CONTRACT CONCEPT REVIEW

NTP Board of Scientific Counselors Meeting
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Concept title: **Quality Assessment Support**

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Purpose

The purpose of the Quality Assessment Support Contract is to conduct audits and inspections of NTP testing facilities, study records, data, materials and reports. The findings of these audits and inspections are communicated to NTP staff and management so that they may be addressed, thus aiding the NTP in producing studies, data, and reports of the highest quality.

Background and Significance

The NTP conducts studies to evaluate the toxicity of various chemical, physical and biological agents. These studies typically assess one or more of prechronic toxicity, chronic toxicity and carcinogenicity, reproductive toxicity, developmental toxicity, immunotoxicity, or neurotoxicity; depending on the type(s) of data required. These studies typically cover a range of activities including chemistry (identity, purity analyses, characterization of dose formulations/exposure concentrations), in-life toxicity endpoints, functional endpoints, determination of internal dose, endpoints to examine potential mechanisms of toxicity, and histopathological assessments. Following completion of a study, pathology data are subjected to quality control by a quality assessment pathologist and then to peer review using a Pathology Working Group (PWG). The data generated from these studies are made available to the public by inclusion in an NTP Report series (current series include Technical Reports, Toxicity Reports, Genetically Modified Models Reports; however, new report series presenting reproductive, developmental, and immunotoxicity data are anticipated). Finally, the NTP makes a large amount of data available via electronic resources (websites, publically accessible databases, etc). These data often contribute to activities aimed at identifying hazards and assessing potential risk to human health that may result from exposure to environmental agents. Thus, generation of high quality data by the NTP is imperative.

The quality assessment support contract provides a resource that allows the NTP to conduct audits and inspections of studies, data, and reports. These activities

occur at multiple points during a given study. The following briefly outlines activities of the quality assessment support contract in the context of an NTP study.

- Audit of a Laboratory Report
  Following completion of a laboratory report by a testing laboratory, the report, study records, and pathology materials (wet tissues, blocks and slides) are submitted to the NTP; the testing laboratory is responsible for Good Laboratory Practice (GLP) compliance and quality assurance of studies it conducts. An audit of a laboratory report involves comparison of the report to study records and contractual standards, including the NTP Specifications applicable to that study[1], in order to assess the accuracy, consistency, and completeness of all factual (qualitative and quantitative) information in the report.

- Audit of Pathology Tables
  Following pathology quality control and peer review, the NTP authorizes revisions to the individual animal pathology data to reflect any NTP-approved diagnostic changes to the data. The audit of pathology tables assesses the accuracy and completeness of all NTP-authorized diagnostic changes made during the peer review process. In addition, pathology data are audited for a small sample of animals for which no changes were recommended to ensure data continuity and stability of unchanged diagnoses.

- Audit of an NTP Report
  Once the pathology data are finalized, the NTP summarizes study data in an NTP report (current and anticipated report series are listed above). The QA support contractor audits a draft of the NTP report, typically the version submitted by the NTP for peer review. This audit assesses the extent to which the data, results, and factual statements presented in the draft NTP report are reported in an accurate, complete, and consistent manner in comparison to study records. In many cases, the peer review drafts of NTP reports are also audited against final versions to assess the quality of the final product.

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[1]Specifications for the Conduct of Studies to Evaluate the Toxic and Carcinogenic Potential of Chemical, Biological and Physical Agents in Laboratory Animals for the National Toxicology Program (NTP) (http://ntp.niehs.nih.gov/ntp/Test_Info/FinalNTP_ToxCarSpecsJan2011.pdf) or the Specifications for the Conduct of Studies to Evaluate the Reproductive and Developmental Toxicity of Chemical, Biological and Physical Agents in Laboratory Animals for the National Toxicology Program (NTP) (http://ntp.niehs.nih.gov/ntp/Test_Info/FinalNTP_ReproSpecsMay2011_508.pdf)

- Audit of Electronic Information
  Much of the data generated by the NTP ultimately is contained in an electronic database or is available via an NTP website; for example, the NTP public website (http://ntp.niehs.nih.gov/). The audit of electronic information assesses the quality of such information.

For many types of data, the quality assessment support contractor audits 100% of the data. In contrast, for large datasets, sampling strategies are utilized. These may include a 10-20% audit for temperature and humidity data and dose/exposure concentration data or an audit of all control and high dose data with a scan of other dose/exposure groups for obvious discrepancies in individual animal toxicity data. If findings from the audit identify discrepancies using these sampling strategies, the NTP may decide that a 100% audit of the data is required.

In addition to the data audits listed above, quality assessment contract staff may also accompany NTP staff on site visits to testing laboratories to assess the extent to which the conduct of studies complies with relevant contractual standards, including the NTP Specifications and federal GLP regulations. These visits may include inspections of study procedures, facilities, and equipment, and audits of data for studies in progress.

The NTP has maintained a quality assessment support contract resource for nearly three decades. Over the 9.5 years of the current contract, ~450 audits have been conducted. The process outlined above highlights the points at which a given test article would require audit or inspection and completion of these tasks generally span several years. In practice, the QA support contractor must have the capability to conduct multiple audits of differing types and audits on data from different test articles simultaneously.

Proposed Changes to the Current Statement of Work

The statement of work (SOW) for the quality assessment support contract will be revised to reflect the need for audit or inspection of NTP studies, data and reports of increasing size, complexity and diversity. In addition, the SOW's capabilities will be expanded to include provision for auditing information and data used in NTP's literature-based evaluations and stored in electronic databases. The data would be extracted from published articles or reports and entered into the database or be calculated from the published data using established mathematical equations.