CONCEPT REVIEW

Contract Title: **Analytical Chemistry Support for NIEHS**

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Objectives

The purpose of these contracts is to provide analytical chemistry support for the National Institute of Environmental Health Sciences (NIEHS) including toxicology bioassays conducted through contract laboratories as part of the National Toxicology Program (NTP) as well as in-house studies conducted by researchers in the Division of Intramural Research, when requested. The analytical services are necessary to ensure that the bioassays are conducted with the intended chemicals (confirmation of identity and purity), at specified dosages (dose formulation, stability, and dose analysis), and with the knowledge of biomarkers of exposure and effect, internal dose, and tissue dosimetry, whenever required. This contract will provide assistance with the identity, stability, formulation, and quantitation issues of chemicals to individual researchers.

Background and Concept Statement

Major efforts to be performed under these contracts are method development, chemical procurement and synthesis, bulk chemical characterization, dosage formulation, formulation analysis, and biological sample analysis as well as toxicokinetics studies. Procurements are usually made through commercial sources and custom syntheses are usually arranged through commercial synthesis laboratories. Once received, unequivocal characterization of the test article is performed, not only to verify identity but also to distinguish any impurities that might confound interpretation of the toxicology results. Formulation and formulation analysis methods are developed specifically for test articles and validated for intra- and inter- laboratory use to ensure that the exposures cited are valid. Also, increasingly, it is important to supplement exposure data with toxicokinetic measurements of elimination rate and internal dose. This information is vital to ensure that toxicological evaluations can be used in developing scientifically valid toxicity information and risk assessment. Finally, tasks such as confirmation of the structure of reaction products and adducts are required to support mechanistic studies of NIEHS researchers.

The extensive level of effort, facilities requirements, and analytical throughput required for the support of the collective carcinogenicity, general toxicology, reproductive and developmental toxicology, immunology, neurotoxicology, cellular and genetic toxicology, and AIDS therapeutics studies conducted by NIEHS as well as support for in-house studies required the award of three chemistry support contracts in the last procurement. Up to three awards are anticipated under this recompetition.

Proposed Changes to the Current Statement of Work

The work to be performed under the recompetition is essentially the same as described above with a few additions. First, a provision will be made to conduct a screening analysis to determine identity and general purity (to within a few percent) of nominally single-component test articles. This change is necessary to support the anticipated initiative for high- and medium-throughput screening studies with high throughput rapid analysis for purity and identity of the test articles to ensure that the right chemical is being studied at some expected level of purity in a cost effective manner. Second, the analytical laboratory may be given an assignment to identify specific low-level impurities in a test article. This is to decouple the requirement for extensive work to identify and perhaps quantitate an impurity in a test article from the general characterization of the test article. It is hoped that this approach will avoid delays in submission of the more general reports. Third, a specific biochemical marker, such as protein binding or quantitation, may be measured using a published well-accepted method in support of mechanistic studies conducted in concert with bioassays. This effort would not constitute discovery or development of a method, but only use of a reported method for chemical measurement of a known biomarker.