

Statement of Work

Independently and not as an agent of the Government, the Contractor shall furnish all of the necessary services, qualified personnel, material, equipment, and facilities, not otherwise provided by the Government, as required to perform the Statement of Work as presented below:

1. Implement and validate appropriate analytical methodology that is sufficiently sensitive, specific, and reproducible for measurement and quantitation of assigned test agents (e.g., small molecule therapeutics and well-characterized biologicals) and metabolites in body fluids and/or tissues of animals and humans at therapeutic and/or toxic concentrations.
2. Conduct pharmacokinetic studies in animals (e.g., mice, rats, optionally larger animals) to support early lead and candidate drug characterization. Various routes of administration (e.g., intravenous, oral, intraperitoneal, subcutaneous, continuous infusion, etc.) may be utilized. Studies may include collection of multiple blood samples obtain plasma or serum and, in some studies, collection of urine, feces, and tissue and/or tumor samples.
3. Utilize analytical methods to determine concentrations of test agents in various matrices (cell extracts, media, plasma, urine, bile, saliva, tumors, and normal tissues) derived from:
 - (a) Pharmacokinetic studies conducted under item 2 above;
 - (b) Other Government-sponsored laboratories
4. Use state-of-the-art modeling software to fit concentration vs. time data (for plasma and possibly tissues) to suitable non-compartmental and/or compartmental pharmacokinetic models and calculate relevant pharmacokinetic parameters (e.g., half-life, volume of distribution, area under the curve, clearance, etc.) for a given agent and route of administration.
5. Calculate systemic bioavailability for various routes (e.g., oral, ip, sc) and determine if bioavailability is dose-dependent. Calculate mass-balance parameters if sufficient data is collected.
6. Determine the suitability of various formulations for the administration of test agents to animals by the desired route and at the desired dose level(s).
7. Conduct *in vitro* plasma protein binding and stability studies of test agents in biological fluids and tissues.
8. Conduce studies in tumor-bearing mice and collect plasma, tissue, and/or tumor samples for drug level determinations and analysis of specified pharmacodynamic endpoints.

9. Measure metabolites and/or degradation products of test agents present in blood, plasma, urine, and/or other fluids.
10. Characterize the plasma and tissue pharmacokinetics of major metabolites.
11. Store samples generated in-house or received from other laboratories under suitable conditions and ship samples to other laboratories upon request.