert Proposal Submission Date.
- ☐ Our organization's System for Award Management (SAM) record is not current or is being updated. If this box is checked or the Offeror does not have a SAM record, follow the link to complete and submit a copy of Representations and Certifications with the proposal to Leidos Biomed: http://oamp.od.nih.gov/sites/default/files/DGS/contracting-forms/rcneg_508.pdf
- ☐ Our organization's DUNS Number is Insert DUNS Number.
- ☐ Our organization certifies that it has Insert # of Employees.

In order to complete their Representations and Certifications , Foreign subcontractors must access <http://ncifrederick.cancer.gov/Cad/Media/Documents/InternationalRepsAndCerts.pdf>

F. Certifications

F.1. Second Tier Subcontracting

Second tier Subcontracting is not permitted in support of this effort.

F.2. E-Verify Compliance (FAR 52.222-54)

To be eligible for award, Subcontractor must provide a copy of the E-Verify generated "Edit Company Profile" page as proof of enrollment.

If Subcontractor is NOT enrolled, Subcontractor will be required to enroll in E-VERIFY within 30 days from date of award and must provide a copy of the Edit Company Profile page. To access E-verify, you may visit <https://e-verify.uscis.gov/enroll>. Subcontractor risks forfeiting award if this requirement is not met.

F.3. Office of Laboratory Animal Welfare (OLAW) Certification (If the work proposed involves 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 applicant 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, applicant organizations must 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. Applicant 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). The PHS Policy is available on the internet at: <http://www.grants.nih.gov/grants/olaw/olaw.htm>.

Please indicate your organization's status by checking the appropriate response: Links to the Animal Welfare Assurance guidance and templates are below.

- ☐ Our organization has an approved Assurance by the Office of Laboratory Animal Welfare (OLAW); our Assurance number is ____.
- ☐ Our organization does NOT have an approved Assurance by the Office of Laboratory Animal Welfare (OLAW); we have submitted one copy of the Animal Welfare Assurance with our Offer.

Link to Animal Welfare Assurance guidance and sample assurance for domestic institutions:
<http://grants1.nih.gov/grants/olaw/sampledoc/assur.htm>.

Link to Animal Welfare Assurance guidance and sample assurance for foreign institutions:
<http://grants1.nih.gov/grants/olaw/sampledoc/foreign.htm>.

G. Offeror Representatives

G.1. Offeror Authorized Representative

The following individual(s) is/are the designated representative of the Offeror. This will be the Official authorized to negotiate and sign the resulting Agreement:

Name

Title

Organization

Address Line 1

Address Line 2

City, State, and ZIP Code

Phone:

Email:

G.2. Offeror Invoice Representative(s)

Name

Title

Organization

Address Line 1

Address Line 2

City, State, and ZIP Code

Phone:

Email:

Attachment 1: Certificate of Accounting and Billing System Adequacy (For Cost Reimbursement and T&M Agreement Types)

Offeror Instructions: If none of the criteria in Section I applies, complete Section II – otherwise, proceed to Section III.

Section I – Approved System(s)

Mark "X" in the appropriate column and provide the applicable letter or report to evidence the audit as indicated below:	Accounting	Billing	Both
Defense Contract Audit Agency (DCAA) audit report No. _____ dated _____ as evidenced by the enclosed report.	☐	☐	☐
Defense Contract Management Agency (DCMA) audit dated _____ as approved by the enclosed letter No. _____ dated _____.	☐	☐	☐
Other Government Agency audit dated _____ as approved by the enclosed letter No. _____ dated _____.	☐	☐	☐

Section II—Evaluation Checklist

If Offeror selects "No" or "N/A" for any of the following questions, Offeror must provide an explanation under Section III – Offeror Remarks for each instance whereby one of these selections is made.

Mark "X" in the appropriate column. (If "N/A" or "No," explain in remarks section below.) If a successful audit has been completed by an independent party, please provide evidence to substantiate this finding.	Yes	No	N/A
1. *Is the accounting system in accordance with generally accepted accounting principles applicable in the circumstances?	☐	☐	☐
2. Accounting system provides for:			
a. *Proper segregation of direct costs from indirect costs.	☐	☐	☐
b. *Identification and accumulation of direct costs by contract.	☐	☐	☐
c. A logical and consistent method for the allocation of indirect costs to intermediate and final cost objectives.	☐	☐	☐
d. Accumulation of costs under general ledger control.	☐	☐	☐
e. *A timekeeping system that identifies employees' labor by intermediate or final cost objectives.	☐	☐	☐

f.	A labor distribution system that charges direct and indirect labor to appropriate cost objectives.	☐	☐	☐
g.	*Monthly accounting of Subcontract costs incurred.	☐	☐	☐
h.	Exclusion from costs charged to Government contracts of amounts which are not allowable in terms of Federal Acquisition Regulation (FAR) 31, Contract Cost Principles and Procedures, or other contract provisions.	☐	☐	☐
i.	*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.	☐	☐	☐
j.	Segregation of preproduction costs from production costs.	☐	☐	☐
3.	Accounting system provides financial information:			
a.	Required by contract clauses concerning limitation of cost (FAR 52.232-20 and 21) or limitation on payments (FAR 52.216-16).	☐	☐	☐
b.	Required to support requests for progress payments.	☐	☐	☐
4.	Is the accounting system designed, and are the records maintained in such a manner that adequate, reliable data are developed for use in pricing follow-on acquisitions?	☐	☐	☐
5.	*Is the accounting system currently in full operation? (If not, describe in the narrative which portions are (1) in operation, (2) set up but not yet in operation, (3) anticipated, or (4) nonexistent.)	☐	☐	☐
6.	Billing system allows for:			
a.	Segregation and exclusion of unallowable costs as required by FAR or Defense Federal Acquisition Supplement (DFARS)	☐	☐	☐
b.	Timely notification to prime contractor of overpayments/underpayments.	☐	☐	☐
c.	Segregation of incurred costs that may be non-billable because the costs may not meet specified criteria	☐	☐	☐
d.	Adjusting submissions for final rates or indirect billing rates that differ from the billed rates	☐	☐	☐

e.	Identifies costs that require specific approvals (special purchases, overtime authorizations, etc.).	☐	☐	☐
f.	Identifying contract overpayments, making refunds in a timely manner, and offsetting contract overpayments against contract underpayments.	☐	☐	☐
*Items marked with an asterisk require Review/Approval and Signature by Ledios Biomed Internal Audit if "No" or "N/A" is selected.				

Section III—Offeror Remarks:

The undersigned attests to the accuracy of the foregoing and agrees to promptly notify Leidos Biomed of any changes to its Accounting, Billing System, and/or related internal control structure that would affect its ability to report hours delivered accurately and completely, and bill costs according to FAR Part 31, Contract Cost Principles and Procedures.

Company Name:

Name of Signatory:

Signature:

Title:

Telephone Number:

Date of Execution:

The following sections are to be completed by Leidos Biomed

Section IV—Leidos Biomed Subcontracts Review/Approval

Name of Signatory:

Signature:

Title:

Date of Execution:

Recommendation:

Section V—Leidos Biomed Internal Audit Review/Approval

Review and approval by Leidos Biomed Internal Audit Department is only required if the Offeror has selected “No or N/A” for the following items listed under Section II – Evaluation Checklist : Items 1, 2a, 2b, 2e, 2g, 2i and 5. (These items are also indicated as applicable in Section II).

Name of Signatory:

Signature:

Title:

Date of Execution:

Recommendation:

	Yes	No	N/A
Corrective Action Plan Received?	☐	☐	☐
Audit Conducted?	☐	☐	☐

Attachment 2: Vertebrate Animal Section (VAS) Worksheet *(If the work proposed involves animals)*

A. Instructions for Offerors

Overview of requirements

If live vertebrate animals are to be used, federal policy requires that the following five points are addressed by applicants in the VAS portion of the Technical Proposal.

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

B. Worksheet to Assist in Addressing the Required Five Points of the VAS

B.1. Performance site(s):

The five points must be addressed for all performance sites.

- If the Offeror's institution is not where animal work will be performed, are all collaborative performance site(s) identified?
- If more than one performance site is proposed, are descriptions of animal care and use addressing the five points provided for each site?

B.1.a. Point 1

Describe the animals and their proposed use; address the following for all species to be used:

- Species

- Strains
- Ages
- Sex
- Number of animals to be used
- A concise, complete description of proposed procedures (i.e., sufficient information for evaluation)

B.1.b. Point 2

Provide justifications for:

- The use of animals
- Choice of species
- Number of animals to be used (cite power calculations, if appropriate) with specific justification for large numbers of animals
- Use of animals that are in short supply or are costly

B.1.c. Point 3

Provide a general description of veterinary care, including veterinary support that is relevant to the proposed procedures. Examples of the kinds of items that may be appropriate to include are:

- A brief account of veterinary staff and their availability
- The regular schedule of monitoring of animals by veterinary staff
- Any additional monitoring and veterinary support that may be required to ensure humane care, if relevant to the procedures proposed (e.g., post-surgical)
- Indicators for veterinary intervention to alleviate discomfort, distress or pain, if relevant

B.1.d. Point 4

Describe procedures to minimize discomfort, distress, pain and injury to that which is scientifically unavoidable in the conduct of research. Examples of the kinds of items that may be appropriate to include are:

- Circumstances relevant to the proposed work, when animals may experience discomfort, distress, pain or injury
- Procedures to alleviate discomfort, distress, pain or injury
- Identify (by name or class) any tranquilizers, analgesics, anesthetics and other treatments (e.g., antibiotics) and describe their use
- Provisions for special care or housing that may be necessary after experimental procedures
- Plans for post-surgical care, if survival surgeries are proposed

- Indicators for humane experimental endpoints, if relevant
- Describe the use of restraint devices, if relevant

B.1.e. Point 5

- Describe methods of euthanasia:
- Describe the method(s) of euthanasia and rationale for selection of method(s)
- Indicate if the method is consistent with AVMA Guidelines on Euthanasia
- Provide a scientific justification for the choice of method if not AVMA recommended

C. Detailed Instructions for Preparation and Review of the VAS

Leidos Biomed will evaluate information provided in the VAS in accordance with the technical evaluation criteria specified in the Solicitation. During discussions, the Leidos Biomed Contracting Officer will provide any concerns expressed during the review and provide the Offeror an opportunity to respond to the concerns. Offerors should be aware that Leidos Biomed may release information contained in Agreement pursuant to a Freedom of Information Act request or pursuant to a protest, either before or after award.

C.1. Preparation of the VAS:

Following the detailed guidelines below, all of the required elements for the VAS typically can be addressed within 1-2 pages.

C.2. Performance site(s):

This is defined as the institutions where procedures with animals will be performed. If the Offeror's institution is not the site where animal work will be performed, the performance site must be identified. If there is more than one performance site, the description of animal care and use at each site must be included in addressing the five points.

C.2.a. Point 1

Description of Animals and How They will be Used

A concise, complete description of the proposed procedures must be included in the VAS. While additional details may be included, a coherent, albeit brief, description of the proposed use of the animals must be provided within the VAS. The description must include sufficient detail to allow evaluation of the procedures. Examples of the types of procedures that may be described include blood collection, surgical procedures, administration of substances, tumor induction and post-irradiation procedures. In describing the animals, the offeror must provide the following information for each species or strain:

- Species

- Strain
- Ages
- Sex
- Number of animals to be used

C.2.b. Point 2

Justifications for Use of Animals

Investigators must justify the use of animals in the proposed research. U.S. Government Principles require contractors to consider mathematical models, computer simulation, and in vitro biological systems. The justification should indicate why alternatives to animals (e.g., computer models, cell culture) cannot be used and the potential benefits and knowledge to be gained. In addressing this point, researchers are encouraged to consider means to replace, reduce and refine the use of animals. Rationale for the choice of species must be provided (e.g. advantages of the species chosen and why alternative species are not appropriate). If less highly evolved or simpler animal models are available, justification should be provided for using more advanced species. For example, the use of non-human primates (NHP), dogs or cats should be thoroughly justified. If NHP species are to be used, a comparison to other NHP species may be appropriate. If animals are in short supply, costly, or to be used in large numbers, an additional rationale for their selection and the number of animals to be used is required.

Estimates for the number of animals to be used should be as accurate as possible. Justification for the number of animals to be used may include considerations of animal availability, experimental success rate, inclusion of control groups and requirements for statistical significance; cite power calculations where appropriate.

C.2.c. Point 3

Veterinary Care

Descriptions of veterinary care should indicate the availability of veterinarians or veterinary technicians. For example, the VAS might indicate the number of veterinarians and veterinary technicians associated with the offeror, and their proximity to the performance site(s). The frequency with which veterinary staff observe or monitor animals may also be stated.

If survival surgeries are proposed, descriptions of veterinary involvement or post-surgical monitoring may be described. For example, if animal use involves invasive approaches that might result in discomfort, distress or pain, the investigator may describe the indicators for veterinary intervention and the ways in which veterinary staff may intervene.

C.2.d. Point 4

Provisions to Minimize Discomfort, Distress, Pain and Injury

Procedures or circumstances that may result in more than momentary discomfort, distress, pain or injury should be identified. Methods to alleviate discomfort, distress or pain should be described. If pharmacological agents are used, the agent(s) may be specified by name or class. Any additional (e.g., non-pharmaceutical) means to avoid discomfort, distress, pain or injury may be briefly described. The manner, circumstances and duration of all post-surgical provisions and care may be described. If special housing is necessary following surgery or manipulations, the VAS may describe these. If procedures (e.g., pharmacological or surgical) might lead to severe discomfort, distress, pain or injury, indicators for humane endpoints and euthanasia (e.g., severe infection, respiratory distress, failure to eat, tumor size) may be described. All of these issues are particularly important for survival surgeries. If multiple surgeries are proposed, these should be well justified and provisions to avoid any potential complications may be described. Describe how restraining devices will be used, if applicable.

C.2.e. Point 5

Euthanasia

The method(s) of euthanasia must be described and must comply with the AVMA Guidelines on Euthanasia. If the method(s) do not comply with AVMA recommendations, the rationale and scientific justification for use of the method(s) must be provided. The indicators for euthanasia (i.e., termination of experiment or humane endpoints) may be stated. It is not sufficient to state simply that humane methods will be used, that are consistent with the recommendations of the AVMA Guidelines on Euthanasia or the Institutional Animal Care and Use Committee (IACUC).

D. References

Guidance in this document is based on PHS Policy and federal requirements. The PHS Policy incorporates the standards in the Guide for the Care and Use of Laboratory Animals and the U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research and Training, and requires that euthanasia be conducted according to the AVMA Guidelines on Euthanasia. Additional background information and references are available on the Office of Laboratory Animal Welfare website (<http://olaw.nih.gov>).

- PHS Policy
- <http://grants.nih.gov/grants/olaw/references/phspol.htm>
- U.S. Government Principles
- <http://grants.nih.gov/grants/olaw/references/phspol.htm#USGovPrinciples>
- Guide for the Care and Use of Laboratory Animals
- http://www.nap.edu/openbook.php?record_id=5140
- AVMA Guidelines on Euthanasia
http://www.avma.org/issues/animal_welfare/euthanasia.pdf

Attachment 3: Leidos Biomed Terms and Conditions

A. Quality Assurance/Inspection

All goods furnished and services performed pursuant hereto shall be subject to inspection and testing by Leidos Biomed at all reasonable times and places during the Agreement term and in any event prior to Final Acceptance as defined in the Statement of Work. No inspection made prior to Final Acceptance shall relieve the Subcontractor from responsibility for defects or other failure to meet the requirements of this Agreement. In the event that goods furnished or services supplied are not in accordance with the Statement of Work and Schedule or other requirements, Leidos Biomed may require the Subcontractor to promptly correct, repair, replace, or re-perform the goods or services. The cost of correction, repair, replacement, or re-performance shall be determined under Section B. Warranty of this Agreement. If the Subcontractor fails to proceed with reasonable promptness to perform the required correction, repair, replacement, or re-performance, Leidos Biomed may terminate the Agreement for default, and procure such materials and services from another source without further obligation to the Subcontractor.

B. Warranty

The Subcontractor represents and warrants only as of the date of signing this Agreement (1) that the rates charged for the goods and/or services purchased pursuant hereto shall be no higher than the Subcontractor's current rates to any other customer for the same quality and quantity of such goods or services; (2) that all goods and services delivered pursuant hereto will be new, unless otherwise specified. Notwithstanding anything to the contrary in this Agreement, Leidos Biomed and Subcontractor acknowledge and agree that the scope of Subcontractor's work under this Agreement constitutes basic, fundamental scientific research, and accordingly the parties acknowledge the experimental nature of the work. Subcontractor does not represent or warrant that it will achieve any particular objectives or results other than to utilize generally accepted scientific standards in the completion of the scope of work. All above representations, warranties and disclaimers of the Subcontractor shall convey to Leidos Biomed and Leidos Biomed's customers. The foregoing warranties and disclaimers shall survive any delivery, inspection, acceptance, or payment by Leidos Biomed.

C. Changes and Suspension

Leidos Biomed may, by written notice to Subcontractor at any time, make changes within the general scope of this Agreement in any one or more of the following: (a) drawings, designs or specifications; (b) quantity; (c) time or place of delivery; (d) method of shipment or packing; and (e) the quantity of Subcontractor furnished property. No such adjustment or any other modification of the terms of this Agreement will be allowed unless mutually agreed upon by the parties by means of a written modification to the Agreement. Leidos Biomed may, for any reason, direct Subcontractor to suspend, in whole or in part, delivery of goods or performance of services hereunder for such period of time as may be determined by Leidos Biomed in its sole discretion. If any such suspension causes a material increase or decrease in the cost of, or the time required for the performance of any part of the work under this

Agreement, an equitable adjustment shall be made in the Agreement price or delivery schedule, or both, provided Subcontractor shall have notified Leidos Biomed in writing of any claim for such adjustment within twenty (20) days from the date of notification of the suspension from Leidos Biomed.

D. Assignment

Neither this Agreement nor any interest herein may be assigned, in whole or in part, without the prior written consent of Leidos Biomed except that the Subcontractor shall have the right to assign this Agreement to any successor of such party by way of merger or consolidation or the acquisition of substantially all of the business and assets of the Subcontractor relating to the subject matter of this Agreement. This right shall be retained provided that such successor shall expressly assume all of the obligations and liabilities of the Subcontractor under this Agreement, and that the Subcontractor shall remain liable and responsible to Leidos Biomed for the performance and observance of all such obligations.

In the event the prime contract of Leidos Biomed with the Government is succeeded by a successor contractor selected by the Government, this Agreement may be assigned to the successor contractor.

E. Insurance Requirements

Prior to award, the Subcontractor must provide Certificates of Insurance, or other documentation evidencing that the insurance coverages required below are in force. Subcontractor must provide no less than thirty days written notice prior to any cancellation or restrictive modification of the policies.

The Subcontractor is responsible for maintaining the minimum insurance coverage's stated herein throughout the term of this agreement including any modifications extending the period of performance or the exercising of any option periods. Should this insurance coverage lapse, be cancelled, or modified in any way Subcontractor will immediately notify Leidos Biomed. The coverage's stated herein in no way lessen nor effect the Subcontractors other obligations or liabilities set forth in this Agreement.

The Subcontractor is self-insured according to the applicable statute under which state funded insurance provisions are determined and maintains the following insurance coverages with minimum limits as stated:

1. Statutory Workers' Compensation in an amount no less than that required by statute in the state of Agreement performance covering its employees.
2. Commercial General Liability in an amount no less than \$1 Million per each occurrence and \$2 Million in this aggregate covering bodily injury, broad form property damage, personal injury, products and completed operations, contractual liability, and independent contractors' liability. Leidos Biomed, its officers, and its employees shall be included as Additional Insureds; and a waiver of subrogation shall be obtained from the carrier in favor of Leidos Biomed
3. Professional Liability in an amount no less than \$1 Million per occurrence covering damages caused by any acts, errors, and omissions arising out of the professional services performed by the Subcontractor, or any person for whom the Subcontractor is legally liable. To the extent that

coverage for the Subcontractor's services are not excluded in (2) above by virtue of being deemed not of a professional nature, this requirement does not apply.

4. All-Risk Property Insurance in an amount adequate to replace property, including supplies covered by this Agreement, of Leidos Biomed and/or Leidos Biomed's customer that may be in the possession or control of the Subcontractor. Leidos Biomed shall be named as a Loss Payee with respect to loss or damage to said property and/or supplies furnished by Leidos Biomed.

The required insurance coverages above shall be primary and non-contributing with respect to any other insurance that may be maintained by Leidos Biomed and notwithstanding any provision contained herein. The Subcontractor and its employees, agents, representatives, consultants, subcontractors, and suppliers, are not insured by Leidos Biomed and are not covered under any policy of insurance that Leidos Biomed has obtained or has in place.

Any self-insured retentions, deductibles, and exclusions in coverage in the policies required under this section shall be assumed by, for the account of, and at the sole risk of, the Subcontractor which provides the insurance and to the extent applicable shall be paid by the Subcontractor. In no event shall the liability of the Subcontractor be limited to the extent of any insurance or the minimum limits required herein.

F. Indemnification

To the extent allowed by law, the Subcontractor shall indemnify, defend and hold Leidos Biomed and Leidos Biomed's customers harmless from and against any and all damages, losses, liabilities and expenses (including reasonable attorneys' fees) arising out of or relating to any claims, causes of action, lawsuits or other proceedings, regardless of legal theory, that result, in whole or in part, from Subcontractor's (or any of Subcontractor's lower tiers, suppliers, employees, agents or representatives): (i) intentional misconduct, negligence, or fraud, (ii) breach of any representation, warranty or covenant made herein; (iii) breach of the confidentiality or disclosure provisions herein; (iv) infringement of any patent, trademark, copyright, trade secret, or any other intellectual property right; or (v) violation of any law or regulation. Notwithstanding the foregoing, Subcontractor's obligations under this Section shall not apply to the extent that a claim is finally determined by a court of competent jurisdiction to be caused by the negligence or willful misconduct of Leidos Biomed

Leidos Biomed shall indemnify, defend and hold the Subcontractor harmless from and against any and all damages, losses, liabilities and expenses determined by a court of competent jurisdiction to have arisen out of any claims, causes of action, lawsuits or other proceedings, that result, in whole, solely from Leidos Biomed's: (i) intentional misconduct, negligence, or fraud related to Leidos Biomed's activities under this Agreement (ii) violation of any law or regulation related to the performance of this Agreement. Notwithstanding the foregoing, Leidos Biomed's obligations under this Section shall not apply to the extent that a claim is finally determined by a court of competent jurisdiction to be caused by the negligence or willful misconduct of the Subcontractor.

Leidos Biomed shall promptly notify the Subcontractor of any claim that is covered by this indemnification provision and shall authorize representatives of the Subcontractor to settle or defend any such claim or suit and to take charge of any litigation in connection therewith.

Notwithstanding this section, should the deliverables or portion thereof be held to constitute an infringement and use as contemplated by this Agreement be enjoined or be threatened to be enjoined, the Subcontractor shall notify Leidos Biomed immediately.

G. Confidential Information

For the purposes of this Agreement, Confidential Information ("Confidential Information") shall mean all information (including functional and technical specifications, data, results, designs, drawings, analysis, research processes, concepts, methods, ideas, inventions (whether patented or not), and "know-how" if written, marked as "confidential" or "proprietary" or with respect to information which is in non-written form, the information is orally or otherwise identified to the receiving party as being Confidential Information at the time it is disclosed and subsequently confirmed as being Confidential Information in a written communication to the receiving Party within thirty (30) days after such disclosure. Neither party shall at any time, and for up to three years after expiration or termination of this Agreement, use or disclose to any person for any purpose other than to perform this Agreement, any Confidential Information it receives, directly or indirectly from the other party in connection with this Agreement, for any purpose other than for the work contemplated in this Agreement, except information that: (i) is or becomes publicly available without restriction from another source that does not have an obligation of confidentiality; (ii) was developed by the receiving party completely independently of the access to the Confidential Information under this Agreement; (iii) is disclosed to the receiving party without restriction; (iv) is disclosed or produced in accordance with a judicial order or governmental request. . Upon request by the other party, the receiving party shall return to the other party all documentation and other material containing such information. Nothing herein shall prohibit Leidos Biomed from providing information the subcontractor discloses in accordance with the statement of work, to Leidos Biomed's government customer who has agreed to maintain the confidential nature of any Confidential Information provided hereunder.

H. Disputes

H.1.

If a decision relating to the Prime Contract is made by the National Cancer Institute Contracting Officer (NCI CO) and such decision is also related to this Agreement, said decision, if binding upon Leidos Biomed under the Prime Contract shall in turn be binding upon Leidos Biomed and the Subcontractor with respect to such matter; provided, however, that if the Subcontractor disagrees with any such decision made by the NCI Contracting Officer and Leidos Biomed elects not to appeal any such decision, the Subcontractor shall have the right reserved to Leidos Biomed under the Prime Contract with the Government to prosecute a timely appeal in the name of Leidos Biomed as permitted by the contract or by law, the Subcontractor to bear its own legal and other costs. If Leidos Biomed elects not to appeal any such decision, Leidos

Biomed agrees to notify the Subcontractor in a timely fashion after receipt of such decision and to assist the Subcontractor in its prosecution of any such appeal in every reasonable manner. If Leidos Biomed elects to appeal any such decision of the NCI Contracting Officer, Leidos Biomed agrees to furnish the Subcontractor promptly of a copy of such appeal. Any decision upon appeal, if binding upon Leidos Biomed, shall in turn be binding upon the Subcontractor. Pending the making of any decision, either by the NCI Contracting Officer or on appeal, the Subcontractor shall proceed diligently with performance of this Agreement.

If, as a result of any decision or judgment which is binding upon the Subcontractor and Leidos Biomed, as provided above, Leidos Biomed is unable to obtain payment or reimbursement from the Government under the Prime Contract for, or is required to refund or credit to the Government, any amount with respect to any item or matter for which Leidos Biomed has reimbursed or paid the Subcontractor, the Subcontractor shall, on demand, promptly repay such amount to Leidos Biomed. Additionally, pending the final conclusion of any appeal hereunder, the Subcontractor shall, on demand promptly repay any such amount to Leidos Biomed. Leidos Biomed's maximum liability for any matter connected with or related to this Agreement which was the subject of a claim against the Government under the Prime Contract shall not exceed the amount of Leidos Biomed's recovery from the Government.

The Subcontractor agrees to provide certification that data supporting any claim made by the Subcontractor hereunder is made in good faith and that the supporting data is accurate and complete to the best of the Subcontractor's knowledge or belief, all in accordance with the requirements of the Contracts Disputes Act of 1978 (41USC601-613) and implementing regulations. If any claim of the Subcontractor is determined to be based on upon fraud or misrepresentation, the Subcontractor agrees to defend, indemnify, and hold Leidos Biomed harmless for any and all liability, loss, cost, or expense resulting there from.

Any dispute not addressed in paragraph above, will be subject to paragraph as described below.

H.2.

Leidos Biomed and the Subcontractor agree to first enter into negotiations to resolve any controversy, claim, or dispute ("dispute") arising under or relating to this Agreement. The parties agree to negotiate in good faith to reach a mutually agreeable resolution of such dispute within a reasonable period of time. If good faith negotiations are unsuccessful, Leidos Biomed and the Subcontractor agree to bring the dispute before a court of competent jurisdiction.

The Parties specifically agree that each Party shall bear the expense of any costs incurred by it for its own counsel, experts, witnesses, preparation of documents, presentations, and logistics related to the proceedings.

Pending any decision, appeal, or judgment referred to in this provision or the settlement of any dispute arising under this Agreement, the Subcontractor shall proceed diligently with the performance of this Agreement.

I. Termination

I.1. Termination for Convenience

Either party shall have the right to terminate this Agreement, in whole or in part, at any time, without cause, by providing written notice to the Subcontractor. Upon receiving notice of such termination, the Subcontractor shall:

Stop all work on this Agreement on the date and to the extent specified.

Place no further contracts hereunder except as may be necessary for completing such portions of the Agreement that have not been terminated.

Terminate all contracts to the extent that they may relate to portions of the Agreement that have been terminated.

Protect all property in which Leidos Biomed has or may acquire an interest and deliver such property to Leidos Biomed

Within twenty (20) days from such termination, the Subcontractor may submit to Leidos Biomed its written claim for termination charges in the form prescribed by Leidos Biomed. Failure to submit such claim within such time shall constitute a waiver of all claims and a release of all Leidos Biomed's liability arising out of such termination. Under no circumstances shall the Subcontractor be entitled to anticipatory or lost profits.

Leidos Biomed reserves the right to verify claims hereunder and the Subcontractor shall make available to Leidos Biomed, upon its request, all relevant, non-proprietary books and records for inspection and audit (e.g., time cards and receipts). If the Subcontractor fails to afford Leidos Biomed its rights hereunder, the Subcontractor shall be deemed to have relinquished its claim.

I.2. Termination for Default

Leidos Biomed may, by written notice of default to the Subcontractor, terminate the whole or any part of this Agreement, in any one of the following circumstances:

The Subcontractor fails to make delivery of the goods or to perform the services within time specified herein or any extension thereof.

The Subcontractor fails to perform any of the other provisions of this Agreement in accordance with its terms and does not cure such failure within a period of ten (20) days after receipt of notice from Leidos Biomed specifying such failure.

The Subcontractor becomes insolvent or the subject of proceedings under any law relating to the relief of debtors or admits in writing its inability to pay its debts as they become due.

If this Agreement is so terminated, Leidos Biomed may procure or otherwise obtain, upon such terms and in such manner as Leidos Biomed may deem appropriate, goods or services similar to those terminated.

The Subcontractor shall deliver to Leidos Biomed, in the manner and to the extent requested in writing by Leidos Biomed at or after termination, such complete or partially completed articles, property, materials, parts, tools, fixtures, plans, drawings, information, and contract rights as the Subcontractor has produced or acquired for the performance of the terminated part of this Agreement, and Leidos Biomed will pay the Subcontractor the contract price for completed articles delivered to and accepted by Leidos Biomed and the fair value of the other property of the Subcontractor so requested and delivered.

The Subcontractor shall continue performance of this Agreement to the extent not terminated. Leidos Biomed shall have no obligation to the Subcontractor with respect to the terminated part of this Agreement except as herein provided.

J. Leidos Biomed Furnished Data and Materials

All items furnished by Leidos Biomed hereunder or equipment purchased by the Subcontractor and specifically charged to Leidos Biomed, are the property of Leidos Biomed

Upon completion, expiration, or termination of this Agreement, the Subcontractor shall return all such items in good condition, reasonable wear only excepted, together with all spoiled and surplus items to Leidos Biomed, or make such other disposition thereof as may be directed or approved by Leidos Biomed. The Subcontractor agrees to replace, at its expense, all such items not so returned. The Subcontractor shall make no charge for any storage, maintenance, or retention of such items. The Subcontractor shall bear all risk of loss for all such items in the Subcontractor's possession.

The Subcontractor also agrees to use any designs or data contained or embodied in such items in accordance with any restrictive legends placed on such items by Leidos Biomed or any third party. If Leidos Biomed furnishes any material, for use hereunder, the Subcontractor agrees: (1) not to substitute any other material for use without Leidos Biomed's prior written consent, and (2) that title to such material shall not be affected by incorporation in or attachment to any other property.

K. Publication/Publicity and Press Release

K.1. Publication/Publicity

In accordance with the NCI Chemical Biology Consortium (CBC) Participants Agreement and upon receipt of confirmation from all Participants (to include the NCI project staff) whom have contributed to the accomplishments outlined in the requested publication, the Subcontractor is

encouraged to make publicly available the results of their activities in support of the CBC Program.

Before the Subcontractor submits a paper or abstract for publication or otherwise intends to publically disclose information generated under the CBC participants agreement, such papers, presentations or abstracts must go to the NCI project team for review. The project team may request a publication delay to file patents, protect intellectual property positions or to protect confidential information/data generated or provided by other members of the project at that member's request.

All manuscripts must include the following language: "This project has been funded in whole or in part with Federal funds from the National Cancer Institute, National Institutes of Health, under Chemical Biology Consortium Contract No. HHSN261200800001E. The content of this publication does not necessarily reflect the views or policies of the Department of Health and Human Services, nor does mention of trade names, commercial products, or organizations imply endorsement by the U.S. Government." In addition to the requirements described above, the Subcontractor will provide the Project Team with a list of their publications related to the CBC on a semi-annual basis.

K.2. Press Releases

Before the Subcontractor submits a request for issuance of a Press release, the Subcontractor must show evidence that all other contributing Participants (to include the NCI project team members) to the effort have given permission for the content to be publically released.

After consensus to proceed with the press release is received from all stakeholders, a formal request for approval shall be submitted to both the NCI CBC Administrator and the Leidos Biomed Subcontracts Administrator; these approvals will not be unreasonably delayed or withheld. All press releases which reference the NCI must be approved by the NCI press office.

Any approved press releases or other documents describing projects or programs funded in whole or in part with Federal money shall clearly state: (1) the percentage of the total costs of the program or project which will be financed with Federal money; (2) the dollar amount of Federal funds for the project or program; and (3) the percentage and dollar amount of the total costs of the project or program that will be financed by nongovernmental sources.

L. General Relationship

The Subcontractor is not an employee of Leidos Biomed for any purpose whatsoever. The Subcontractor agrees that in all matters relating to this Agreement it shall be acting as an independent contractor and shall assume and pay all liabilities and perform all obligations imposed with respect to the performance of this Agreement. The Subcontractor shall have no right, power, or authority to create any obligation, expressed or implied, on behalf of Leidos Biomed and/or the Government and shall have no authority to represent Leidos Biomed as an agent.

M. Non-Waiver of Rights

The failure of Leidos Biomed to insist upon strict performance of any of the terms and conditions in the Agreement, or to exercise any rights or remedies, shall not be construed as a waiver of its rights to assert any of the same or to rely on any such terms or conditions at any time thereafter.

N. Legal Construction and Interpretations

This Agreement shall be governed by and interpreted in accordance with the principles of Federal Contract Law, and to the extent that Federal Contract Law is not dispositive, and the state law becomes applicable, the laws of the State of Maryland shall apply without regard to its conflict or choice of law provisions.

O. Export Control Compliance for Foreign Persons

The Subcontractor warrants that it has in place a system or process for compliance with all U.S. export control laws, including but not limited to the regulations of the U.S. Department of Commerce and/or U.S. Department of State. At all times, the Subcontractor shall comply with all applicable federal, state and local laws applicable to the export of any process, goods and/or technical data and information from the United States and within the U.S. to foreign nationals. Subcontractor acknowledges that when applicable, a failure to comply with all applicable laws may subject the Subcontractor to criminal liability under U.S. law and may result in termination of this Agreement. The Subcontractor shall include in all lower tier contracts similar provisions as contained herein requiring compliance with all applicable laws.

Furthermore, Subcontractor agrees that it shall not disclose, export, or re-export any Leidos Biomed information, or any process, product, or services produced under this Agreement, in violation of any restrictive legends placed on such items by Leidos Biomed, without the prior notification to Leidos Biomed. In addition, the Subcontractor agrees to immediately notify Leidos Biomed if the Subcontractor is listed on any of the Department of State, Treasury, or Commerce proscribed persons, organizations or destinations lists, or if the Subcontractor's export privileges are otherwise denied, suspended, or revoked in whole or in part. Subcontractor shall not be required to accept any information or any work under this Subcontract that requires access to information that is subject to export controls.

P. Standards of Business Ethics & Conduct

Leidos Biomed believes in fair and open competition and is committed to conducting its business fairly, impartially, and in an ethical and proper manner. Leidos Biomed's expectation is that the Subcontractor also will conduct its business fairly, impartially, and in an ethical and proper manner. If the Subcontractor has cause to believe that Leidos Biomed or any employee or agent of Leidos Biomed has acted improperly or unethically under this Agreement, the Subcontractor shall report such behavior to the Leidos Ethics Hotline 855-753-4367. Copies of the Leidos Biomed's Code of Ethics and contacts for such reports are available under Corporate Governance at the following link: [Standards of Business Ethics and Code of Conduct](#).

Q. Audit

At any time before final payment Leidos Biomed may request and perform an audit with reasonable advance written notice to Subcontractor of the invoices and substantiating material. This may be an onsite audit at Subcontractor's facility or a request for sufficient documentation to audit in accordance with generally accepted audit standards. Each payment previously made shall be subject to reduction to the extent of amounts that are found by Leidos Biomed not to have been properly payable in accordance with the terms of this Agreement. Audit will include, but not be limited to, effort reporting documentation, invoices for material, storeroom requisitions, expense reports, and other substantiation supporting invoiced amounts.

R. Compliance with Laws and Regulations

The Subcontractor shall submit all certifications required by Leidos Biomed under this Agreement and shall at all times, at its own expense, comply with all applicable Federal, State, and local laws, ordinances, administrative orders, rules, or regulations.

S. Gifts

The Subcontractor shall not make or offer a gratuity or gift of any kind to Leidos Biomed's employees or their families. The Subcontractor should note that the providing of gifts or attempting to provide gifts under Government Agreements might be a violation of the Anti-Kickback Act of 1986 (4 U.S.C. 51-58).

T. Maryland Sales and Use Tax

The State of Maryland has issued Direct Payment Permit #3, effective date August 29, 1996, a copy of this Permit is available upon request. As a holder of a Direct Payment Permit, Leidos Biomed is authorized to make direct payment of sales and use tax to the State of Maryland. Accordingly, Subcontractors that provide goods and services to Leidos Biomed are relieved from collecting sales tax from Leidos Biomed. Therefore, Subcontractors to Leidos Biomed shall not place a separate line item for tax on any invoice sent to Leidos Biomed Please note that the Permit is not to be used by Subcontractors to make purchases free of sales tax, nor shall the Permit be transferred or assigned.

U. Notice of Delay

The Subcontractor agrees to immediately notify Leidos Biomed in writing of any actual or potential delay in the Subcontractor's performance under this Agreement. Such notice shall, at a minimum, describe the cause, effect, duration, and corrective action proposed by the Subcontractor to address the problem. The Subcontractor shall give prompt written notice to the Leidos Biomed of all changes to such conditions. This notification shall be informational only, and compliance with this provision shall not be construed as a waiver by Leidos Biomed of any delivery schedule or date or of any rights or remedies provided by law or under this Agreement.

V. Notification of Debarment/Suspension

By acceptance of this Agreement either in writing or by performance, the Subcontractor certifies that, as of the date of award of this Agreement, neither the Subcontractor, lower tiers, nor any of its principals, is debarred, suspended, or proposed for debarment by the Federal Government. Further, Subcontractor shall provide immediate written notice to the Leidos Biomed Contracting Officer in the event that during performance of this Agreement the Subcontractor or any of its principals is debarred, suspended, or proposed for debarment by the Federal Government.

W. Security

Under its prime contract with the Frederick National Laboratory for Cancer Research, Leidos Biomed may be required to conduct, on persons performing work on Government Owned or controlled installations, individual background checks prior to the commencement of effort. As part of this process, information will be required to enable Leidos Biomed to conduct the appropriate background checks, including name (including any aliases), daytime phone number, SSN, date of birth, and country of birth. Individuals who are unable or unwilling to provide the required information and/or receive the required authorizations will not be allowed access to the Frederick National Laboratory for Cancer Research or any controlled premises.

X. Tobacco Use at the Frederick National Laboratory for Cancer Research

In accordance with the Department of Health and Human Services (HHS) directive, the Frederick National Laboratory for Cancer Research campus is a tobacco free workplace. Use of tobacco in any form is prohibited on the entire Frederick National Laboratory for Cancer Research campus. This includes personal vehicles while on Frederick National Laboratory for Cancer Research property and all Government vehicles, regardless of their location.

This policy applies to all employees, Government and Contractor, visitors, subcontractors, vendors, and guests of the Frederick National Laboratory for Cancer Research and extends to all HHS owned or leased facilities and properties external to the Frederick National Laboratory for Cancer Research campus where the sole tenant(s) are HHS and/or Leidos Biomed employees.

Y. Severability

If any term contained in this Agreement is held or finally determined to be invalid, illegal, or unenforceable in any respect, in whole or in part, such term shall be severed from this Agreement, and the remaining terms contained herein shall continue in force and effect, and shall in no way be affected, prejudiced, or disturbed thereby.

Z. Interpretation

The captions and headings used in this Agreement are solely for the convenience of the parties, and shall not be used in the interpretation of the text of this Agreement. Each party has read and agreed to

the specific language of this Agreement; therefore no conflict, ambiguity, or doubtful interpretation shall be construed against the drafter.

AA. Electronic and Information Technology Standards

The Subcontractor agrees to comply with Section 508 of the Rehabilitation Act of 1973 (29 U.S.C. 794d) as amended by P.L. 105-220 under Title IV (Rehabilitation Act Amendments of 1998). Electronic and Information Technology (EIT) developed, procured, maintained, and/or used under this contract shall be in compliance with the "Electronic and Information Technology Accessibility Standards" set forth by the Architectural and Transportation Barriers Compliance Board (also referred to as the "Access Board") in 36 CFR Part 1194. The complete text of Section 508 Final Standards can be accessed at <http://www.section508.gov/index.cfm?FuseAction=content&ID=12>. Applicable standards to this requirement are set forth in 36 CFR Part 1194.21 through 26.

The Subcontractor further agrees to include this provision in any Subcontract awarded pursuant to this Agreement. Failure to comply to these requirements may constitute cause for termination under Section L.10 Termination of this Agreement.

BB. Acceptance of Agreement and Modification of Terms

No modifications, additions or changes in the terms and conditions proposed herein or after execution of the definitive agreement by the parties shall be binding unless mutually agreed upon in a formal written modification executed by duly authorized representatives. No waiver of any kind to the terms and conditions contained herein shall be valid unless made in writing and executed by Leidos Biomed and the Subcontractor. The Subcontractor agrees to perform in accordance with the Description/Quantity schedule set forth in this Agreement and all attachments thereto.

CC. Information Security

The Subcontractor agrees to comply with the Information Technology (IT) systems security and/or privacy specifications set forth in this Agreement and as further defined by the Federal Information Security Management Act of 2002 (FISMA), Title III, E-Government Act of 2002, Pub. L. No. 107-347 (Dec. 17, 2002); <http://csrc.nist.gov/drivers/documents/FISMA-final.pdf>.

The Subcontractor further agrees to include this provision in any Agreement awarded pursuant to the Agreement. Failure to comply with these requirements may constitute cause for termination under Section L.10 Termination of this Agreement.

The Subcontractor shall be responsible for properly protecting all information used, gathered, or developed as a result of this Agreement. The Subcontractor shall establish and implement appropriate administrative, technical, and physical safeguards to ensure the security and confidentiality of sensitive Government information, data, and/or equipment. Any Subcontractor employee who may have access to sensitive information under this Agreement shall complete the form entitled, "Commitment to Protect Non-Public Information – Contractor Agreement," which may be found at the following website: <https://ocio.nih.gov/aboutus/publicinfosecurity/acquisition/Documents/Nondisclosure.pdf>.

A copy of each signed and witnessed Non-Disclosure Agreement shall be submitted to the Leidos Biomed Contracting Officer prior to performing any work under this Agreement.

The Subcontractor shall assure that each employee has completed the NIH Computer Security Awareness Training (<http://irtsectraining.nih.gov>) prior to performing any work under this Agreement.

In addition, the Subcontractor shall submit a roster, by name, position, email address, phone number, and responsibility, of all staff (including 2nd tier Subcontractor staff) working under the Agreement who will develop, have the ability to access, or host and/or maintain a Federal information system(s). The roster shall be submitted to Leidos Biomed within 14 calendar days of the effective date of the Agreement along with scanned copies of the completed training certificates for each staff member. Any revisions to the roster as a result of staffing changes shall be submitted to Leidos Biomed within 15 calendar days of the change. Additional training certifications will then be due to be submitted to Leidos Biomed every 12 months thereafter on the anniversary date of contract award.

In addition, during all activities and operations on Government premises, the Subcontractor shall comply with DHHS, including National Institutes of Health (NIH), rules of conduct. Should the Subcontractor have questions concerning these requirements or need of procedural guidance to ensure compliance they may contact the cognizant Leidos Biomed Subcontract Specialist.

DD. 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 DHHS Inspector General's Office in writing or on the Inspector General's Hotline. The toll free number is 1-800-DHHS-TIPS (1-800-447-8477). All telephone calls will be handled confidentially. The email address is Htips@os.dhhs.gov and the mailing address is:

Office of Inspector General
Department of Health and Human Services
TIPS HOTLINE
P.O. Box 23489
Washington, D.C. 20026

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

Pursuant to the current HHS annual appropriations act, the Subcontractor shall not use Agreement 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 (21 U.S.C. 812), 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.

FF. Force Majeure

Neither party shall be liable for any failure of or delay in performance of its obligations under this Agreement to the extent such failure or delay is due to circumstances beyond its reasonable control, including, without limitation, acts of God, acts of a public enemy, terrorism, fires, floods, wars, civil disturbances, sabotage, accidents, insurrections, blockades, embargoes, storms, explosions, labor disputes (whether or not the employees' demands are reasonable and/or within the party's power to satisfy), acts of any governmental body, failure or delay of third parties or governmental bodies from whom a party is obtaining or must obtain approvals, authorizations, licenses, franchises, or permits, or inability to obtain labor, materials, power, equipment, or transportation (collectively referred to herein as "Force Majeure"). Each party shall use its reasonable efforts to minimize the duration and consequences of any failure of or delay in performance resulting from a Force Majeure event and to promptly notify the other of any actual or potential Force Majeure event.

GG. Entire Agreement

The parties hereby agree that this Agreement, including all documents incorporated herein by reference or attached hereto, shall constitute the entire Agreement and understanding between the parties hereto and shall supersede and replace any and all prior or contemporaneous representations, agreements, or understandings of any kind, whether written or oral, relating to the subject matter hereof.

HH. Survival

The provisions for the Sections Entitled Key Personnel, Warranty, Assignment, Indemnification, Confidential Information, Disputes, Termination, Leidos Biomed Furnished Material, and Export Control shall survive the termination or expiration of this Agreement.