

SMALL BUSINESS SOURCES SOUGHT NOTICE

Notice Number: HHS-NIH-NCI-SBSS-TSB-37007-11

Title: "Development and Production of Parenteral Dosage Forms for Clinical Studies"

This amendment changes the following section as well as the attached Statement of Work (changes are underlined):

Capability Statement/Information Sought:

Capability Statements shall demonstrate an understanding of and experience with the development and production of pharmaceutically acceptable parenteral dosage forms of promising new agents with activity against cancer in humans. If a Request for Proposals (RFP) is issued following this Small Business Sources Sought announcement, offerors will need to demonstrate, at the time of proposal submission, that they have recent prior experience 1) manufacturing and delivering batches of sterile injectable drugs for human use, and 2) handling, developing, and manufacturing cytotoxic drugs. 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. Respondents must provide a detailed Technical Approach that demonstrates a clear understanding of the draft SOW with discussions of the following relative to cytotoxic agents for human use: a) formulation development; b) production of parenteral dosage forms; c) quality control and assurance; 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.
3. **Common Cut-off Date:**
Electronically submitted tailored capability statements are due no later than 12:00 PM (EST) on March 28, 2013. **CAPBILITY STATEMENT RECEIVED AFTER THIS DATE AND TIME WILL NOT BE CONSIDERED.**

STATEMENT OF WORK

I. BACKGROUND AND PROJECT OBJECTIVES

The primary objective of this project is to develop and produce pharmaceutically acceptable parenteral dosage forms of cancer drugs for human use. Certain agents selected by the NCI, DCTD will be assigned for development and production as parenteral products. Batch sizes shall range from small batches (100 - 200 units) to intermediate size batches to be used in Phase I and II trials (1,000 - 5,000 or more units). The capability to develop and manufacture other pharmaceutical dosage forms (i.e. sterile emulsions, liposomes and sterile micro-dispersions) is desirable.

Data obtained from resulting 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.

II. 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 sterile, freeze-dried, liquid-filled, and other injectable dosage forms. This facility and equipment shall conform to and be maintained for the production of human drugs in accordance with FDA prescribed Current Good Manufacturing Practices. They shall be capable of handling, developing, and manufacturing cytotoxic drugs.

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.

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 drugs for clinical trials in humans. All new Task Orders 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 Contracting Officer's Representative. 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 Task Orders will be for:

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

Other specialized dosage forms such as 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 Contracting Officer's Representative. 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 Control

The Contractor shall perform quality control 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 Contracting Officer's Representative.

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 Contracting Officer's Representative:

- a) Identity Test
- b) Chromatographic Tests including assay, related substances, uniformity of dosage units.
- 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
- k) Assay validation
- l) Process validations

Other tests will be assigned by NCI when necessary. All other aspects of quality control 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 Control/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 Contracting Officer's Representative. 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 Task Orders will be required per annum:

Development Projects - 4 Task Orders

Production Projects - 4 Task Orders

(Average batch size 1,000 vials)

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 Contracting Officer's Representative.