REQUEST FOR INFORMATION NOTICE

Notice Number: HHS-NIH-NCI-RFI-TSB-37000-11
Title: **"Development and Production of Parenteral Dosage Forms for Clinical Studies"**

This is a Request for Information notice. This is **NOT** a solicitation for proposals, proposal abstracts, or quotations. The purpose of this notice is to obtain information regarding: (1) the availability and capability of qualified business sources. Your responses to the information requested will assist the Government in determining the appropriate acquisition method.

This National Cancer Institute (NCI), National Institutes of Health (NIH) project is a recompetition of an existing requirement. This Request for Information notice is for information and planning purposes only and shall not be construed as a solicitation or as an obligation on the part of the National Cancer Institute. Interested parties are expected to review this Notice and the draft **Statement of Work** to familiarize themselves with the requirements of this project; failure to do so will be at your firm's own risk.

Purposes and Objectives:
The National Cancer Institute is seeking qualified businesses to develop and produce pharmaceutically acceptable parenteral dosage forms of promising new agents with activity against cancer. Data obtained from any contract that may be awarded will: 1) be used to support IND applications submitted by the National Cancer Institute to the U.S. Food and Drug Administration as well as foreign agencies, 2) be provided to other NCI contractors engaged in large scale dosage form manufacture and analytical evaluation of these dosage forms and 3) be provided to physicians, pharmacists, nurses, and other medical personnel handling these products in a clinical setting.

Capability Statement/Information Sought:
Capability Statements shall demonstrate an understanding of the development and production of pharmaceutically acceptable parenteral dosage forms of promising new agents with activity against cancer. If a Request for Proposals (RFP) is issued following this Request for Information announcement, offerors will need to demonstrate, at the time of proposal submission, that they are registered with the Food and Drug Administration (FDA) as a pharmaceutical manufacturing facility for sterile products. The Capability Statements for this requirement shall address the following four (4) areas: 1) technical approach, 2) personnel; 3) facilities and equipment and 4) corporate experience with similar projects.

1. A detailed Technical Approach that demonstrates a clear understanding of the draft SOW with discussions of a) formulation development; b) production of parenteral dosage forms; c) quality assurance and evaluation and d) packaging and labeling of finished products. Standard Operating Procedures used in the preparation and manufacture of dosage forms should be described as well as Standard Operation Procedures for protecting personnel from cytotoxic agents being formulated and quality control tested.

2. Personnel described must have experience with parenteral product development, especially freeze-drying, as well as expertise in the areas of sterile emulsions, liposomes and microdispersions. In addition, staff should possess experience with a variety of analytical instrumentation and the development of stability indicating assays.

3. A description of the facility that will be directly utilized and available for this proposed project, including laboratory, equipment and storage areas, should be provided.

4. The description of your firm's corporate experience with similar projects should include your firm's general background, experience, and qualifications particularly with projects involving development and production of specialty parenteral formulations. A special notation should be made of similar or related programs performed for the Government including documentation with reference to the applicable contract numbers and the supervising agencies.

A copy of the draft Statement of Work (SOW) pertaining to this requirement, which is subject to revisions, may be accessed online.

Anticipated Period of Performance:
The period of performance for this requirement will be a one-year base period with four (4) successive one-year options, for a total of five years if all options are exercised. The anticipated start date is December 15, 2012. Multiple awards are anticipated.

Information Submission Instructions:

1. **Page Limitations:**
   Interested qualified organizations should submit a tailored capability statement for this requirement not to exceed twenty-five (25) single-sided pages including attachments, resumes, charts, etc. (single-spaced, 12 point font minimum) that clearly details the firms ability to perform aspects of the notice described above and the draft Statement of Work. Tailored capability statements should also include point of contact, address, and DUNS number.
2. **Number of Copies/Delivery Point:**
   All capability statements sent in response to this Request for Information Notice must be submitted electronically (via e-mail) to Brenda Oberholzer, Contracting Officer, at oberholzerb@mail.nih.gov in MS Word, or Adobe Portable Document Format (PDF). The e-mail subject line must specify HHS-NIH-NCI-RFI-TSB-37000-11. Facsimile responses will not be accepted.

3. **Common Cut-off Date:**
   Electronically submitted tailored capability statements are due no later than 2:00 PM (EST) on March 2, 2012. **CAPBILITY STATEMENT RECEIVED AFTER THIS DATE AND TIME WILL NOT BE CONSIDERED.**

   DISCLAIMER AND IMPORTANT NOTES: This notice does not obligate the Government to award a contract or otherwise pay for the information provided in this response. The Government reserves the right to use information provided by respondents for any purpose deemed necessary and legally appropriate. Any organization responding to this notice should ensure that its response is complete and qualifications to perform the work. Respondents are advised that the Government is under no obligation to acknowledge receipt of the information received or provide feedback to respondents with respect to any information submitted. After a review of the responses is received, a pre-solicitation synopsis and solicitation may be published

in Federal Business Opportunities. However, responses to this notice will not be considered adequate responses to a solicitation.

CONFIDENTIALLY: No proprietary, classified, confidential, or sensitive information should be included in your response. The Government reserves the right to use any nonproprietary technical information in any resultant solicitation(s).

DRAFT STATEMENT OF WORK

a. BACKGROUND AND PROJECT OBJECTIVES

The primary objective of this project is to develop and produce pharmaceutically acceptable parenteral dosage forms of promising new agents with activity against cancer. Certain agents selected by the NCI, DCTD will be assigned for development and production as parenteral products. Batch sizes shall range from small batches (less than 100 units) to intermediate size batches to be used in Phase I and II trials; however, escalation to large batch sizes (10 - 30,000 or more units) for advanced Phase II/III trials is also possible. The capability to develop and manufacture other pharmaceutical dosage forms (i.e. large volume parenterals, sterile emulsions, liposomes and sterile micro-dispersions) is desirable.

Data obtained from resultiung contract(s) may 1) be used to support IND applications submitted by the National Cancer Institute to the U.S. Food and Drug Administration as well as foreign agencies, 2) be provided to other NCI contractors engaged in large scale dosage form manufacture and analytical evaluation of these dosage forms and 3) be provided to physicians, pharmacists, nurses, and other medical personnel handling these products in a clinical setting.

b. Mandatory Qualification Requirement

The Contractor must be registered with the FDA as a pharmaceutical manufacturing facility for sterile products. The Contractor should show proof (FDA form 483) of routine FDA inspection(s) within the last two years. This requirement shall be met at the time of proposal submission. Moreover, the Contractor must be in compliance with FDA requirements during the course of the contract performance. In this regard, the Contractor shall notify the Project Officer of any outstanding FDA form FD 483s resulting from routine inspection and proposed timetable for corrective action during the course of contract performance.

DRAFT DESCRIPTION OF WORK

A. STATEMENT OF WORK

The Contractor shall furnish services, qualified personnel, materials, and a complete, ongoing and fully operational facility including all necessary equipment for all aspects of the manufacture and testing of freeze-dried, liquid- filled, and ampoules parenterals. The facility shall be capable of filling, sealing and testing ampules. This facility and equipment shall conform to and be maintained in accordance with FDA prescribed Current Good Manufacturing Practices.

The Contractor shall:

1. Provide all materials used in the manufacture, testing, packaging and labeling of the formulated parenteral products unless provided by the Government. (Note: The active drug substances will in most cases be supplied by NCI).

2. Provide adequate analytical instrumentation and pharmaceutical equipment to perform a thorough and complete quality control evaluation of both the active drug substance and the formulated products. Such equipment shall include the in-house capability to perform gas liquid chromatography, high performance liquid chromatography, ultraviolet and infrared spectroscopy, pH and moisture determination and the USP sterility test.

B. The following tasks may be required under this contract as determined by the Project Officer:

1. Formulation Development

Development and production of injectable dosage forms of investigational anti-cancer drugs for clinical trials in humans: All new assignments shall require some preliminary pre-production evaluation. Some projects will require only familiarization studies with an existing formulation. However, other projects will require thorough dosage form development including development of a stability indicating assay, accelerated stability study of final dosage form, compatibility studies in vehicles suitable for parenteral use, pilot scale freeze drying studies, analysis, and validation studies of these dosage forms at the discretion of the Project Officer. Information will be provided on the chemical purity of the bulk drug substance as well as some preliminary solubility data. The Contractor shall develop suitable analytical methods to adequately evaluate the stability of the experimental products under various end-use conditions. Drugs which present aqueous solubility difficulties shall require the use of low temperature vacuum drying capabilities, or nonaqueous or two-solvent systems. The NCI will in most cases supply the investigational drug substances and the Contractor shall be

responsible for acquisition of other supplies for development and production including but not limited to analytical reagents, diluents, excipients, containers, closures, and labels.

2. Production of Parenteral Dosage Forms

Parenteral production assignments will be for:

a) Sterile freeze-dried products
b) Liquid filled vials

Other specialized dosage forms such as Large Volume Parenterals (LVP), liposomes, micro-dispersions, or sterile emulsions may be required to be produced. If the Contractor is not equipped to manufacture these dosage forms, sub-contractors may be utilized.

Validated standard operating procedures should be in place for all phases of production and compendial testing.

The projects are initiated by work assignment letter from the Project Officer. The specifications for production, batch size, labeling and packaging will be included in the work assignment letter or developed during the course of formulation research and development.

3. Quality Assurance

The Contractor shall perform quality assurance testing of all final formulation ingredients as well as the finished products. The testing shall include identity and purity characterization of the bulk investigational drug substance to assure conformance with the previously obtained independent analytical results. Chromatographic methods of analysis developed by the Contractor shall be validated. The amount and type of such testing will be specified by NCI. All applicable compendial and other pharmaceutical testing for all other components used in the formulation shall be required. Bioload testing shall be required for some bulk substances as directed by the Project Officer.

Quality control evaluation of the finished dosage forms to assure conformance to the NCI specifications shall be required. An evaluation may consist of the following tests as determined by the Project Officer:

a) Identity Test

b) Chromatographic Tests including potency, assay, related substances, uniformity of dosage form.

c) Residual Moisture

d) USP Completeness and Clarity of Solution

e) pH

f) USP Sterility Test

g) USP Pyrogen Test

h) LAL Testing

i) 100% Visual inspection

j) USP Particulate Matter (for small and large volume parenterals)

k) Assay validation

l) Process validations

Other tests will be assigned by NCI when necessary. All other aspects of quality assurance as specified in the U.S. Food and Drug Administration Current Good Manufacturing Practices pertinent to parenteral manufacture shall be required.

The Contractor shall be responsible for Quality Assurance of materials produced by sub-contractors and shall provide detailed plans for monitoring sub-contract work.

4. Packaging and Labeling of Finished Products

All products shall be labeled and packaged according to specifications supplied by the Project Officer. Label preparation may be subcontracted, but labeling shall be performed on the contract site. Finished products shall be stored at the labeled storage condition until released to the NCI. All products shall be sent directly to the National Cancer Institute's designated storage facility (currently located in the Washington Metropolitan area) upon release and to arrive within two (2) days under appropriate storage conditions. In some instances, an emergency drop shipment of drugs may be required directly to a clinical investigator or to the NCI

storage contractor.

5. The following estimated number of assignments will be required per annum:

Development Projects - 6 assignments
Production Projects - 12 assignments
(Average batch size 1,000 vials/ampules)

The active drug substance will in most cases be supplied by the NCI. The Contractor shall provide all other ingredients, containers, stoppers, boxes, labels and other necessary supplies as specified by the Project Officer.