



**AMENDMENT COVER PAGE - REQUEST FOR PROPOSAL**

<b>REQUEST FOR PROPOSAL NO:</b>	<b>RM-04-0001 (Posted in FedBizOpps as NIMH-04-DB-0001)</b>
<b>TITLE:</b>	<b>“Molecular Libraries Small Molecule Repository”</b>
<b>AMENDMENT:</b>	<b>One (1) Dated: January 30, 2004</b>
<b>OMB No.:</b> 0990-0115	<b>PURCHASE AUTHORITY:</b> Public Law 92-218 as amended; <u>Note:</u> The issuance of this solicitation does not commit the Government to make an award, or to pay any costs for the preparation and submission of a proposal.
<b>ISSUED BY:</b> Bruce E. Anderson Contracting Officer Contracts Management Branch NIMH, NIH, DHHS Neuroscience Center Building, 8155 (MSC 9661) 6001 Executive Blvd. Bethesda, MD 20892-9661  <b>POINT OF CONTACT:</b> Bruce E. Anderson E-mail: <a href="mailto:ba9i@nih.gov">ba9i@nih.gov</a> Phone (301) 443-2696 or 2234 Fax at (301) 443-0501 Collect calls will not be accepted.	<b>RFP ISSUE DATE: December 29, 2003</b>  <div style="border: 1px solid black; padding: 2px;"><b>DUE DATE: March 2, 2004 (Unchanged)</b></div> <b>4:00 p.m., local prevailing time</b>  <u>Note:</u> The official Point of Receipt for the purposes of determining timely delivery is the Contract Management Branch, NIMH. A <u>paper</u> copy with original signatures is the official copy for recording timely receipt. If the Contracting Officer or Designee does not receive your proposal at the place and time specified, then it will be considered late and handled in accordance with PHS Clause 352.215-10 entitled “Late Proposals, Modifications of Proposals and Withdrawals of Proposals” located in this solicitation. <u>Facsimile submissions are not acceptable.</u>
<b>TO: ALL OFFERORS</b>	<b>PURPOSE: THE PURPOSE OF THIS AMENDMENT IS TO PROVIDE ANSWERS TO QUESTIONS ABOUT THE RFP RECEIVED TO DATE.</b>

NOTE: OFFERORS ARE RESPONSIBLE FOR ROUTINELY CHECKING THE NIMH WEBSITE AT <http://www.nimh.nih.gov/grants/indexcon.cfm> or <http://www.fedbizopps.gov> FOR ANY POSSIBLE SOLICITATION AMENDMENTS THAT MAY BE ISSUED. THIS OFFICE WILL PROVIDE NO ADDITIONAL NOTIFICATION OF ANY AMENDMENTS.

Enclosed: RFP Questions and Answers (8 pages)

[Questions Grouped by Subject Matter/Task]

### **General Statement Regarding the Questions Received and Preparing Cost Proposals**

As evidenced below, many questions have been received asking for details regarding the estimation of costs for this initiative. In general, it is difficult to estimate costs for this contract due to certain *unknowns* and *uncertainties*, which are described in some of the answers to questions.

We have provided as much information as is available at this time; when more information is available, it will be disseminated.

Offerors should base their costs upon the information provided in the RFP, but should also draw upon their own expertise and past experience in this area to discuss any assumptions used in preparing your cost proposal. We have provided a level of effort estimate as a *guide*; since there is no reasonable way of estimating what compounds will actually cost, the amounts to budget for compound acquisition are stated; these two items together are a major portion of the direct costs and should provide a good basis for the cost proposals.

The issue of capital expenditure for a compound storage and retrieval system is addressed in Q.1, below. While the budget for this acquisition does not include funds for purchase of such a system, as stated this will be “negotiated” as necessary.

### **Compound Storage and Retrieval Systems**

**Q.1.** Reference Page 8, Task 3, Storage and Quality Control, paragraph 1 states ‘the contractor shall provide all the necessary expertise and facilities to store, maintain and track the small molecule repository inventory’.

***Does the Government purchase the "compound store", or is the Contractor expected to bear this cost?***

**A.1.** This is negotiable; however, the contract emphasis is on the acquisition/purchase of high quality compounds, and it is the Government’s intent to apply the majority of the funds allocated to this contract for that purpose. Offers that propose Government purchase (or lease) of a compound store with a significant amount of contract funds will be considered less advantageous than those that bear at least *some* (or all) of this cost themselves.

It is important to reiterate the Government’s requirement for storage and retrieval of compounds: *The Contractor must provide a storage and retrieval system allowing for rapid and efficient selection and retrieval of compounds for the creation of plates. This system must be capable of retrieving compounds rapidly enough to allow for the shipment of the equivalent of an estimated two complete sets of the total library per year to the screening centers (see answer to question #2, below), plus additional subsets of compounds to extramural requestors. It is estimated that the collection will grow at the rate of up to 250,000 compounds per year, to a total collection of up to 1,000,000 compounds.*

The Statement of Work, Tasks 1 and 3, provides more detail on the acquisition, storage, retrieval, and tracking of compounds. While the RFP states a preference for a “micro tube-based compound storage and retrieval system” in order to allow for the efficient cherry-picking of compounds, it allows “alternative systems” which will accomplish the same objectives, as above.

The proposed storage and retrieval system should be one that meets the basic contract needs in this area, while also meeting the stated goals and objectives of the contract. The Government will evaluate the suitability of the proposed system under Evaluation Criteria 3. FACILITIES AND MANAGEMENT, worth a total of 20 Points (see p. 25 in the RFP).

The estimated requirement for Periods 1 and 2 of the contract would be a suitable system that could store and retrieve a collection of approximately 100,00-250,000 compounds by the end of Period 2 (or September 2005). As the small molecule collection grows, it will of course require additional space and equipment. Since we don't know exactly how quickly compounds will be acquired, it is important that offerors have some flexibility in providing for the actual storage and retrieval needs.

Offerors should be aware that this is a competitive acquisition, and award will be based upon the best value to the Government. While technical merit is paramount, cost and past performance is also considered. Total proposed cost is always a consideration in the selection of a Contractor for award. If, for example, two or more offerors are considered essentially technically equal, then cost will become a significant evaluation criterion in the selection for award.

***Q.2. Can the contractor lease or purchase equipment from a pharmaceutical or biotechnology company that has an operational repository facility in place?***

**A.2.** Yes, the Contractor can propose lease or purchase of equipment from a pharmaceutical or biotechnology company. However, it should be demonstrated that any equipment which is not housed at the Contractor's location can be accessed and is available to the Contractor, and that the necessary logistics have been arranged.

#### **Task 1. Compound Identification and Acquisition**

***Q.3. What percentage of this 1 million collection would you expect from academic sources, industry and commercial suppliers, respectively?***

**A.3.** It is impossible to anticipate specifically who the suppliers will be and what portion each type would supply. We anticipate that all these sources will be used.

***Q.4. Are there currently identified sources of compounds from which samples will be obtained? If so, what portion of the one million samples does the government anticipate will come from known sources? For what portion will the contractor first have to identify potential suppliers and work with suppliers on establishing a means for receiving compound information in a standardized format?***

**A.4.** While the contractor is expected to serve as a resource for identifying potential suppliers, they will not be the sole source of this information. A notice will be placed in the NIH Guide, and the program will be advertised in various other settings, seeking interested suppliers. The external scientific review group is also expected to identify sources of compounds. It is likely that some work will need to be done establishing a means for receiving compound information in a standardized format from the majority of suppliers.

***Q.5. What portion of compounds does the government anticipate will be purchased and what portion donated?***

**A.5.** In the initial stages of the contract, we anticipate that the majority of compounds will be acquired through direct purchase.

**Q.6. *Could you tell us how the funds for direct compound acquisition (\$1.4M in Period 1 and \$3M in each 12-month period thereafter) were calculated? For example, does it imply that each compound (including acquisition and replenishing) will cost \$13.4?***

**A.6.** The total funds set-aside for purchases was a rough estimate of funds required to acquire a library of up to 1,000,000 compounds, and may or may not be representative of the actual costs during the contract. Since at this time we don't know specifically what compounds will be acquired (and the source of these compounds), it is of course very difficult to estimate costs. It is also unknown what portion of the library will be donated or come from Government sources. The cost for each particular compound is anticipated to vary highly depending on the type of compound, the source, the amount to be acquired, purity, etc. In addition, our estimation of the size of this collection (1,000,000 compounds) is an objective, and not a certainty.

**Q.7. *Would nonprofits such as the Centers of Excellence in Chemical Methodologies and Library Development be expected to supply compounds at a significant discount to the \$13.4/compound rate?***

**A.7.** As stated, we expect to acquire compounds at widely variable costs. In general, we would expect compound acquisition costs from a non-profit organization supplying compounds to be more representative of their type of organization (i.e. a pass-through cost) as opposed to similar acquisition costs from a commercial organization.

**Q.8. *Would there be an opportunity for the Contractor to supply a portion of this repository? If so, is the cost supposed to be the same as compounds purchased directly from a commercial supplier?***

**A.8.** Yes, the Contractor will be afforded the opportunity to supply compounds, and as is the case for all suppliers, will be encouraged to provide these at a "discounted" price.

**Q.9. *If the Contractor has protocols ready for value-added compounds but needs to re-synthesize them to meet the requirement for quantities, can they be included in the collection? If so, is the Contractor supposed to calculate the cost of supplying these compounds or supposed to go with the \$13.4 per compound estimate?***

**A.9.** For the most part, compounds must be currently available to be offered for potential inclusion in the collection. If a compound supplier believes that certain compounds would be valuable additions to the collection they may offer them for evaluation by the panel; but if selected for inclusion, compound suppliers must make them physically available before they will be purchased under the contract. Synthesis efforts under the contract are only intended to be for the purpose of replenishment of depleted compounds.

## **Task 2. Arrayed Sets and Distribution**

**Q.10. *How many mother and daughter plates does the government anticipate creating for each plate array? Will the replicates be limited to the 7-10 research sites/ screening centers or will more be required?***

**A.10.** The volume of plates to be created and shipped is difficult to estimate at this time, as the number of screening centers and their capacities, or the volume of external requests for subsets of the library, known at this time. We anticipate that each of the 7-10 screening centers will be receiving the equivalent of two complete sets of the library per year.

We expect that compound plates sent to the screening centers will contain a sufficient amount of compound per well for the creation of enough screening plates to run 2-3 assays, each requiring approximately anywhere between one (1) nano-liter and one (1) micro-liter of compound, though this will be dependent on the type of assay being run.

The quantity of compound per plate may also vary depending on the type of compound (i.e. different amounts for plates of natural products). We expect that the number of plates shipped in response to external requests will be similar to the number of plates sent to the screening centers, though at this point we cannot provide an estimate of the quantity of compound per well to be provided to external requestors, nor have we determined whether compounds would be distributed dry or in solvent. Volume is dependent on many factors and may change over contract period.

**Q.11.** We would like to better understand the boundaries of throughput requirements.

*Since the Contractor is supposed to supply the 7-10 HTS Centers on a weekly basis without charging extras, how many plates and how much quantity of each compound in a plate shall we assume per week for estimating the costs?*

**A.11.** See above answer to Q. 10.

**Q.12.** *Section B-Task 2: How many replicates of 96 and 384 well plates do you envisage requiring initially?*

**A.12.** See above answer to Q. 10.

**Q.13.** *What is the expected number of shipments and the expected number of plates to be shipped per period?*

**A.13.** See above answer to Q. 10.

**Q.14.** *What assumptions should we use on plate formats? What percentage of plates sent out will be on 96-well, 384-well, 1536-well, or even 3456-well plates? Will all wells be filled or will one or more rows of wells be left open on plates for use of standards and/or blanks?*

**A.14.** It is anticipated that for the most part compounds will be sent in 96 or 384 well plate format. We expect that the plates sent to the screening centers will contain a sufficient amount of compound to be used for a number of screens and that the screening plates will be created by the screening centers themselves. Typically plates should include rows left open for standards or blanks.

**Q.15.** *Would the Contractor be expected to supply customer-specified quantities of compounds in customer-specified plate types, or could there be a limited number of formats?*

**A.15.** A limited number of formats will be provided to extramural customers. Screening centers will generally use standard compound plates, but may require additional specialized plates containing additional quantities of compounds found to be hits in an assay.

**Q.16.** *Does the NIMH have a strong preference in the types of plates and vials utilized?*

**A.16.** There is no specific preference for types of plates or vials utilized. Compound plates must be capable of being utilized by standard equipment used for high-throughput screening.

**Q.17.** *According to Page 8 of 36 under Task 2, the Contractor is supposed to provide to other interested HTS facilities and extramural investigators on a fee for service basis, at a cost of \$3-4 per compound (i.e. per well). How much quantity of each compound is expected?*

**A.17.** At this point we cannot provide an estimate of the quantity of compound to be provided to extramural requestors (nor have we determined whether compounds would be distributed dry or in solvent). We are seeking input from the field as to what would best meet the needs of the potential users of this service.

**Q.18.** *Do you envision that plate shipment to the screening centers will be provided in DMSO on wet ice, dry ice or neat?*

**A.18.** We expect that, for the most part, shipment would be provided in DMSO on dry ice.

**Q.19.** *What volumes are anticipated for the microtubes and microtiter plate?*

**A.19.** Volumes in tubes and plates for long-term storage have not been specified as this is dependent on currently unknown variables, including storage conditions, compound stability, and rate of consumption. Offerors may make recommendations for volume based on their expertise and past experience in this area.

**Q.20.** There have been a number of questions received about *access* to compounds in the library, and if the degree of access might be influenced by the offeror's status regarding their type of organization (e.g., profit or nonprofit, etc.) or whether the organization has supplied compounds themselves or not.

*What is the policy on access to compounds?*

**A.20.** The Government has not yet finalized a policy on the issue of access to the compound library. However, it is likely that all requests will not be considered as *equal* in priority during the contract, and that compounds will be distributed in accordance with a Government-assigned priority status.

The degree of access to compounds shall be determined based upon overall demand, priority given to the request, and contract resources. If demand for compounds exceeds the supply, contract resources needed to re-supply will be too high, and the Government shall limit the distribution in a manner it sees fit. Regarding the priority of a request, in general academic investigators *may* receive higher priority status than commercial investigators, and those who deposit compounds in the repository *may* be given a higher priority access than non-suppliers, at the discretion of the Government.

Also, it is important to note that an offer to supply the repository as part of your proposal to the Government is not part of the review criteria in the solicitation and as such cannot be considered in the scoring and evaluation of a proposal. Therefore, we are neither encouraging nor discouraging this. Offers to supply the repository in return for a higher priority access status cannot be accepted by the Government as a *condition* of the award; if you are awarded a contract and wish to supply the repository, we will discuss access issues after award; but again access to compounds will in part be dependant upon the overall demand, which cannot be determined at this time.

It is important to note that not all compounds *offered* may be *accepted* for inclusion in the library. The final decision on this will be made by the government and based on scientific review of the compounds and whether or not it is believed they will enhance the overall collection.

**Q.21.** Reference Page 5, Objectives section states, " The objectives of the contract are: ... (3) to distribute arrays to the Molecular Libraries Screening Centers, and to other interested HTS facilities..." Also, page 8, Task 2. Arrayed Sets and Distribution states, "Compound arrays shall also be provided to other interested HTS facilities and to extramural investigators on a fee for service basis, as a cost of approximately \$3-4 per compound (i.e. per well)."

***Are for-profit organizations in private industry( e.g. pharmaceutical and biotechnology companies), included as "interested HTS facilities" and "extramural investigators", and will they have access to the compound library? If so, will the same cost structure, i.e. \$3-4 per well, fee for purchase, be applied?***

**A.21.** Yes, for-profit organizations such as pharmaceutical and biotechnology companies may have access to the repository library, based upon the access policy, overall demand for compounds, and the priority established by the Government for each particular request. However, the Government reserves the right to establish a potentially higher price structure for these types of organizations.

**Q.22.** *Is it expected that a cost of \$3-4 per well is a break-even cost for the storage and distribution of compounds to potential customers? Can any potential direct cost "profit" be applied towards reagents, equipment and lab ware costs?*

**A.22.** This represents a nominal amount and in our experience it may or may not cover the actual costs. All *income* generated by distribution of compounds to outside investigators will be applied as a "credit" on invoices submitted to the Government under the contract; therefore indirectly this income will offset and make available more funds to be utilized under the contract.

### **Task 3. Storage and Quality Control**

**Q.23.** Section B-Task 3: *When talking about inert atmosphere storage, are compounds sealed under inert atmosphere but stored in an air environment, or sealed and stored under inert atmosphere? Please provide clarification to this language.*

**A.23.** When discussing inert atmosphere storage we were referring to compounds sealed under inert atmosphere, but stored in an air environment.

**Q.24.** *Since reweighing compounds takes much more time than simply checking compounds in, it is important to know the condition of incoming compounds. For purposes of assumption, what portion of compounds might we anticipate receiving pre-weighed and pre-labeled in a standard-sized vial? What portion of compounds will be received in non-standard vials that will have to be reweighed?*

**A.24.** For at least the 1st several contract periods, we anticipate that the majority of compounds acquired for the repository will be through direct purchase, and that for the most part these purchased compounds will be received pre-weighed in standard-sized vials. The remaining compounds are likely to be acquired through other means, such as donation, and may require re-weighing and packaging, though efforts will be made to ensure that compounds sent in for inclusion in the repository will be in a standard, pre-weighed format.

**Q.25.** *Does the government anticipate receiving any samples from existing plated inventories (i.e., already solubilized and plated)? If so, what percentage of compounds would they anticipate receiving in this format?*

**A.25.** While our preference is for compounds in powder form, it is likely that some of the samples acquired will be from existing plated inventories. The percentage of compounds that will be acquired in this format is unknown at this time.

#### **Task 4. Re-Supply and Re-Synthesis**

**Q.26.** *If a HTS center finds a hit, how much of that compound is the Contractor expected to re-supply? We are trying to understand how frequently the Contractor needs to replenish each compound to get a better estimate of cost.*

**A.26.** Screening centers would generally need to be re-supplied with a sufficient amount of compound to do some basic secondary screening, such as a dose-response curve, negative controls, and possibly a limited counter-screen at related targets. On average, we estimate that this would be approximately 1-5mg, though this would vary depending upon the assay involved.

#### **Task 5. Informatics**

**Q.27.** *According to page 13 of 36 under Schedule of Work, the Contractor is supposed to set up from scratch the website and database and start to distribute the compounds in the first 4 months (Period 1). Considering that the SRC needs to review and prioritize compounds and it takes time to set up a new informatics infrastructure, we would like to better understand if this expectation of schedule could be more flexible.*

**A.27.** The schedule given in the RFP is flexible. It is unclear at this point how much compound distribution will be required in the early phase of the project, as this is dependent on the number of extramural requests received, the readiness of the first of the ML screening centers, and the rate of compound acquisition under the contract.

**Q.28.** *Does NIMH already know required fields and field types for the database (e.g. GUI strings preferences, barcode preferences etc, variable, numeric and fixed text preferences...)?*

**A.28.** Specific information on required fields and field types is not known at this time. It is likely that much of this will be open to suggestions by the contractor. For the most part sample tracking information will be primarily for internal use only by the repository, though some aspects of the database will need to be interfaced with the Molecular Libraries public database, PubChem. There are some important requirements with respect to how the repository should exchange chemical structure data with PubChem. These requirements include:

- The repository will assign unique, stable identifiers of their own design to each chemical sample as it is received from a vendor or other source. These will be included in PubChem depositions as a means to distinguish new samples from old samples with updated descriptions.

- The repository will submit chemical structure information for all samples to PubChem, making periodic depositions as new samples are obtained or chemical structure or description fields updated. Depositions will be in one or more standard exchange formats, e.g. SD files, as specified by PubChem.

- The repository will record PubChem-assigned accession codes for each sample and include this information in all sample descriptions provided to screening centers or other users. These accession codes will allow users to refer to chemical structure information stored centrally in PubChem.

### **Other Miscellaneous Questions**

**Q.29.** *Will the NIH expect or request later stage licensing, royalties or milestone payments resulting from positive biological screening results? What is the IP ownership for positive screening results? Q. Will for-profit organizations be expected to submit screening results back to the NIH?*

**A.29.** This issue is being discussed but a final policy has not been established. NIH is not anticipating requesting later stage licensing, royalties, or milestone payments from positive screening results. For non-proprietary compounds used, IP ownership of positive screening results will reside with the investigator who conducted the screen. Though we encourage the submission of screening results by all investigators making use of repository compounds, it has not yet been fully determined what the requirements, if any, for submitting screening results back to NIH will be.

**Q.30.** *Is there a cost reimbursement to organizations, for-profit and not-for-profit, that provides compounds, equipment, software, "know-how" or IP, to the Repository?*

**A.30.** This subject can be discussed during negotiations. As already stated above, all suppliers will be paid for their compounds (unless they are donated) at prices determined to be fair and reasonable. If it is agreed that the Government will reimburse the Contractor for certain costs, (e.g., equipment, software, etc.), they will be reimbursed through the Contractor's invoices, and in accordance with the contract terms. A position on IP issues has not been reached.

**Q.31.** *According to page 10 of 36, all databases/websites developed with contract funds will be the property of the Federal government. Is it possible for the Contractor to spend its own money to set up a duplicate of the Small Molecule Repository infrastructure for its own use, including purchasing some of the same compounds as the Small Molecule Repository?*

**A.31.** Contractors are free to use their own funds in this manner if they so choose. However, any proprietary compounds or data provided to the program could not be used for any activities outside of the contract, unless the contractor sought and obtained permission for such use from the provider.

**[End of Amendment 01]**