

July 30, 2004



Request for Proposals

Facilities for Chemical Optimization and Synthesis of Small Molecules for
the SMA Project

RFP No: JL-19704-3

In support of:

**The National Institute of Neurological Disorders and Stroke (NINDS)
The SMA Project: A Collaborative Program to Accelerate Therapeutics
Development for Spinal Muscular Atrophy**



*An SAIC-managed program to support the NINDS, National Institutes of Health,
Department of Health and Human Services*

SAIC Prime Contract No.: N01-NS-3-2356



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1. Introduction

The [National Institute of Neurological Disorders and Stroke](http://www.ninds.nih.gov) (NINDS) launched The SMA Project: A Collaborative Program to Accelerate Therapeutics Development for Spinal Muscular Atrophy (SMA) in September 2003. The program aims to identify and rapidly develop a treatment for SMA, a paralyzing neurodegenerative disease of childhood. More information about the program can be found at <http://www.SMAProject.org>.

The purpose of this solicitation is to identify a facility or facilities to (1) conduct chemical optimization of lead compounds for SMA through medicinal chemistry and/or (2) provide larger-scale (multi-gram) synthesis services for promising compounds. Offerors may submit proposals to support either or both of these services.

1.1 Spinal Muscular Atrophy and the SMA Project

SMA is an autosomal recessive neuromuscular disease with variable severity ranging from limited motor neuron loss and normal life expectancy (type III) to progressive infantile paralysis and death (type I). All forms of SMA are caused by loss of function of the survival motor neuron 1 gene (*SMN1*). Reduced levels of SMN protein result in the specific death of motor neurons but not of other cell types in which the gene is normally expressed. *SMN2*, a nearly identical gene, is present in variable copy numbers and produces low levels of full-length SMN protein. SMA disease severity inversely correlates with the number of copies of *SMN2*; patients with higher *SMN2* copy numbers have a less severe form of the disease than patients with a low copy number. This suggests that therapeutic strategies to increase the level of *SMN2* produced in motor neurons may compensate for loss of *SMN1* and result in an improved clinical outcome for SMA patients.

The *SMN2* gene differs from *SMN1* by a single nucleotide polymorphism. This sequence change causes alternative splicing so that *SMN2* produces two different transcripts. These transcripts differ by the presence or absence of exon 7 and only a fraction of the transcripts produced by the *SMN2* gene are full length. Thus, an increase in the level of full-length *SMN* may be achieved either by increasing *SMN2* promoter activity or by influencing alternative splicing to produce a higher fraction of full-length transcripts.

A number of small molecules have been identified that increase *SMN2* expression in cell culture, including phenylbutyrate, valproic acid, and aclarubicin. These appear to act by increasing *SMN2* promoter activity and/or altering the splicing of *SMN2* message, which leads to increased levels of full-length *SMN2* RNA. To maximize the chances that members of these and other similarly active compound classes might improve the condition of SMA patients, the SMA Project will undertake to further develop and optimize such compounds for clinical testing.

The SMA Project is establishing a Lead Development Team that will identify candidate compounds for preclinical testing. These compounds may come from small molecule screens conducted by the SMA Project or may be submitted for consideration by the research community. Through service contracts,¹ the SMA Project seeks to establish the necessary services for the Lead Development Team to identify the most favorable compounds, direct their chemical optimization, and determine their potential for treatment of SMA (**Figure 1**). Three types of contract facilities will conduct (1) medicinal chemistry optimization through synthesis of small molecule analogs of active compounds (this RFP), (2) testing of the bioactivity of compounds in a battery of in vitro assays relevant to SMA, and (3) determination of the efficacy of compounds in in vivo mouse models of SMA. (Copies of SMA Project Solicitations for the

¹ Awards will be made in the form of contracts. SMA Project contracts will be "subcontracts" to SAIC to support the NINDS. However, for simplicity, in this RFP, the term "Contractor" is used to refer to an organization that will serve as an SMA Project Chemical Optimization/Synthesis facility; the term "Subcontractor" refers to any organization that reports directly to the organization that is serving as the SMA Project Chemical Optimization/Synthesis facility.

mouse testing facility and the in vitro testing facility, as well as previous RFPs, are available on the SMA Project website, <http://www.SMAProject.org>.)

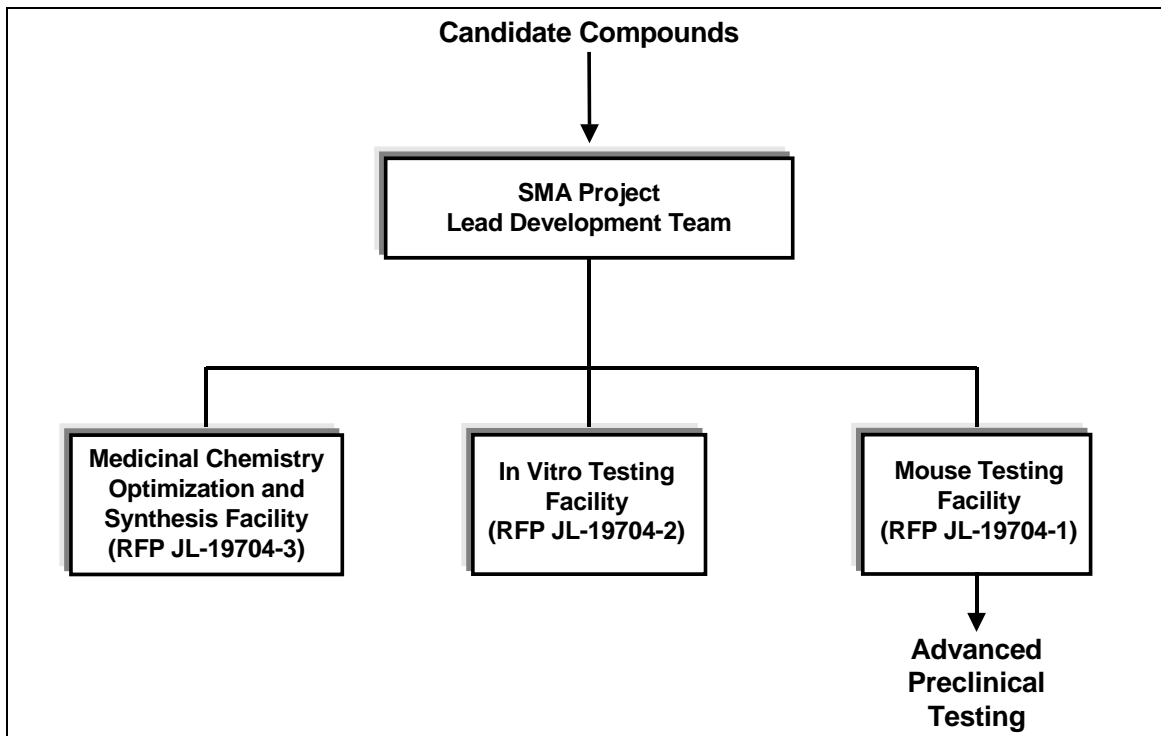


Figure 1 – Developmental Overview for the SMA Project

This RFP is intended to identify a facility or facilities for collaborative design, synthesis, and characterization of small molecule compounds. These resources will be critical components of the SMA Project effort to identify and optimize candidate compounds for clinical testing.

1.2 Schedule for This Solicitation

Key dates related to this RFP are as follows:

- Offeror's² Intent to Submit Due September 3, 2004
- Proposals Due September 10, 2004
- Review of Proposals and Supporting Documentation ~October 8, 2004
- Initiation of Negotiations ~November 22, 2004
- Anticipated Start Date ~December 22, 2004
- Notification of Unsuccessful Offerors ~January 22, 2005
- Anticipated End Date ~September 1, 2007

2. Focus of This Solicitation

Proposals are requested for a service facility or facilities with capabilities for (1) designing and preparing appropriate test molecules for chemical optimization of lead compounds through medicinal chemistry (Section 2.1) and/or (2) synthesizing larger scale quantities of small molecules (Section 2.2) that are required for the preclinical development of candidate compounds for SMA. Additionally, Offerors proposing to perform at least one of the aforementioned services can apply for an optional task to provide radiolabeled chemicals for

² "Offerors" are the institutional entities that respond to an RFP.

use in biodistribution assays (Section 2.3). The following sections (2.1-2.3) describe components of the statement of work and capabilities of the Offerors and for performance of this contract.

Offerors should note that the SMA Project may make more than one award (i.e., Contract) for a chemical optimization and synthesis facility. In addition, the SMA Project may make separate awards for chemical optimization and synthesis services. To be considered for an award, each Offeror (inclusive of any proposed subcontractors) must provide the complete range of chemical optimization services required under Section 2.1, or the complete range of synthesis services required under Section 2.2. Offerors may respond to both requirements if they are able to supply the complete range of services for both chemical optimization and synthesis.

All Offerors will be required to submit a proposal demonstrating that they have capabilities in the required critical methodologies, appropriate equipment, and experience in collaborating and conducting work on similar types of projects. The SMA Project has not yet identified the specific small molecules that will be chemically modified or synthesized under this contract. Therefore, a sample task for developing a chemical optimization scheme (see Section 2.1.2) is being used to guide Offerors who are submitting a proposal to conduct chemical optimization services in the structuring of their proposals and to assist reviewers in their assessment of technical merit.

Successful Offerors (i.e., Contractors) will be participants in the SMA Project's iterative process for developing small molecule therapeutics (**Figure 2**). This process will require frequent communication and collaboration between the different contract facilities to ensure that materials and data are transferred efficiently, thereby avoiding unnecessary delays in the overall process. Therefore, Offerors must also demonstrate that they have a successful history of efficient data and material exchange with outside facilities.

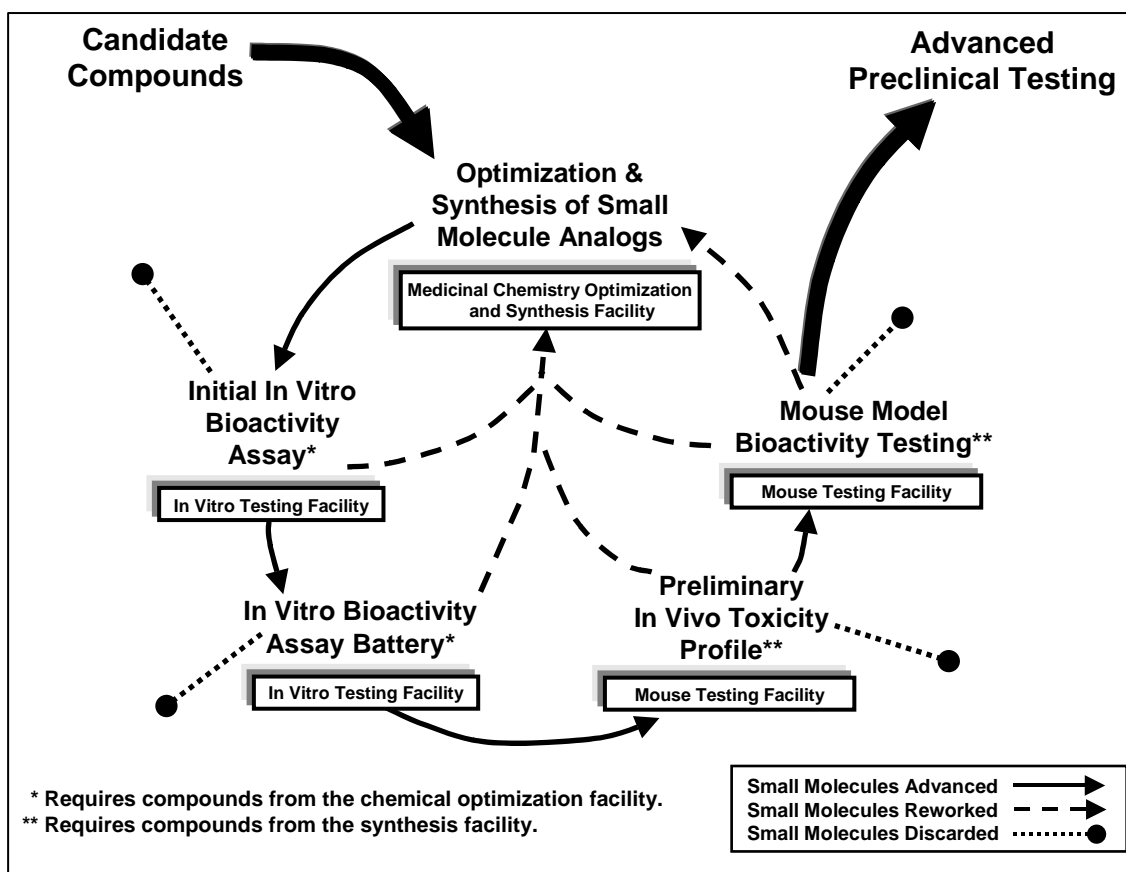


Figure 2 – Flow Plan for Development of SMA Project Small Molecule Therapeutics.

Efficient time lines are critical to the success of the SMA Project's accelerated program for therapeutics development. In preparing time lines for proposals, Offerors should note at what stage(s) their proposed services/products would be required in the SMA Project's Flow Plan (Figure 2). Of note, the end date for all facility contracts will be ~September 1, 2007.

2.1 Chemical Optimization of Lead Compounds for SMA

Under the direction of the SMA Project Lead Development Team, the Contractor shall produce, through medicinal chemistry and/or commercial acquisition, chemical analogs of small molecules (milligram quantities) with the potential for treating SMA. The Contractor shall supply these chemical analogs to an SMA Project in vitro testing facility for evaluation in a battery of biological assays relevant to SMA. The production and testing of chemical analog compounds will be an iterative process, with the goal of optimizing the bioactivity and pharmaceutical suitability of lead compounds (Figure 2). The SMA Project Lead Development Team will manage and guide this process; however, the Contractor is expected to significantly contribute to the successful improvement of compound activity through creative intellectual input into the molecule design as well as the design and execution of synthetic strategies.

2.1.1 Offerors' Capabilities

Offerors who are submitting a proposal to conduct chemical optimization services must demonstrate a successful track record at:

- Developing and implementing creative and successful strategies to chemically optimize the biological properties of small molecules.
- Based on multi-dimensional similarity to hit or lead compounds, identifying and acquiring chemical analogs likely to have increased potency and reduced toxicity from reliable commercial sources.
- Confirming the identity and assessing the purity of synthesized compounds through analytical techniques that include the usual spectroscopic and chromatographic technologies.

Offerors must demonstrate that they have experience in collaborating with investigators from other institutions, including the ability to ship compounds reliably, use data from a variety of bioassays to design a medicinal chemistry strategy, and accurately conduct frequent data exchanges, preferably in electronic format.

For the purposes of preparing a proposal and demonstrating relevant experience, the Offeror should assume a requirement to undertake chemical optimization efforts on as many as three different lead structures per year. These will be iterative projects requiring chemists skilled in the development of structure activity relationships (SAR).

2.1.2 Sample Task: Developing a Chemical Optimization Scheme

Identification of specific compounds to be developed and synthesized under the contract will not be made prior to award. Therefore, Offerors who are submitting a proposal to conduct chemical optimization services must submit technical proposals for the sample task outlined in this section, which will be used to gauge their capability to perform similar work. An award that is based upon a proposed sample task does not guarantee that the specific task will be funded. (See Section 8.1 for information on how tasks will be funded post-award for successful offerors.)

To demonstrate the high-level, creative medicinal chemistry expertise required by this RFP, please describe two sample chemical optimization schemes: one scheme for developing a lead optimization effort based upon phenylbutyrate, a drug approved for use in urea cycle disorders, and one scheme for developing a lead optimization effort based upon aclarubicin, a drug with a

history as an anti-cancer agent. Both of these compounds have been found to have bioactivity in in vitro models of SMA.

Data on which to base the SAR analysis will come from:

- Drug-likeness of the compounds based on observed and calculated chemical properties, such as the Lipinski rule of 5.
- Pharmaceutical suitability of the compounds based on in vitro tests such as microsomal oxidation data, serum protein binding, etc.
- Bioactivity of the compounds in in vitro assays relevant to SMA, such as effects on expression or splicing of *SMN2*.

The SMA Project in vitro testing facility will provide in vitro data on prepared compounds and these data will guide the development of the SAR. The majority of the assays will involve cultured cells and will be amenable to 96 well or higher density format, requiring milligram quantities of 90% or greater purity compounds. For proposal preparation purposes, the Contractor can expect to receive the results of in vitro testing of new compounds within one week of sending the compounds for analysis.

Offerors may use traditional medicinal chemistry approaches and/or parallel medicinal chemistry approaches, but the strategy guiding the SAR should be clearly described in the proposal. The assessment of drug likeness of the compounds produced will be the responsibility of the Medicinal Chemistry Contractor, and Offerors should propose how this will be assessed.

2.2 Compound Synthesis of Small Molecules for In Vivo Testing

Through testing to be conducted at the SMA Project in vitro testing facility, the Lead Development Team will identify specific compounds for larger scale synthesis that will ultimately be used in in vivo studies (see Figure 2).

The Contractor shall produce multigram quantities of non-Good Manufacturing Process (cGMP)-grade compound that is selected for in vivo testing at a scale and purity necessary for: (1) preliminary preclinical pharmacokinetic and toxicity testing necessary to justify and develop treatment protocols in mice and (2) efficacy studies in at least two mouse models of SMA requiring compound administration for periods as long as 3 months. Although the scale of this work will, of course, depend on the success of the SMA Project chemical optimization effort, the SMA Project may need as many as 5-10 compounds per year and as much as 50 g of the target compound.

Animal testing of compounds will be conducted at a SMA Project mouse testing facility under a separate contract (see Figures 1 and 2). However, the Contractor shall assist other Contractors in devising appropriate methods for dissolving and administering compounds for in vivo study.

The Contractor shall provide the detailed descriptions of the synthetic schemes to the SMA Project for compounds that will be used in in vivo studies. The description should be sufficiently detailed to allow publication of the results in scientific journals and provide all required information to ensure successful cGMP scale up at another facility.

2.2.1 Offerors' Capabilities

The Offeror must demonstrate a successful track record at producing non-cGMP-grade compounds for in vivo studies. Please describe previous experience with synthesis of compounds of sufficient quantity and purity for animal studies. For the purposes of preparing a proposal for this RFP, please assume that the Contractor will produce approximately 5-10 compounds per year for these preliminary animal studies. Please demonstrate that your facility

has sufficient capacity to meet this goal. Additionally, Offerors are requested to submit cost information about prior similar work (see Section 4.10 for details).

2.3 Optional Service: Radiolabeling Chemicals

Radiolabeled chemicals will be required for performing in vivo biodistribution studies of some compounds. Offerors (inclusive of any proposed subcontractors) with the capability of synthesizing radiolabeled compounds are invited to demonstrate their ability to provide radiolabeled chemicals for use in biodistribution assays.

The SMA Project will not obligate funds to optional components of the work statement. If an option is exercised, it will be at a later date (i.e., not at the time of contract award). Only Offerors with facilities licensed and in good standing with the Nuclear Regulatory Commission (NRC) should respond to this request for optional services.

3. Offerors Provide Information on Intent to Submit

Potential Offerors are strongly encouraged to complete the Intent to Submit form on the [Open Solicitations](#) page of the SMA Project website or to send an e-mail to smaproject-fd@saic.com.

4. Proposal Preparation Procedures

Before preparing a proposal, Offerors should read over this entire document and visit the SMA Project website (<http://www.SMAProject.org>) to learn more about the program and the nature of SMA Project contracts and task orders. Offerors should also review the Subcontract Agreement and the Representations and Certifications document, which are posted on the [Open Solicitations](#) page of the SMA Project website.

NOTE: Unlike previous SMA Project RFPs, there will only be one deadline for Proposals and all Supporting Documentation; pre-proposals will not be accepted or evaluated.

Proposals must contain a response to provide *chemical optimization* and/or *synthesis* services.

To assist Offerors in assembling all the required documents, a Checklist for Submitting a Proposal and Supporting Documentation has been included as Attachment A. *Note:* Items covered in Sections 4.1–4.5, 4.7, and 4.9–4.10 should be copied onto a CD.

4.1 Proposal Face Page

The face page of the proposal must contain the following items:

- Proposal Title
- Name of Offeror Institution
- Principal Investigator's First Name, Middle Initial, Last Name, and Degree(s)
- Principal Investigator's Signature
- Contracting Officer's First Name, Middle Initial, Last Name, and Degree(s)
- Contracting Officer's Signature
- Principal Investigator's Contact Information: mailing address, telephone number, fax number, e-mail address, and, if available, alternate telephone number and e-mail address.
- Contracting Officer's Contact Information: mailing address, telephone number, fax number, e-mail address, and, if available, alternate telephone number and e-mail address.
- The following statement "Response to Facilities for Chemical Optimization and Synthesis of Small Molecules for the SMA Project, JL-19704-3."

- As appropriate, specify whether the proposal is for *chemical optimization* and/or *synthesis* services. Also specify whether the optional task is included.
- The following Statement: “This proposal complies with the Salary Rate Limitation pursuant to P.L. 108-199, and the Offeror certifies that no costs for independent research and development, to include any indirect costs have been claimed under this submission.” (Please note the certification regarding IR&D applies only to commercial institutions. If IR&D costs are a part of your institution’s indirect cost application that portion must be excluded for this proposal.)

4.2 Proposal Executive Summary

One-page limit. The proposal must contain a 1-page Executive Summary that demonstrates an understanding of the objectives/goals to be met, summarizes the Offeror’s capabilities, and includes a summary of their approach for performing the proposed work. The Executive Summary will be forwarded to the SMA Project Steering Committee after review as part of the material that will be used to make a funding recommendation (see also Section 7.5). The format specifications outlined in Section 4.6 are also applicable to this summary.

4.3 Proposal Body

- Offerors proposing to conduct chemical optimization of lead compounds for SMA through medicinal chemistry must follow instructions in Section 4.3.1 (Parts 1 and 2)
- Offerors proposing to provide larger scale (multigram) compound synthesis services of small molecules for promising compounds for use in in vivo testing must follow instructions in Section 4.3.2.
- Offerors who have proposed either of the aforementioned services can also propose radiolabeling services and must follow instructions in Section 4.3.3.

4.3.1 Proposal Body for Chemical Optimization of Lead Compounds for SMA

Part 1: Overall Capabilities

Offerors shall provide a Background Information/Demonstrated Capabilities **no longer than 7 pages in length**, inclusive of any figures, tables, and graphs. This section should demonstrate that the Offeror has a comprehensive understanding of the goals/objectives to be met (as described in Section 2.1) along with a description of the Offeror’s capabilities for meeting them.

The description of capabilities should address experience, facilities, equipment, supplies, special resources, personnel, management structure, and any subcontractor organizations that are being proposed. If any subcontractor organizations are being proposed, it is necessary to include a description of the Offeror’s subcontract management capabilities and a description of each subcontractor’s capabilities for performing any work to which they will be assigned.

The description should include an overall project Management Plan and address the Offeror’s capability to coordinate multiple concurrent tests and scheduling. The Offeror’s intellectual property management plan should be covered in the overall project management plan. The plan should include a proposed monthly reporting plan to concisely summarize overall project efforts.

Part 2: Sample Task

Offerors shall provide an approach to performing the Sample Task summarized in Section 2.1.2 that is no longer than **20 pages**, inclusive of any figures, tables, and graphs. Please note that additional technical information can be included in an appendix to the proposal (see Section 4.5 Appendix: Standard Operating Procedures). If not clearly indicated in the background

information/capabilities section, this section should include where the work will be performed, the personnel who will be performing the work, and unique equipment.

The technical approach should include a demonstration of the understanding of the requirements (Section 2.1) and, at the minimum, detail the following:

- Source suppliers for unusual supplies or reagents.
- The problems that are most likely to occur and how they will be corrected.
- Capacity for performance of the work (i.e., maximum number of compounds that can be synthesized in parallel).
- Any procedures or methods that will be used for ensuring standardization.
- A standardized format for submitting synthesis results to the SMA Project.
- A Time Line* for performance of the work.

* Time Lines: Time Lines should be as efficient/short as possible and should include performance milestones. Milestones should be brief descriptions of expected and required outcomes, not just completion of tasks. For a sample Time Line, see the [Open Solicitations](#) page of the SMA Project website.

4.3.2 Proposal Body for Compound Synthesis of Small Molecules for In Vivo Testing

Offerors shall provide a Background Information/Demonstrated Capabilities **no longer than 10 pages in length**, inclusive of any figures, tables, and graphs. This section should demonstrate that the Offeror has a comprehensive understanding of the goals/objectives to be met (as described in Section 2.2) along with a description of the Offeror's capabilities for meeting them.

The description of capabilities should address experience, facilities, equipment, supplies, source suppliers for unusual supplies or reagents, special resources, personnel, management structure, and any subcontractor organizations that are being proposed. The Offeror should include a Time Line/Schedule³ for synthesizing individual compounds and their capacity for performance of the work (i.e., maximum number of compounds that can be synthesized in parallel).

If any subcontractor organizations are being proposed, it is necessary to include a description of the Offeror's subcontract management capabilities and a description of each subcontractor's capabilities for performing any work to which they will be assigned.

The description should include an overall project Management Plan and address the Offeror's capability to coordinate multiple concurrent tests and scheduling. The Offeror's intellectual property management plan should be covered in the overall project management plan. The plan should include a proposed monthly reporting plan to concisely summarize overall project efforts.

4.3.3 Optional Task: Radiolabeling Chemicals

Offerors shall provide their Demonstrated Capabilities **no longer than 3 pages in length**, inclusive of any figures, tables, and graphs. This section should demonstrate the Offeror's capability to radiolabel chemicals that have been identified through efforts described in Section 2 of this RFP.

The description of capabilities should address experience, facilities, equipment, supplies, source suppliers for unusual supplies or reagents, special resources, personnel, and management structure. The Offeror should include a Time Line/Schedule to synthesize radiolabeled chemicals, to provide these compounds for use in biodistribution assays, and their capacity for

³ See Section 4.3.1 for a description of Time Lines.

performance of the work (i.e., maximum number of compounds that can be synthesized in parallel).

If this service is provided by a subcontractor, information on communication/data exchange between the subcontractor and the contractor should be included.

4.4 References

No page limit. List relevant references using a standard reference format that includes the full citation (i.e., author(s), year published, title of article, publication, volume, chapter, page numbers, and publisher, as appropriate).

4.5 Proposal Appendix: Standard Operating Procedures (SOPs)

No page limit. List and briefly state the purpose of the SOPs currently used by your organization that are relevant to the work being proposed in the Technical Approach section. If desired, a sample SOP may be included in this appendix.

4.6 General Format Specifications

The following format instructions must be followed when preparing the Executive Summary, Proposal Body, References, and the Proposal Appendix **or the application may be returned without review**. Prepare the documents single-sided. The proposal should not be stapled or otherwise bound. The documents must be clear, readily legible, and conform to the following requirements:

- Type font: Must be 10 point or larger (suggested font = 11-point Arial).
- Type density: Must not be more than 15 characters per inch (cpi) including spaces. For proportional spacing, the average for any representative section of text must not be more than 15 cpi or 114 characters per line.
- Spacing: Single-spaced; must not be more than 6 lines of type within a vertical inch.
- Margins: Must be a minimum of ½ inch in all directions.
- Paper size: 8½ x 11 inch.
- Header or Footer: The Principal Investigator's (PI's) name and consecutive page numbers should be included on the Proposal Executive Summary, Body, References, and the Proposal Appendix.

Charts, tables, figures, figure legends, and footnotes may be smaller in size but must be readily legible. Do not use photo reduction. Prepare all graphs, tables, diagrams, and charts in black ink. The application must contain only material that reproduces well when photocopied or printed in black and white since some reviewers may only receive a printed version. Do not use Internet website addresses to provide information necessary to the review because reviewers are under no obligation to view the Internet sites. Moreover, reviewers are cautioned that directly accessing an Internet site could compromise their anonymity.

4.7 Biographical Sketches

Four-page limit for each biosketch; unlimited number of biosketches allowed. Include a biosketch for key personnel, including the PI. The National Institutes of Health's (NIH's) biosketch form (<http://grants1.nih.gov/grants/funding/phs398/biosketch.pdf>) can be used.

Required elements of a biographical sketch are:

- Education/Training: List all degrees received, universities attended, and other pertinent information.

- **Positions and Honors:** List previous positions in chronological order, concluding with your present position. Include present membership on any advisory committee. List any honors.
- **Publications:** List selected peer-reviewed publications, manuscripts in press, and manuscripts submitted (in chronological order). Do not include manuscripts in preparation.
- **Research Support:** List both selected ongoing research projects and projects completed within the last 3 years (federal or non-federal support). Beginning with the most relevant projects, compare this Offer to ongoing project(s) and include information on the degree of scientific uniqueness and overlaps. Briefly indicate the overall goals of the ongoing projects and responsibilities of the Offeror. *Note:* Do not include percent of effort or direct costs.

4.8 Letters of Intent

No page limit. Provide letters of intent from all proposed subcontractors and consultants.

4.9 Publication and/or Patent Information

Five-document limit. Include up to five relevant publication reprints and/or patent abstracts. A patent application abstract should provide a nonproprietary description of the patent application.

4.10 Proposed Budget/Pricing Information

No page limit. An Indefinite Delivery/Indefinite Quantity (ID/IQ) subcontract will be issued for one or more offers received in response to this RFP. A time and material or cost-reimbursement contract is anticipated. The offer shall provide separate budgets for:

- **Project Management** – This budget should cover overall Project Management, inclusive of preparing monthly reports, time to consult with the Lead Development Team and SMA project investigators, and participation in two, 2-day SMA project meetings per year.
- **Chemical Optimization Sample Task** (if applicable) – The budget should support the work and schedules provided by the Offeror for work in response to the Sample Task.

In addition, Offerors proposing to serve as a Compound Synthesis facility should provide:

- **Full Time Equivalent (FTE) costs** for personnel that perform the synthesis. Indicate labor category (e.g., Senior Chemist, Chemist, Technician) and the approximate labor category mix, with percentages, that is typically used to perform this type of work.
- **Costs for synthesizing multi-gram quantities of 10 compounds** that were delivered over the past 24 months. Cost information should include chemical structure (optional), the date work was initiated, the date and quantity of the compound that was delivered, and the number of steps used in the synthesis. Additionally, the Offeror may provide clarification if there were some unusual costs associated with this synthesis (e.g., high cost for starting reagents).

The Summary of Costs form, which is available on the [Open Solicitations](#) page of the SMA Project website, may be used to submit pricing information. The summary of costs should be accompanied by a budget justification.

4.11 Past Performance and Customer Surveys of Performance

To demonstrate successful performance on work that is similar to that required for the SMA Project, the Offeror should submit a Summary of Pertinent Contracts and Grants and Customer Surveys of Performance.

- **Summary of Pertinent Contracts and Grants:** This document should summarize either ongoing or completed projects that are comparable or related to the work required by this RFP. Pertinent Contracts and Grants should be limited to those in which work is ongoing or completed in the last 3 years. This document should include (1) who performed the work, i.e., the Offeror or a subcontractor; (2) the contract/grant number; (3) the client; (4) the dollar value; (5) the period of performance; (6) a description of the work performed; and (7) an explanation of relevance of the work to this RFP.
- **Customer Surveys of Performance:** For Offerors submitting proposals for either chemical optimization or synthesis services, the Customer Survey of Performance form in Attachment B of this RFP should be completed by **three clients** for which the Offeror has already completed or is presently conducting work. For Offerors submitting proposals for both chemical optimization and synthesis services, Customer Survey of Performance forms should be completed by **up to six clients** (three clients for each service). For each proposed subcontractor organization, Customer Survey of Performance forms should be completed by one to **two clients** for which the subcontractor has already completed or is presently conducting similar work.

Offerors shall mail or e-mail the Customer Survey of Performance form to previous clients, collect the surveys from previous clients, and submit the surveys with their proposal. Offerors may provide information on problems encountered on the identified contracts and the Offeror's corrective actions.

A MS Word version of the Customer Survey of Performance is also available on the [Open Solicitations](#) page of the SMA Project website.

5. Supporting Documentation

NOTE: Only **two paper copies** of the following documents need to be provided with your proposal. This information does not need to be provided electronically on the CD.

Offerors shall send in the following Supporting Documentation **at the same time** as their proposals:

- **Subcontract Agreement:** Available on the [Open Solicitations](#) and [Supporting Documentation](#) pages of the SMA Project website. When completing this document, pay particular attention to the Contract Clauses in Schedule B, Part II. This section contains numerous items pertinent to laboratory research (e.g., Animal Welfare Assurance, Continued Ban on Funding of Human Embryo Research, Recombinant DNA and Human Gene Transfer Research, and Research Misconduct). **This section also contains intellectual property management provisions.**
- **Representations and Certifications:** Available on the [Open Solicitations](#) and [Supporting Documentation](#) pages of the SMA Project website.

6. Submission of Proposals and Supporting Documentation

A complete submission consists of a proposal (as described in Section 4) and supporting documentation (as described in Section 5). Details on the required format (i.e., paper vs. electronic) for submission, number of copies needed, and address to which your documents must be sent are provided below.

Please submit:

- **Eight** identical paper copies of the proposal,
- **One** electronic copy of the proposal on a CD (exclusive of signatures, Past Performance and Customer Surveys of Performance, and Letters of Intent), and
- **Two** paper copies of the Supporting Documentation,

all complying with the requirements described in this RFP, via **mail** or **overnight carrier** by **5:00 P.M. ET** on **September 10, 2004** to:

Science Applications International Corporation (SAIC)
Attn: Jonathan Logan
5340 Spectrum Drive, Suite N
Frederick, MD 21703-7357
Phone: 301-228-3149

A Checklist for Submitting a Proposal and Supporting Documentation is included as Attachment A to assist Offerors in the preparation of the required documents for submission.

7. Procedures for Evaluation of Proposals and Selection of Award

7.1 General Information

Final funding decisions will be based on (1) review of proposals that will be performed in accordance with the evaluation review criteria outlined in Section 7.4, (2) recommendations of the Steering Committee, (3) priorities of NINDS, and (4) availability of funds.

7.2 Compliance Check

Prior to forwarding proposals for review, all documentation will be compliance checked to ensure:

- The proposal contains a cover page with signatures, an Executive Summary, a technical approach with required time lines, a biographical sketch for the PI, letters of intent from all proposed subcontractors and consultants, a budget, and customer surveys.
- The Supporting Documentation contains required signatures.

Proposals that do not meet the aforementioned requirements will be returned to the Offeror without review.

7.3 Proposal Review Process

A review panel composed of scientists with appropriate expertise will evaluate the proposals. Reviewers will evaluate proposals based on the criteria listed in Section 7.4. Evaluations of chemical optimization and synthesis services will be made independently. If both services are proposed, certain sections of the proposal (e.g., biographical sketches) will be evaluated twice, in the context of each service.

Offerors should be prepared to be available by telephone during the review meeting to answer questions pertaining to their proposal; details of this procedure will be provided to Offerors approximately 1 week prior to the scheduled review meeting.

7.4 Proposal Review Criteria

Reviewers will evaluate proposals against the review criteria listed below. The relative importance of these criteria is indicated by the assigned point weights. The maximum total score possible is **100 points**.

- **Past Experience (40 points)** –
 - *For proposals for chemical optimization services:* Do the Overall Capabilities and Sample Task sections demonstrate successful experience in creatively designing and conducting chemical structural optimization schemes?

- *For proposals for synthesis services:* Does the Overall Capabilities section demonstrate successful experience in organic synthesis and purification, determination of chemical identity, and characterization of physicochemical and pharmaceutical properties for the purposes of in vivo testing?
- *For all proposals:* Do the completed Customer Surveys of Performance demonstrate that the Offeror has successfully performed the type of work required on a contractual basis? Does the Offeror have a successful history of collaboration?
- **Technical Approach and Time Lines (25 points) –**
 - *For proposals for chemical optimization services:* Does the Sample Task section propose creative, thorough, and feasible strategies for chemical optimization?
 - *For proposals for synthesis services:* Does the Offeror propose feasible strategies for compound synthesis for in vivo testing?
 - *For all proposals:* Have quality control and assurance issues been addressed? Are the proposed schedules for optimization, synthesis, purification, and identity determination as efficient as possible, yet realistic? Have all conceivable efficiencies been considered?
- **Personnel and Project Management (20 points) –** Is there a proposed Project Manager with education and experience commensurate with the level of responsibility to be assumed? Are there Medicinal Chemists on staff with demonstrated expertise in small molecule optimization? Is the management plan well thought out? Do the Background Information/Demonstrated Capabilities and the Management Plan demonstrate a thorough understanding of the requirements and the broader goals and objectives of the SMA Project? Are personnel adequately trained and experienced in use of the equipment and reagents needed for the work to be performed? Are there sufficient personnel to simultaneously conduct work on multiple compounds?
- **Facilities/Equipment (15 points) –** Do the Overall Capabilities and Sample Task sections and Supporting Documentation demonstrate that the Offeror has an appropriately equipped and licensed facility for conducting the proposed work? Is the analytical instrumentation adequately described? Is the equipment in good repair and being maintained according to manufacturer specifications? Are adequate measures in place to ensure the safety of all personnel and the proper disposal of all hazardous waste? Is the capacity of the facility suitable to meet the goals of the SMA Project?

If proposed, the Optional Task will be deemed acceptable or not acceptable based upon the capabilities, personnel, and facilities. (Please note that the Optional Task will not be funded at the time of award and may be exercised at a later date.)

In addition to the review criteria listed above, reviewers will consider the appropriateness of the **pricing information** supplied by the Offeror.

7.5 Funding Recommendations and Award Negotiations

Upon completion of peer review, Steering Committee members will be provided a copy of each proposal's Executive Summary and a summary of reviewers' evaluation. The Steering Committee will use this information to make funding recommendations to SAIC and NINDS for approval by NINDS.

Site visits may be conducted for some Offers within 6 weeks of review. With prior notification from SAIC, each Offeror should make the facility available during normal business hours.

SAIC will formally notify organizations of technical merit results. Notification of award status will be made in accordance with Federal Acquisition Regulation 15.503.

8. Additional Information for Offerors

8.1 General Information

The Offeror is to furnish all information required by this RFP to SAIC. Any erasures or changes to a proposal must be initialed by an individual authorized to submit the offer, on behalf of the Offeror. The individual submitting the offer must have the authority to contractually bind the offer.

This RFP does not commit SAIC to pay any costs associated with the Offeror's preparation and submission of a proposal. The SAIC Subcontracts Representative is the only individual legally authorized to contractually bind SAIC for this solicitation. This is not an authorization to proceed with the work referenced herein.

8.2 Contact Information

For technical questions regarding this RFP, please contact Adam Book at 301-228-3114. For contractual questions related to this RFP, please contact Jonathan Logan at 301-228-3149. Alternatively, technical or contractual questions can be e-mailed to smaproject-fd@saic.com.

8.3 Progress Monitoring of Awards

Progress on each contract and task order will be monitored. Offerors who receive funding will be asked to submit brief monthly reports/updates on overall progress and separate reports with detailed chemical optimization and synthesis results. Offerors will propose a monthly reporting plan to concisely summarize overall project efforts in their proposal and means to share data. A format and schedule for delivery of data and reports will be negotiated.

Through open communication between SMA Project investigators and SAIC's professional staff of doctoral-level scientists, regulatory affairs specialists, and project control specialists, any issues or concerns will be efficiently addressed. As needed, SMA Project Steering Committee members and technical experts who are formally associated with SAIC will also review reports/updates.

Offerors should note that continued funding for issued Task Orders during the period of performance of the SMA Project contract will be dependent on successful completion of assays according to the time lines specified in the proposal. SAIC will work with a SMA Project contractor to adjust time lines if necessary to best meet the needs of the SMA Project.

8.4 Resource Sharing, Data Sharing, and Intellectual Property Management

The SMA Project is "A Collaborative Program to Accelerate Therapeutics Development for Spinal Muscular Atrophy." Collaboration is deemed essential for being able to identify and rapidly complete preclinical development of the SMA therapeutics that are most likely to be safe, effective, and approved for clinical use by the U.S. Food and Drug Administration. In vivo efficacy screening of candidate compounds is important for the success of this program, and the screening results must be made freely available for use in any component of this program. In awarding funds to successful Offerors, SAIC will act as a Contractor to NINDS. As such, these funds are subject to the provisions of the *Principles and Guidelines for Recipients of NIH Research Grants and Contracts on Obtaining and Disseminating Biomedical Research Resources* (64 FR 72090, December 23, 1999) and the *NIH Grants Policy Statement* concerning the availability of research results: publications, intellectual property rights, and sharing of biomedical research resources. An intellectual property plan will be negotiated as part of the [Subcontract Agreement](#). To facilitate data and resource sharing and the generation of new ideas, funded investigators will be required to participate in investigator teleconferences

and meetings as arranged by SAIC (for more information, see [About the Program](#) on the SMA Project website).

To ensure that intellectual property claims are adequately protected and/or appropriately pursued, program participants who are not employees of the federal government will be required to read and sign the program's Data Sharing Plan (see the Subcontract Agreement). Enforcement of the Plan will be carried out by NINDS with assistance from SAIC. In addition, as part of the Subcontract Agreement with SAIC, the Contractor agrees that an Intellectual Property Plan will be established for products developed under the contract. This plan will be in compliance with the provisions and spirit of the Bayh-Dole Act (35 U.S.C. 200, et seq.) and will not impose inappropriate reach-through royalty terms on the sale of an end item developed using the product. (See the Subcontract Agreement for a full description of the Intellectual Property Plan requirements.)

To help ensure the resource sharing, data sharing, and intellectual property management plans of the Offerors are consistent with the goals of this program and NIH policies, SAIC and the Steering Committee will consider whether each Offeror's plans are consistent with the goals of this program prior to making funding recommendations to NINDS.

The following section is intended primarily for the Offeror's Business Office. Offerors should familiarize themselves with the information contained in this section and forward the material to their Business Office as soon as possible.

9. Information Related to SMA Project Contracts

9.1 General Information

SAIC reserves the right to make multiple awards. Indefinite Delivery/Indefinite Quantity (ID/IQ) subcontract(s) will be issued in response to this RFP. Awards will be made for base subcontracts for managing the facility. Contracted facilities will be asked to develop protocols for providing chemical optimization and synthesis services, as appropriate, for a specific (candidate) compound. Protocols will be refined and modified based on consultation with the Lead Development Team, NINDS, and SAIC prior to initiating work.

Any SMA Project contract resulting from this solicitation shall resemble the Subcontract Agreement posted on the SMA Project website, with the exception of appropriate modifications made at the time of award, including all applicable provisions required for flowdown by the prime contract to SAIC and any provisions required by law on the date of execution of the SMA Project contract. The terms and conditions set forth or referenced herein shall apply, and SAIC objects to and shall not be bound by any additional alternate terms and conditions proposed by the Offeror. The Offeror agrees, if an offer is accepted, to furnish any or all services for which the offer is submitted at the price(s) proposed and upon the terms and conditions contained in this RFP, and the proposal shall be inclusive of all costs associated with performing the work, including profit/fee.

9.2 Restrictions on the Use of Human Subjects and Human Tissues/Specimens

Research involving human subjects shall not be conducted under SMA Project contracts. Research involving tissues or other biological specimens derived from living or deceased humans and cell lines derived from human tissues may only be conducted if Offerors have demonstrated their compliance with all appropriate guidelines pertaining to the use of human specimens and approval of the Contracting Officer. Please see the NIH brochure [Research on Human Specimens: Are You Conducting Research Using Human Subjects?](#) based on *Regulations for Protection of Human Subjects (45 Code of Federal Regulation Part 46)*, for more information.

9.3 Proposal Validity

To be considered valid, your proposal must be addressed to Jonathan Logan and remain firm for 180 calendar days.

9.4 Qualifications of Prospective Offeror

The Offeror must have adequate resources to perform any resulting SMA Project contract, in accordance with the terms and conditions of this RFP, and upon request furnish proof of the same. The SAIC Subcontracts Representative may request verification of the Offeror's financial status, cost data related to the proposal, verification of insurance, anticipated technical approach, preliminary project scheduling, and/or any other pertinent data needed to establish the responsibility of the Offeror. Offers will not be accepted from any SAIC employee or business unit.

9.5 Procurement of Certain Equipment

Offerors will not be reimbursed for the purchase, lease, or rental of any item of equipment listed in the following Federal Supply Groups, regardless of the dollar value, without the prior written approval of the government contracting officer:

- 67 – Photographic Equipment
- 69 – Training Aids and Devices
- 70 – General Purpose ADP Equipment, Software, Supplies, and Support
(Excluding 7045-ADP Supplies and Support Equipment)
- 71 – Furniture
- 72 – Household and Commercial Furnishings and Appliances
- 74 – Office Machines and Visible Record Equipment
- 77 – Musical Instruments, Phonographs, and Hometype Radios
- 78 – Recreational and Athletic Equipment

When equipment in these Federal Supply Groups is requested by the Offeror and determined essential by the Contracting Officer, the government will endeavor to fulfill the requirement with equipment available from its excess personal property sources, provided the request is made under a cost reimbursement contract. Extensions or renewals of approved existing leases or rentals for equipment in these Federal Supply Groups are excluded from the provisions of this article.

Additional unallowable items include accountable government property (defined as both real and personal property with an acquisition cost of \$1,000 or more and a life expectancy of more than 2 years) and "sensitive items" (defined and listed in the Contractor's Guide for Control of Government Property, <http://knownet.hhs.gov/log/AgencyPolicy/HHSLogPolicy/contractorsguide.htm>, 1990), regardless of acquisition value.

9.6 Late Offers

Formal offers, amendments, or requests for withdrawal of offers received after the date specified for submittal may not be considered.

9.7 Offer Acceptance and Award

SAIC reserves the right under all circumstances to select and award to the Offeror, in whole or in part, any portion of this project that is in the best interest of SAIC and its client.

Of note:

- SAIC may accept any offer regardless of whether there are negotiations conducted subsequent to its receipt. Any such negotiations shall not constitute a rejection or counteroffer on the part of SAIC.
- SAIC reserves the right to reject the offer, to waive minor informalities in offers, and/or to conduct further negotiations with the Offeror.
- SAIC assumes no responsibility for any promise or representation, either oral or written, that an SMA Project contract award will be made, unless done so by the SAIC Subcontracts Representative and only when an SAIC Pro-Forma Subcontract of the type referenced in this RFP is executed with the Offeror.
- SAIC reserves the right to make multiple awards.

9.8 Right of Denial

SAIC reserves the right to deny the services of an Offeror due to inadequate qualifications and/or failure to complete a contract or demonstrated poor performance on contracts similar in nature or an Offeror who, under investigation, is shown not to be in a position to perform the contract.

To form a complete offer, the Offeror is required to provide a detailed cost proposal in accordance with this solicitation, a technical proposal that demonstrates the Offeror's understanding of the requirements, and other pertinent documents as outlined in Section 5 of this RFP.

Checklist for Submitting a Proposal and Supporting Documentation

Proposal

Submit 8 identical paper copies and a CD with one electronic copy of the following (items marked with an * are not needed in electronic form):

- Proposal Face Page (with signatures on original paper copy)
- Proposal Executive Summary (1-page limit)
- Proposal Body
 - Chemical Optimization Facility
 - Overall Capabilities (7-page limit)
 - Sample Task (20-page limit)
 - Synthesis Facility (10-page limit)
 - Optional Task – Radiolabeling Chemicals (3-page limit)
- References (no page limit)
- Proposal Appendix with Standard Operating Procedures (no page limit)
- Biographical Sketches (4-page limit for each biosketch; unlimited number of biosketches)
- Letters of Intent* (no page limit)
- Proposed Budget/Pricing Information and Budget Justification (no page limit)
- Customer Surveys of Performance*
 - Forms from 3 current or past clients (up to 6 clients if proposing both chemical optimization and synthesis services)
 - For proposed subcontractors, forms from 1-2 current or past clients of the subcontractor

Supporting Documentation

Submit 2 identical paper copies of the following:

- Subcontract Agreement

The entire document must be read and completed as necessary. Of note, signatures are needed in the following places:

 - Schedule A, page 13
 - Attachment II (Memorandum – Requirements Related to Human Subjects, Specimens, and Recombinant DNA Research), page 31

Also note that as part of the Subcontract Agreement you must provide:

 - An approved Animal Welfare Assurance from the Office of Laboratory Animal Welfare, page 22
 - An intellectual property management plan that satisfies the requirements outlined in the Subcontract Agreement, page 25

In addition, prior to the start of research involving animals you must provide:

 - Verification of approval (including the date of most recent approval) by the Institutional Animal Care and Use Committee (IACUC) with appropriate documentation, page 22
- Representations and Certifications document

This document must be read and completed as necessary, including a signature of the person authorized to bind Offeror on page 12.



The SMA Project: Customer Survey of Performance

Please complete Parts 1, 3, and 4 of the questionnaire and return via regular mail or fax to the attention of:

(Name) By _____
(Date)

(Address)

(Fax Number)

Our organization is planning to submit a proposal to the SMA Project. The Request for Proposals to which we intend to respond involves providing support services for conducting chemical optimization of lead compounds for SMA through medicinal chemistry and/or providing larger-scale (multi-gram) synthesis services for promising compounds.

PART 1: GENERAL INFORMATION

Name of Contracting Organization: _____

Department/Component: _____

Contract Number: _____

Contract Type: _____

Contract Value (including options): \$_____

Period of Performance (including option periods): _____

Approximate percentage of work being performed (or completed) by subcontractor (s): _____ %

Contracting Officer's Name and Telephone Number: _____

Program Manager's Name and Phone Number: _____

Please provide a brief description of how this contract relates to providing services similar to those indicated at the top of this page. In addition, please provide a general description of products/services required under this contract:

Part 2: RATINGS

Use the table below as a guide to complete Part 3.

	Quality of Product or Service	Cost Control	Timeliness of Performance	Business Relations
0 – Unsatisfactory	Contractor is not in compliance and is jeopardizing achievement of contract objectives	Contractor is unable to manage costs effectively	Contractor delays are jeopardizing performance of contract objectives	Response to inquiries, technical/service/administrative issues is not effective
1 – Poor	Major problems have been encountered	Contractor is having major difficulty in managing costs effectively	Contractor is having major difficulty meeting milestones and delivery schedule	Response to inquiries, technical/service/administrative issues is marginally effective
2 – Fair	Some problems have been encountered	Contractor is having some problems in managing costs effectively	Contractor is having some problems meeting milestones and delivery schedule	Response to inquiries, technical/service/administrative issues is somewhat effective
3 – Good	Minor inefficiencies/errors have been identified	Contractor is usually effective in managing costs	Contractor is usually effective in meeting milestones and delivery schedule	Response to inquiries, technical/service/administrative issues is usually effective
4 – Excellent	Contractor is in compliance with contract requirements and/or delivers quality products/services	Contractor is effective in managing costs and submits current, accurate, and complete billings	Contractor is effective in meeting milestones and delivery schedule	Response to inquiries, technical/service/administrative issues is effective
5-Outstanding: The contractor has demonstrated an outstanding performance level in any of the above four categories that justifies adding a point to the score. It is expected that this rating will be used in those rare circumstances when contractor performance clearly exceeds the performance levels described as "Excellent."				

Assign each area a rating of 0 (Unsatisfactory), 1 (Poor), 2 (Fair), 3 (Good), 4 (Excellent), or 5 (Outstanding).

PART 3: SMA PROJECT CUSTOMER SURVEY OF CONTRACTOR PERFORMANCE

Circle the appropriate rating using the table in Part 2. If you do not have enough personal knowledge or feedback from internal customers who directly received products and services from the Contractor to make a determination on any of the performance criteria below, please circle "N/A" (not applicable/no opinion).

QUALITY OF PRODUCT OR SERVICE

1. Compliance with contract requirements	0	1	2	3	4	5	N/A
2. Accuracy of reports	0	1	2	3	4	5	N/A
3. Effectiveness of personnel	0	1	2	3	4	5	N/A
4. Technical Excellence	0	1	2	3	4	5	N/A

COST CONTROL

1. Record of forecasting and controlling target costs	0	1	2	3	4	5	N/A
2. Current, accurate, and complete billings	0	1	2	3	4	5	N/A
3. Relationship of negotiated costs to actuals	0	1	2	3	4	5	N/A
4. Cost efficiencies	0	1	2	3	4	5	N/A

TIMELINESS OF PERFORMANCE

1. Met interim milestones	0	1	2	3	4	5	N/A
2. Reliability	0	1	2	3	4	5	N/A
3. Responsive to technical directions	0	1	2	3	4	5	N/A
4. Completed on time including wrap-up and contract administration	0	1	2	3	4	5	N/A
5. Met delivery schedules	0	1	2	3	4	5	N/A
6. Liquidated damages assessed: Yes No (circle one)							

BUSINESS RELATIONS

1. Effective management, including management of subcontracts	0	1	2	3	4	5	N/A
2. Reasonable/cooperative behavior	0	1	2	3	4	5	N/A
3. Responsive to contract requirements	0	1	2	3	4	5	N/A
4. Notification of problems	0	1	2	3	4	5	N/A
5. Flexibility	0	1	2	3	4	5	N/A
6. Pro-active vs. reactive	0	1	2	3	4	5	N/A

