RFI for cGMP Endotoxin – April 8, 2009

General Information:

This Sources Sought Notice (SS) is for information and planning purposes only and shall not be construed as a solicitation or as an obligation on the part of SAIC-Frederick, Inc. (SAIC-F) or the National Cancer Institute at Frederick (NCI-F). SAIC-F does not intend to award a contract on the basis of responses to this Sources Sought Notice, nor otherwise pay for the preparation of any information submitted. As a result of this Sources Sought Notice, SAIC-F may issue a Request for Proposal (RFP) in the future. THERE IS NO SOLICITATION SCHEDULED AT THIS TIME. However, should such a requirement materialize, no basis for claims against SAIC-F shall arise as a result of a response to this Sources Sought Notice or the SAIC-F's use of such information as either part of our evaluation process or in developing specifications for any subsequent requirement. Any questions concerning this solicitation must be directed through the SAIC-F Point Of Contact (SAIC-F POC).

RFI Number: S09-135

Posted Date: April 8, 2009

Intended Offeror's Response Date: May 1, 2009 by 4:00PM Eastern
Final day to submit questions: June 5, 2009 by 12 Noon Eastern
Final Response Date: June 30, 2009 by 3:00PM Eastern

Contracting office address: SAIC-Frederick, Inc.
92 Thomas Johnson Drive, Suite 250
Frederick, MD 21702-1201

Purpose of RFI:

SAIC-F is to seeking to identify a qualified contract research organization that is able to economically produce a new batch of clinical grade bulk endotoxin that is compliant with current Good Manufacturing Practices to replace the > 30 year old bulk endotoxin currently in storage. PLEASE NOTE: An appropriate strain of E. coli would be required to be acquired by any potential Subcontractor should a Request for Proposal (RFP) and subsequent Subcontracting Agreement be offered to a selected offeror.

Project Goal:

The goal included in this statement of work is to produce a new batch of clinical grade bulk endotoxin that is compliant with current Good Manufacturing Practices to replace the > 30 year old bulk endotoxin currently in storage. This project will be broken down into a Development Section, including MCB production, and purification process development. An engineering run of bulk endotoxin along with a pilot lyophilization

study. The final stage includes cGMP Production; including GMP bulk endotoxin manufacture and GMP vialing and lyophilization plus a manufacturing report.

Anticipated Milestones and Deliverables:

Milestone 1 – Activity A: Production and characterization of a 200 vial Master Cell Bank.

The previous cGMP endotoxin was produced from the Escherichia coli (Braude strain) group O 113:H10:K negative strain that was isolated and characterized at the Bacteriology Division, Bureau of Laboratories, Center for Disease Control, Atlanta, Georgia (Ewing WH, Hucks MC, and Taylor MW (1952) J Bacteriology 63: 319-325). The BDP will contact Dr. Epstein to determine if this bacterial strain is available from the NIH Clinical Center, the FDA, or the CDC.

The potential Subcontractor will obtain the appropriate strain of E. coli and then manufacture and characterize the 200 vial MCB according to current standards. The potential Subcontractor will provide a list of tests to be performed. SAIC-F may provide the potential Subcontractor a source of the required strain if necessary.

Milestone 1 – Activity B: Purification Development.

R&D grade E. coli cultures will be produced using the previously recommended chemically defined media and conditions. These cultures will be produced in the potential Subcontractor's laboratories using standard R&D procedures and it is expected that this process will require minimal development work.

The resulting cell pellets will be used for purification development following the previous purification process used > 30 years ago. The potential Subcontractor will provide a proposal for process modification (if any) to meet the required scale, cGMP compliance, and product quality. Such studies may include:

1. A 10 liter culture will be produced and subjected to phenol extraction to produce a single unpurified bulk that can be used for purification development studies.
2. Tests to replace a dialysis step with transmembrane flow filtration (TFF).
3. Determine whether the deoxyribonuclease digestion can be replaced with Benzonase digestion.
4. Testing chromatography as a replacement for the sodium acetate/ethanol concentration step.
5. Determine whether the final dialysis step can be replaced with TFF.

Milestone 1 – Activity C: R&D Assay Development.

The potential Subcontractor will identify any method development necessary to perform the required release testing for the bulk and final vialed product shown in Tables 1 and 2.

SPECIAL NOTE: SAIC-F, with the NCI, will contact the US FDA for review of the proposed methods of analysis and specifications prior to initiation of the cGMP phase of

the program. The results of that future discussion will be shared with the potential Subcontractor.

Milestone 2: Engineering Run/Pilot Lyophilization

The potential Subcontractor's laboratories will be used to perform a cGMP pilot run. A full scale production and purification will be performed to test the process and produce bulk drug substance. This drug substance will be used as an internal reference standard for the following studies:

1. QC assay development.
2. QC testing for comparability to previous endotoxin CC-RE-Lot3.
3. Drug Substance stability studies.

The potential Subcontractor may perform any or all of these studies. The potential Subcontractor will also perform pilot formulation and lyophilization studies based on requirements to produce final vialed product listed in Table 3.

Milestones 3 &4: Production of cGMP Endotoxin

The potential Subcontractor will perform a full scale production and purification to produce cGMP grade endotoxin including the following activities:

1. Controlled fermentation will be conducted in a batch mode.
2. Purification will be performed to produce bulk drug substance.
3. QC/QA release of the drug substance.
4. Formulation, vialing, and labeling of endotoxin drug product (FVP).
5. QC/QA release of the FVP.
6. Stability program for FVP and, if required, bulk biological substance
7. Preparation of a Manufacturing Report (Appendix 1) to be included in submissions to the US FDA with authorization to cross-reference any required potential Subcontractor submissions to enable full review of the manufacturing and testing documents by the US FDA for IND studies.

Table 1: Methods of Analysis and Specification for Bulk Biological Substance

Method	Product Specification
Kinetic – QCL Potency Assay (EU/mL) [3]	NLT 50,000 EU/mL
Gel Clot Potency Assay (EU/mL) [3]	NLT 50,000 EU/mL
Sterility[1]	Negative per 21CFR610.12
Residual host cell protein	For Information Only
Residual host DNA	For Information Only
Residual phenol[2]	For Information Only
Mass spectrometry; method to be proposed by Contractor	For Information Only
Polysaccharide characterization; method to be proposed by Contractor	For Information Only

[1] Bacteriostasis & fungistatsis analysis to be performed on representative sample

[2] Additional residuals analysis may be required based on the potential process-related contaminants.

[3] Stability indicating assay

Table 2: Methods of Analysis and Specification for Final Vialed Product

Method	Product Specification
Kinetic – QCL Potency Assay (EU/vial)	5,000 – 15,000 EU
Gel Clot Potency Assay (EU/vial)	5,000 – 15,000 EU
Sterility	Negative per 21CFR610.12 & cUSP
Residual moisture	<=3.0%

Note: All methods are stability indicating assays

Table 3: Required Deliverables for Milestone 3 & Milestone 4

CGMP Production Stage	Minimum Quantity	Configuration
Final Bulk Biological Substance	1.25×10^8 EU from 62.5 liters	Final buffer is 1% lactose, 0.1% PEG-6000 to be bulk filled into sterile glass 10L bottles (8 L per bottle) and stored at 2-8^{o}C
Final Vialed Product, Lyophilized	10,000 vials, net stability and release sampling; 2,000 EU/mL when reconstituted with 5 mL Water-For-Injection (WFI)	10,000 EU per vial in Type II borosilicate glass vials with 20mm stoppers and 20 mm West Aluminum seals. Sterile, single use vials stored at 2-8^{o}C

Project Management:

The potential Subcontractor will describe the facilities to be used to perform the Statement of Work and will provide a program management plan that includes the structure for project management, frequency and content of project status communications and the contents of financial and technical reports. SAIC-F will require technical reports for each completed development study and manufacturing activity (e.g., MCB production, bulk biological substance production) and will require monthly financial status reports of technical progress and budget expenditures. The potential Subcontractor will provide a program schedule and budget that clearly delineates each program milestone by schedule and cost. SAIC-F will require review of program deliverables from each milestone prior to authorization to proceed with the next scheduled milestone.

Quality Systems and cGMP Compliance:

The potential Subcontractor will be responsible for compliance with all local, state and federal regulatory statutes. For specific cGMP compliance, the potential Subcontractor will be required to enter into a Quality Agreement with SAIC-F.

Offeror Instructions:

1) Any potential Offeror who desires to respond to this RFI, must submit their intention to the SAIC-F POC below via email NO LATER THAN June 30, 2009 at 3:00 PM Eastern Standard Time.

2) Offerors must submit a capability statement describing their organization's experience and abilities to further develop the proposed material as described which includes: (a) the professional qualifications, experience, and listing of key staff who may be assigned in the developing/manufacturing of the prototype (CV's are to be provided); (b) listing of any/all current and relevant certifications from a qualified neutral third-party and contact information; (c) a description of the facilities and other resources available to develop/manufacture the material; (d) an estimate cost broken down in a time and material (T&M) format; (e) an estimated project schedule; and (f) detailed project management plan.

   The final response should include the following Business Information in addition to the capability statement:

   A. RFI Number
   B. DUNS number
   C. Company Name
   D. Company Address
   E. Company Point of Contacts, Phone, FAX, and Email Address. POC's should include individual(s) who is(are) duly authorized in managing any/all technical issues and/or questions, and individual(s) who is(are) authorized in managing any/all contractual issues and/or questions.
   F. Type of Company (i.e. small business, large business, educational institution, etc.)

3) The final date to submit questions for this RFI is 12 noon EDT, June 5, 2009.
4) The last date to submit final responses to this RFI is 3:00PM EDT, June 30, 2009.

Point of Contact

Primary:
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