

CONTRACT CONCEPT REVIEW

NTP Board of Scientific Counselors Meeting

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Concept Title: Statistical Support for NTP and DIR

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Purpose

We propose having one contract to provide statistical support for research within DNTP and DIR:

1. **Statistical support for DNTP studies (67%).** Statistical support would include analysis of data from short-term and long-term rodent studies, particularly those having complex study designs (e.g., reproductive and continuous breeding and modified one-generation studies). Additionally, support would include analyses of data from high- and medium-throughput assays, toxicokinetics studies, laboratory experiments, and human studies.
2. **Statistical support for DIR studies (33%).** Statistical support would include analysis of data from laboratory experiments and human studies.

Background and Significance

The National Toxicology Program (NTP) is a federal, interagency program, headquartered at the NIEHS, whose goal is to safeguard the public by identifying substances in the environment that may affect human health. Toward that end, the NTP collects data using a variety of study designs that require varying methods of data analysis and/or modeling¹. Current NTP initiatives include examining the effects of cell phone radiation, endocrine disruptors, herbal supplements, chemical mixtures and nanomaterials, as well as high- and medium-throughput screening of chemicals. To fulfill its mission, in part, the NTP conducts short-term and long-term rodent studies; these studies may include unique design features that require customized statistical analyses, such as exposure of pregnant females with the likelihood of within-litter correlations among littermates. The NTP also conducts high- and medium-throughput assays, human studies in the NIEHS Clinical Research Unit (CRU) and surveys, as well as in-house research in the NTP laboratories.

The NIEHS Division of Intramural Research (DIR) conducts in vitro and in vivo research on biological and chemical processes, the role of environmental agents in human disease and dysfunction, underlying mechanisms of environmentally-associated diseases, and intervention/prevention strategies to reduce the effects of exposures to environmental agents². Examples of studies involving the current statistical support contract include modeling

¹ Specific NTP studies are described at <http://ntp.niehs.nih.gov>.

² Specific DIR studies are described at branch and laboratory links on <http://www.niehs.nih.gov/research/atniehs/dir/index.cfm>.

brain wave patterns and analysis of National Health and Nutrition Examination Survey (NHANES) data for associations of potential risk factors with myositis.

NIEHS invests much time and money into the collection of mission-related data; appropriate data analyses are required to support accurate and precise interpretation of study results.

Statistical support for NTP studies

The NTP conducts rodent toxicity and carcinogenicity studies for which the data may include survival times, organ and body weights, tissue concentrations, hematology and clinical chemistry, reproductive assessments, and indicators of presence or absence of tumors and non-neoplastic lesions of individual animals. Routine statistical analyses for these studies are automatically generated by the database in which the data resides. However, complex study designs or unique design characteristics (e.g., reproductive assessment by continuous breeding, modified one generation, double control groups, extra tissue sectioning, special lesion pooling, etc.) require customized statistical analyses. Furthermore, some NTP study designs include additional evaluations, such as immunotoxicity and/or neurobehavioral endpoints, which require customized statistical analyses.

Through the Tox21 program³ and other efforts, the NTP conducts high throughput and medium throughput screening assays on hundreds to several thousand chemicals. This large volume of data requires statistical and computational support to assess data analysis methodologies, model dose-response associations and evaluate responses across assays and across chemicals.

NTP conducts basic research to elucidate responses observed in rodent studies. Examples of recent laboratory studies include evaluations of effects of mixtures of chemicals; use of non-neoplastic endpoints to predict eventual cancer; use of in vitro data to predict in vivo pharmacokinetics; and mechanistic studies. Support activities include assisting with statistical issues related to experimental design and data analysis, carrying out analyses of data, and developing statistical and/or mathematical models to describe relationships and associations.

NTP occasionally conducts human studies, such as biomonitoring studies, pharmacokinetics studies, product use assessments, etc. Support activities include assisting with sample size and power calculations, carrying out analyses of data, and developing statistical and/or mathematical models to describe relationships and associations.

Statistical support for DIR studies

Most DIR researchers conduct basic research at the molecular, cellular, and organismal level. Statistical and mathematical modeling support activities include assisting with issues related to experimental design and data analysis, carrying out analyses of data, and developing statistical or mathematical models for describing associations or mechanisms.

³ <http://ncats.nih.gov/research/reengineering/tox21/tox21.html> and <http://ntp.niehs.nih.gov/results/hts/index.html>

Several DIR researchers collect or use human data from large-scale surveys, such as NHANES, or from studies at the NIEHS CRU. Statistical support for this research includes providing sample size and power calculations and statistical analysis of data.

Proposed Changes to the Current Statement of Work

The current statistical support contract provides statistical, mathematical and bioinformatics support to NTP and DIR. The approximate proportions of support for DNTP and DIR are, respectively, 67% and 33%, and are not expected to change. It is anticipated that the new contract will be up to 10 years.

The statement of work for the proposed new statistical support contract will be revised to remove the provision of bioinformatics support for DNTP. For DNTP, it is anticipated that a different, new contract will provide bioinformatics support. DIR bioinformatics support is currently provided by another contract and will not be included in the new contract, so that there is no duplication of effort.