STATEMENT OF WORK

TITLE: Chemical Biology Consortium Screening Library Center

Introduction/Background:

The Chemical Biology Consortium (CBC) has been established through the NCI Division of Cancer Treatment and Diagnosis (DCTD) in conjunction with the Center for Cancer Research (CCR) and the Office of the Director (OD). The CBC is a multidisciplinary network comprised of academic, government and private entities that interacts collaboratively to support execution of drug discovery and development projects within the NCI Experimental Therapeutics Program (NExT). The CBC centers along with DCTD's existing resources, establishes a complete drug discovery and development platform for oncology therapeutics. One critical infrastructure resource within the CBC is small molecule screening library services in support of high throughput screening (HTS) projects. The CBC Screening Libraries Center (CBCSLC) provides this resource capability. The CBCSLC was originally established in 2010 under the name Chemical Biology Consortium Small Molecule Repository (CBCSMR). The CBCSLC will be responsible for the storage, distribution, replenishment and expansion of our current 130,000 compound small molecule screening library and providing associated infrastructure, technical and informatics **services.**

<u>Objectives and Capabilities:</u>

1. Store and maintain the CBCSLC 130,000 small molecule screening collection (solid/film vialed stores, working Matrix tube stores and microliter plates) to support NExT HTS projects. The collection contains a 83,000-compound diversity library used for general screening and 15-20 specialized focused sets that total 47,000 compounds and are selected for distribution based on individual project needs.
2. Generate mother and replicate plates of the CBCSLC small molecule screening collection to support HTS projects as demand warrants. These are generally formatted in 384-well plates but the capability should exist to work in 96-well or 1536-well environments.
3. Generate and distribute diversity and focused plated sets based on project demand to the CBC screening centers. These are generally formatted in.384-well plates but the capability should exist to work in 96-well or 1536-well·environments.
4. Generate and distribute cherry-picked plated sets, based on project demand to the CBC screening centers. These are generally formatted in 384-well plates but the capability should exist to work in 96-well or 1536- well environments.
5. Monitor the compound inventory to ensure that threshold quantities of all compounds, both dry samples and solutions, are available to support screening needs. Re-acquire depleted compounds to replenish the inventory.
6. Provide the necessary informatics support to register, maintain and update chemical information on each Sample and track compound inventory and distribution.
7. Serve as the chemical structure registrar for all screening molecules of interest to the CBC. This will include evaluating each structure entered into the CBCSLC database for correct and full structure integrity, including relative and absolute stereochemistry, and assigning a unique identifier to each unique structure. This unique identifier will then be used as an index for all subsequent test results.
8. Provide library design, analysis and procurement capabilities, including commercial vendor universe knowledge, for potential expansion of the current library collection.

SERVICES TO BE PERFORMED:

A. Organizational Structure

All work under this contract shall be monitored by the Contracting Officer's Representative (COR), the COR shall be the Contractor's primary point of contact for technical matters under this contract.

B. Specific Technical Requirements

Independently, and not as an agent of the Federal government, the Contractor shall furnish all necessary labor, services, equipment, materials, supplies, and facilities, except as otherwise specified herein, as needed to perform the work set forth below. The contract may be used to purchase new compounds, as directed by the COR, but compounds acquired from other sources may also be managed under this contract. The Contractor shall have a suitable facility, equipment and staff available at the time of proposal submission.

Task 1. Library Storage, Operational Maintenance, Security and Safety

The listed tasks will be performed on an on-going basis throughout the contract life.

a. Storage- Storage of the 130,000 compound CBCSLC library in suitable facility under conditions that ensure optimal stability and purity, along with background tasks related to the maintenance of associated infrastructure. The library collection is maintained as a mix of: 1) 4 dram vialed neat solid/films, 2) working solution stores in Matrix tubes and 3) 384-well microliter plates. The Contractor shall have the capability to store all samples long-term at -78, -20, and 0°C under inert 'atmosphere as appropriate for maintaining quality in a cost effective manner.· The standard storage conditions are -20°C under an inert atmosphere employing DMSO as a solution solvent. There shall be sufficient storage space and flexibility to accommodate changes in the mix of storage types. The Contractor shall provide all the necessary expertise, equipment, and facilities to store, maintain, and track the inventory. Storage and handling shall comply with all applicable local, state and Federal regulations.

b. Quality Control – The Contractor shall perform rapid, low throughput analyses of chemical purity (e.g., LC/MS, HPLC, and for NMR) as requested by the COR. It is anticipated that this will involve 50-250 samples annually. The Contractor shall be required to have an on-going Quality Assurance plan for instruments and other equipment. The QC requirement (purity and identity) shall include but is not limited to ability to carry out high throughput analysis by GC-MS or LC-MS and interpret results as passing or failing to meet QC criteria by showing specified purity (as specified by the COR). The primary method of analysis shall be LC-MS and/or.GC-MS. When these methods are not suitable the Contractor shall have the capability to routinely perform purity analysis by lH-NMR. It is anticipated that <1% of samples will require 1H-NMR analysis. Structure not confirmed by lack of observed molecular ion by MS or NMR spectra inconsistent with structure is deemed as failing.

c. Distribution - The Contractor shall have the capability to ship plated sets (e.g. diversity library, focused libraries and single-use sets) to the CBC screening centers and external investigators, as requested by the COR. The Contractor shall have capability to ship on a weekly basis using "next business day" for domestic shipments. The Contractor shall also have the capability to ship internationally including regions in India and China. It is estimated that international shipments will be minimal. It is anticipated that 10-15 institutes will comprise the CBC including 5-8 screening centers. Compound shipments shall be made in such a way as to ensure the integrity of the contents (e.g. packed in dry ice) and shall comply with all applicable federal, state, and local regulations and international shipping and custom regulations. It is anticipated that 15-20 individual shipments will be made annually that include existing libraries and cherry-picked sets. The direct shipping costs will be charged to the recipient through their Fedex number while the cost associated with packaging will be the responsibility of the Contractor.

d. Inventory - Monitoring and Repurchase- The Contractor shall monitor and maintain adequate compound inventory, both solution and dry store, to ensure that sufficient threshold quantities, as specified by the COR, of all compounds are available to support screening needs. As compounds fall below threshold inventory (e.g. 5 mg), either by depletion or degradation, the Contractor shall- undertake all activities necessary to purchase sufficient quantities of the compound to replenish the inventory upon approval by the

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COR. It is anticipated that no more than 0.5% of the sample collection will need to be replenished annually. It is estimated that this would be -300 compounds over the life of the contract.

e. CBC Synthetic Compounds – The Contractor shall also have the capability to manage CBC member generated dry powder synthetic samples. It is anticipated that the number of compounds will be minimal over the life of the contract (i.e. <50). Management of samples will involve receipt, registration, inventory, storage, analysis and distribution activities.

f. Disposal – The Contractor shall comply with all local, state and Federal regulations in the disposal of chemical samples, personal protective equipment, solvents and chemically contaminated vials, tubes and plates.

g. Informatics and Documentation - The Contractor shall maintain and update the CBCSLC electronic database containing individual chemical structures, descriptors, associated physiochemical data along with distribution and inventory information. The Contractor's database shall be functionally compatible with the internal Oracle-based NCIICBC database. The Contractor shall be responsible for regularly synchronizing the CBC-related information between the databases. In addition, the Contactor shall produce archival documents that describe the design history, physiochemical characteristics and content of new libraries added to the collection over the life of the contract.

h. Reporting Requirements - The Contractor shall provide quarterly reports, annual reports and a final report describing contract-related activities spanning the time period, including issues encountered and solutions implemented. The subject emphasis within the reports should be based on magnitude of resource allotted. The reports should contain a 1-paragraph executive summary of important activities and issues. The reports should include any significant personnel changes that may impact the execution of work. The annual and final reports should be a summary of work completed over the time period. Additionally, the contractor will be required to submit annually a Section 508 compliance report. Reporting requirements can be found in section C of this contract.

Task 2. Production of Arrayed Sets and Distribution

a. Compound Arrays and Replicates – The Contractor shall have the capability for automated arraying of compounds in DMSO or other suitable solvent in-a format suitable for rapid re-formatting (e.g. deep-well mother plates) and long-term storage. In addition, the Contractor should have the capability for production of daughter plates for distribution to high-throughput screening (HTS) centers. It is anticipated that most libraries will be plated and distributed 384-well format although the Contractor should also have the capability to work in a 96-well and 1536-well environment. Depending on demand, up to 4 replicates of the collection may be produced annually (-500,000 wells). All arrayed sets will become property of the Federal government.

b. Distribution- The Contractor shall distribute compound arrays to the CBC screening centers, as requested by the COR. The Contractor shall have capability to ship on a weekly basis using "next business day" for domestic shipments. The Contractor shall also have the capability to ship internationally including regions in India and China. It is estimated that international shipments will be minimal. It is anticipated that I0-15 institutes will comprise the CBC including 5-8 screening centers. Compound shipments shall be made in such a way as to ensure the integrity of the arrays and shall comply with all applicable federal, state, and local regulations and international shipping and custom regulations. It is anticipated that 15-20 individual shipments will be made annually that include existing libraries and cherry-picked sets. The direct shipping costs will be charged to the recipient through their Fedex number while the cost associated with packaging will be the responsibility of the Contractor.

Task 3. Production of Single-Use Sets

a. Single-Use Sets - The Contractor shall have the capability for automated arraying of the Diversity Collection (83K) and selected focused libraries in DMSO or other suitable solvent in 384-well, single-use and assay-ready formats (e.g. 384-well Greiner 781280, luL vol) for long-term storage and for distribution to external investigators. All stored arrayed sets will become property of the Federal government.

Task 4. Production of Cherry-Pick Sets and Distribution

a. Cherry-pick Production – The Contractor shall have the capability for automated cherry-picking of the screening collection to produce plated sets based on screening hits or other selected criteria as directed by the COR. The general format will be 384-well but other formats may be selected. Cherry-picks to support up to 4 HTS screens annually may be requested (5,000 wells).

b. Distribution- The Contractor shall distribute cherry-picked sets as requested by the COR. The Contractor shall have capability to ship on a weekly basis using "next business day" for domestic shipments. Shipments shall be made in such a way as to ensure the integrity of the arrays and shall comply with all applicable Federal, state, and local regulations. It is anticipated that 5-10 individual shipments will be made annually. The direct shipping costs will be charged to the recipient through their Fedex number, while the cost associated with packaging will be the responsibility of the Contractor.

Task 5. Expansion of Screening Collection

a. Design and Identification - The Contractor shall, in coordination with specifications provided by the COR, employ state-of-the-art computational methods to identify candidate compounds from government and commercial sources for inclusion in new focused libraries. The libraries may, for example, be based on structure subtypes, molecular targets or biological activity.

b. Acquisition – The. Contractor shall undertake all activities necessary to acquire sufficient quantities (typically 5-30 mg) of compounds selected for expansion of the current CBCSLC screening collection. It is anticipated that the collection will not expand beyond an additional 5,000-10,000 compounds although this will be based on future needs and available funding resources. Compounds will be obtained primarily through direct purchase from commercial vendors but may also be obtained from CBC synthetic efforts and other NIH programs (e.g. CMLD, Chemical Methodologies and Library Development). All compounds, either in solution or dry solid, will become property of the Federal government.

C. Project Management

The Contractor may designate a Project Manager (PM) in addition to a Project Director (PD). The PD and PM shall act as points of contacts with the COR, the PM will act as the day-to-day point of contact. Based on workload the PD and PM may be the same person.

D. Confidentiality

The Contractor shall protect the confidentiality of any proprietary compound synthesized or received under the contract. The Contractor shall not release information regarding a proprietary compound or associated proprietary data to parties exclusive of the CBC program without the express written consent of the NCI. The Contractor shall agree to sign CBC Participant agreements, Material Transfer Agreements, and Confidentiality and Nondisclosure Agreements (e.g. see http://ott.od.nib.gov).

E. Licenses and Permits

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The Contractor will be required to maintain all necessary licenses and permits throughout the life of the contract. The Contractor shall have in place at the time of proposal submission all local, state and federal licenses and permits necessary for the execution of the proposed work. This shall include, but may not be limited to, permits to occupy a suitable repository facility and permits to store, distribute and dispose of hazardous materials (e.g. EPA hazardous waste generator identification number).

F. Safety

The Contractor shall operate in compliance with OSHA Safety regulations, State and local regulations. They shall provide a satisfactory Chemical Hygiene plan. The Contractor shall update the plan as required by regulation.

G. Security

The Contractor shall take adequate measures to insure the security of all Government property, including compounds, arrayed sets and associated data. All IT systems and procedures shall conform to NIH IT Security policies and procedures. The Contractor shall update their procedures and systems as necessary. In addition to the standard background investigations, non-disclosure agreements, and IT security awareness training, a system security plan conforming to NIST 800-18, Guide for Developing Security Plans for Federal Information Systems (http://csrc.nist.gov/publications/nistpubs/800-18-Revl/sp800-18-Revl-final.pdf) covering security controls recommended in NIST 800-53, Recommended Security Controls for Federal Information Systems and Organizations (http://nvlpubs.nist.gov/nistpubs/Specia!Publications/NIST.SP.800-53r4.pdf) shall be implemented, if required. Additionally, the IT systems containing sensitive information shall be covered under a certification and accreditation that includes an independent agent System Test and Evaluation as well as written and annually tested contingency plans as outlined in NIST Guide for the Security and Certification and Accreditation of Federal Information Systems (https://www.fismacenter.com/SP800-37-final.pdf) and NIST Contingency Planning Guidelines (http://csrc.nist.gov/pub]ications/nistpubs/800-34-rev-1/sp800-34-revl_errata-Nov11-2010.pdf.

H. Section 508 Compliance

All products and deliverables associated with the tasks described within this Statement of Work that are intended for distribution via the Internet or have the potential for access through the Internet must be compliant with requirements specified in Section 508 of the Federal Rehabilitation Act, as amended in 1998. This Act addresses any/all electronic and information technology (EIT). As such, those procured through this effort must meet the applicability accessibility standards at 36 CFR 1194.36. CFRJ194 implements Sec'tipn508 of the Rehabilitation Act of 1973, as amended, and is viewable at http://www.section508.gov. The contractor is responsible for reviewing this regulation, which can also be reviewed on http://www,accessclroard.gov/index.php.
The following Section50.standard applies to this project:
1194.22-Web-based Intranet and Internet Information and Application

I. Period of Performance

The base period of performance of the proposed contract is estimated from July 30, 2015 to July 29, 2020.

J. Schedule of Work

July 30,2015 to July 29,2020: The Contractor shall be able to perform the tasks in the Statement of Work at any time period throughout the life of the contract. It is expected that Task 1 will be on-going throughout the entire contract.

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There shall be a 60 day overlap in the Schedule of Work to accommodate a 60-day transition period (July 30, 2015- September 29, 2015) to any other than the incumbent contractor. This time period will be used to transfer the inventory to a new facility and resume normal operations.

K. Transition to the Subsequent Contractor

I. At least twelve (12) months prior to the completion date of this contract, the Contractor shall submit a written plan/system to the COR for the potential transfer of all compounds, arrayed sets and Government property to an offsite storage facility {potentially a successor Contractor or the NCI). A general inventory of compounds, arrayed sets and other Government property shall be included.

2. Upon request by the COR, at least three (3) months prior to the completion of the contract, a full and complete inventory of compounds and arrayed sets in the repository and all Government-owned property including scientific equipment, software programs and databases, data files, etc., shall be provided. At this time, the Contractor shall also describe their specific plans for packaging and shipping all such compounds, arrayed sets, data and Government property to a successor Contractor or the NCI, and a cost estimate for this transition.

3. The Contractor shall fully cooperate with any successor Contractor and the NCI to ensure the smooth, efficient and timely transfer of all such data and Government property, including providing access to any essential uniquely trained staff to complete the transfer of informatics and any other critical components of the operation.

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