

TECHNICAL PROPOSAL INSTRUCTIONS

A detailed work plan must be submitted indicating how each aspect of the statement of work is to be accomplished. Your technical approach should be in as much detail as you consider necessary to fully explain your proposed technical approach or method. The technical proposal should reflect a clear understanding of the nature of the work being undertaken including information on how the project is to be organized, staffed and managed. Information should demonstrate your understanding and management of important events and tasks.

Recommended Technical Proposal Format: The following format is recommended for submission of technical proposals:

- I. TITLE PAGE (COVER PAGE)
- II. TABLE OF CONTENTS (with page numbers)
- III. INTRODUCTION - Summarize the importance that this project and your proposed approaches will have in achieving the goals of the NCI program.
- IV. TECHNICAL -

Prepare a technical proposal in response to the instructions below. The Technical Evaluation Criteria will be used to evaluate the scientific aspects of the proposal.

The technical discussions included in the technical proposal should respond to the items set forth below:

A. Personnel

Describe the experience and qualification of personnel who will be assigned for direct work on this program. Information is required which will show the composition of the task or work group, its general qualifications, and recent experience with similar equipment or programs. Special mention shall be made of direct technical supervisors and key technical personnel, and the approximate percentage of the total time each will be available for this program.

OFFERORS SHOULD ASSURE THAT THE PRINCIPAL INVESTIGATOR, AND ALL OTHER PERSONNEL PROPOSED, SHALL NOT BE COMMITTED ON FEDERAL GRANTS AND CONTRACTS FOR MORE THAN A TOTAL OF 100% OF THEIR TIME. IF THE SITUATION ARISES WHERE IT IS DETERMINED

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THAT A PROPOSED EMPLOYEE IS COMMITTED FOR MORE THAN 100% OF HIS OR HER TIME, THE GOVERNMENT WILL REQUIRE ACTION ON THE PART OF THE OFFEROR TO CORRECT THE TIME COMMITMENT.

The Principal Investigator should possess a Ph.D. in Pharmaceutics, Physical Pharmacy, or Medicinal Chemistry with at least five years experience in the development of injectable formulations. The Principal Investigator should be an employee of the offeror's organization and should devote about 500 direct labor hours annually to this project.

Identify the Principal Investigator (by name) and describe the background, training, recent experience and scientific accomplishments that qualifies the individual to lead this Project. Include the Principal Investigator's complete, updated curriculum vitae. Indicate this individual's availability and proposed level of effort.

All proposed senior personnel must possess capabilities and experience commensurate with their assigned responsibilities. One member of the group should have experience in the development of freeze dried dosage forms. A total of 2080 direct labor hours annually should be at the Ph.D. or M.Sc. level employee. The proposal should describe in detail the work these individuals have completed in improving drug solubility and/or stability, and how these improvements have been incorporated into parenteral pharmaceutical dosage forms. Describe the experience of the proposed staff in the area of pharmaceutical analysis. Describe the experience of the project staff with ultraviolet, infrared and proton magnetic resonance spectroscopy, gas chromatography, high performance liquid chromatography, optical rotation techniques, and thermal analysis. Describe the experience of the project staff in the development and application of stability- indicating assays.

Identify these professional staff members (by name) and describe the background, training, recent experience, and scientific accomplishments that qualifies each individual to perform in their area of responsibility. State the estimated time each will spend on the project, proposed duties on the project, and the areas or phases for which each will be responsible. Include each individual's complete, updated curriculum vitae that indicate their educational background, recent dosage form development experience, and scientific accomplishments.

For all proposed personnel who are not currently members of the offeror's staff, a letter of commitment or other evidence of availability is required. A resume does not meet this requirement.

A. Consulting arrangements

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It is desirable to maintain as much of the work and expertise as possible in one location in order to maintain control over priorities of work and delivery schedules. If consultants are proposed a statement in writing from the consultants detailing the following information must be included in your proposals:

- a) The specific items or expertise they will provide;
- b) Their availability to the project and the amount of time anticipated;
- c) How rights to publications and patents will be handled; and,
- d) Willingness to comply with a confidentiality of information clause.

A consultant may not serve as Principal Investigator.

B. Understanding the Problem and Technical Approach

The National Cancer Institute expects to encounter compounds with potential activity in cancer and other indications that exhibit, from a pharmaceutical viewpoint, a range of complexity. Some projects may be straight forward, however, some compounds may present significant solubility problems not resolved by pH adjustment or the use of water miscible solvents. New approaches may be necessary to improve the solubility and intravenous delivery of these agents. To demonstrate the offeror's understanding of this project, the offeror should:

1. Describe his/her approach to the development of an intravenous dosage form
2. Describe new and novel formulation approaches which he/she would recommend for compounds that are not successfully solubilized using traditional methods
3. In addition to describing the mode of solubilization, also describe aspects of the method as it affects the intended application. These may include:
 - a) Physical and chemical stability of the delivery system
 - b) Sterilization techniques
 - c) Potential adverse biological effects of the delivery system
 - d) Suitability for manufacture on a production scale
 - e) Viscosity as it would affect "syringeability"

4. Discuss problems which may be encountered with the application of each solubilization technique. Include a clear definition of the development problems encountered as well as approaches used in their resolution.
5. Describe recent formulation problems which the proposed project team has resolved.

C. Facilities and Equipment

Describe in detail the laboratory space and equipment available for the performance of these studies. A detailed floor plan, including dimensions, should be provided for all laboratory space available for this project, identifying the areas where different facets of the work will be conducted. In situations where more than one building or institution is involved, a clear description of the locations of all sites and the distances and travel time between them should be given. Some of the antineoplastic agents are considered very toxic. Describe your proposed approach for the safe handling and disposing of toxic substances.

A description of all major equipment available for the work and their locations should be provided. While it is expected that most equipment will be under the direct control of the PI and Project team members, special mention should be made when this is not the case. When equipment is only available on a shared basis, some evidence should be provided as to who is responsible for controlling access and how the determination of priority of usage will be made (letter of commitment from Department Head, etc.). Describe supplemental facilities available to improve effectiveness of performance, e.g., library, computer.

In particular, the Contractor shall describe the following equipment for project use:

1. Equipment necessary for the determination of equilibrium solubility and stability of drugs in various media.
2. Analytical instrumentation (e.g., HPLC, GC) including make and model numbers.
3. Other equipment used to determine chemical and physical characteristics of the investigational compounds.
4. Development scale "shelf type" freeze dryer, ampoule sealer (crimpers) and other equipment and facilities necessary for manufacturing 50-150 units of the experimental dosage form for intravenous and oral use.

5. The substances to be studied under this project should be considered as potent, potentially hazardous agents, and thus, handled very carefully. Describe your organization's policy for handling potentially hazardous materials. If your organization has a safety manual, please reference it in your discussion and submit three (3) copies with your proposal.
6. Describe your organization's procedures for disposal of chemical and hazardous waste materials. Indicate your compliance with all relevant federal, state and local regulations regarding such waste materials.

D. Organizational Background and Experience

1. Describe the qualifications of your organization to provide support for this project, including previous experience in the development of pharmaceutical dosage forms.
2. Indicate the priority to be placed on this project compared to other existing commitments that may preclude or delay completion of this effort.