

## CONTRACT CONCEPT REVIEW

### NTP Board of Scientific Counselors Meeting December 15, 2022

**Title:** Toxicology Support Contract Services for the Division of Translational Toxicology (DTT), National Institute of Environmental Health Sciences (NIEHS)

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#### **Background and Significance:**

The Division of Translational Toxicology (DTT) has a long history (> 40 years) of conducting toxicology studies to characterize the effects of agents of public health concern via contract mechanisms. DTT scientists conduct research using cutting-edge approaches and technologies to better understand how environmental exposures may impact human health. DTT scientists work in multidisciplinary teams and may collaborate with other federal agencies, institutes, industry, and academia. Research initiatives are further described at the following website: <https://www.niehs.nih.gov/research/atniehs/dtt/index.cfm>.

#### **Justification for Use of Contract Mechanisms:**

DTT requires support for conducting toxicity evaluations. The overall research approach utilized by DTT is designed to identify potential environmental contributors to human health effects and disease-based outcomes. The research approach for individual projects may be tiered, with early phases informing study design of later phases, and facilitating timely dissemination of information to the public. Test agents may include chemical, physical and biological agents, as well as non-chemical stressors. The Division has a need to evaluate the utility and relevance of rapidly evolving technologies and determine the potential for routine incorporation into toxicology evaluations. There is also a need to conduct in vitro studies, as well as short-term and long-term in vivo studies. In many cases, projects will require the generation and integration of in vitro and in vivo data to inform translation to human health effects. The scope of the required capabilities and the facilities, equipment, and personnel with relevant expertise needed to conduct these studies, exceed the resources available at NIEHS; therefore, we request approval to obtain support through contract mechanisms.

#### **Capabilities:**

Toxicology Support falls under the following functional areas: DTT anticipates the frequent need for support with expertise and capabilities in the following areas:

- **Problem formulation** : identify a discrete set of research questions based on a broad set of objectives.

- **Analytical chemistry support for inhalation studies:** characterization of the bulk material and development and validation of a generation and monitoring system.
- **On-test analytical chemistry support for non-inhalation studies:** confirmation of identity and purity and formulation preparation and analysis.
- **Conduct of in chemico reactivity assays or in vitro studies:** using immortal or primary cells, cell suspensions, cells grown on an air-liquid interface, or 3D complex tissue models with multiple cell types, including microphysiological systems.
- **In vivo animal studies:** with exposure beginning in utero or in young animals and by routes of administration including inhalation (whole body or nose only), oral (dosed feed, dosed water, gavage), dermal, or parenteral (intraperitoneal, subcutaneous, intravenous, intratracheal).
- **Evaluations for in vitro and in vivo studies:** RNA isolation, gene expression analysis, histopathology, biochemical and molecular assays, and characterization/fate/reactivity of materials in biological systems.

The proposed requirements encompass the current capabilities of the existing toxicology support contracts with an expanded focus on in chemico and in vitro capabilities and functional in vivo outcomes critical for human translation.