STATEMENT OF WORK

A. PROJECT OBJECTIVES

The Pharmaceutical Resources Branch (PRB), Developmental Therapeutics Program (DTP), Division of Cancer Treatment and Diagnosis (DCTD), National Cancer Institute (NCI) is seeking contractors for formulation development services. Formulation for intravenous, oral and other routes of administration will be required for all clinically evaluated compounds. Some compounds exhibit adequate pharmaceutical properties per se. However, some compounds present significant solubility, stability, and or bioavailability problems that are not amenable to solvent approaches or pH adjustment, but may require long range studies depending on Program needs and/or judgment of the P.O.

The National Cancer Institute is seeking contractors to 1) develop acceptable dosage forms for compounds to be subsequently evaluated in cancer patients and 2) to carry out innovative approaches and studies leading to more effective delivery of compounds possessing limited solubility, stability and/or bioavailability. The workload, for each contract, will likely be two to three (2-3) compounds for full-scale, and several small projects per year. NCI will select and provide the compounds to be studied. When available, analytical chemistry data will also be sent by the NCI.

In addition to solubility studies, the projects may require analytical work, particularly the development of a stability-indicating assay to monitor the integrity of the parent compound during the formulation development and in the final formulated product. Also, depending on the desired dosage form, the P.O. will guide the contractor to conduct necessary pre-formulation studies on the compounds of interest. These investigations will be directed toward a pharmaceutical dosage form that will meet certain solubility and adequate stability acceptable by the Government. The Contractor will provide a pilot batch of finished dosage forms and a written final project report. The contractor may also be asked to conduct bioavailability enhancement studies; therefore, capability to conduct bioavailability studies in experimental animal is also required. The National Cancer Institute at its discretion will perform toxicity testing in laboratory animals of new dosage forms and/or delivery systems, new excipients and/or vehicles and confirmation of biologic activity of experimental formulations.

B. STATEMENT OF WORK

The Contractor shall furnish services, qualified personnel, material, equipment, and facilities not otherwise provided by the Government under the terms of this contract as needed to perform the work described below:

1. Determine the solubility profile of the supplied bulk drug substance in various physiologically acceptable aqueous and certain water miscible and least-toxic organic solvents.
2. Carryout physicochemical studies to characterize molecules including but not limited to solubility and stability profiles of the supplied bulk drug substance.

3. Develop approaches for intravenous, oral, and other delivery routes of drugs exhibiting inadequate solubility, stability, and/or bioavailability depending on the need of the Program in collaboration with the P.O.

4. Develop if necessary suitable stability-indicating assays to detect the active drug substance subject to a variety of experimental conditions including the formulation *per se*, heat, light, oxygen, and other parameters.

5. Prepare kinetic profiles to predict the stability of the drug substance in various physiologically acceptable aqueous vehicles and certain organic solvents as determined by NCI. Determination of pKa and partition coefficient of drug substance may be required.

6. Apply the solubility and stability enhancement approaches when needed to prepare experimental dosage formulations on small scale for subsequent therapeutic and toxicological evaluation by NCI in animals. Pack, label, and ship the experimental products according to instructions provided by the Government.

7. Evaluate the experimental dosage form under simulated use conditions, i.e., completeness and clarity of the constituted solution after freeze drying, stability of this solution *per se* and after dilution with intravenous fluids in glass bottles and in polyvinyl chloride (pvc) bags and other suitable containers or bags for intravenous administration.

8. Carry out a short-term stability study of the finished dosage form under accelerated stability condition at $50^{O}C$, $37^{O}C$, $25^{O}C$, and under refrigeration condition as needed and directed by the Government in collaboration with P.O. per Program needs.

9. Depending on the Program needs and/or agent under investigation, it may be necessary to study and develop different types of dosage forms such as controlled release or targeted delivery systems as well as dosage forms for different routes of administrations. If the expertise or capabilities are not available to the offeror, they shall acquire the cooperation of experts or consultants with approval by the Project Officer.

10. The contractor may also be asked by P.O. to develop other dosage forms like controlled release or targeted delivery system as well as dosage forms for different route of administration other than parenteral. The contractor thus should have the capability to evaluate the bioavailability and/or effectiveness of the drug in the said formulation to be able to use the result in optimization of the said delivery system.

C. **Travel**

1. The Contractor shall expect that a senior investigator will attend a scientific meeting annually to present the developmental results. This travel will be recommended by Project Officer and must be approved in advance by the Contracting Officer.