CONTRACT CONCEPT REVIEW

Scientific Advisory Committee on Alternative Toxicological Methods (SACATM) Meeting

September 5-6, 2012

Concept Title: Support Contract for the National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM)

Presenter: Dr. William Stokes, Director, NICEATM

Purpose of the Support Contract

The purpose of this contract is to provide scientific, technical, and administrative support for the National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM). NICEATM administers the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) and is responsible for ensuring compliance with specific duties and provisions of the ICCVAM Authorization Act of 2000 (42 U.S.C. 285*l*-3). In general, ICCVAM's duties include (1) advising on test method development and validation, (2) conducting interagency technical reviews of proposed new safety testing methods, (3) transmitting formal test method recommendations to Federal agencies, (4) promoting regulatory acceptance of scientifically valid test methods, and (5) fostering national and international harmonization of test methods.

Consistent with the NTP mission to develop and validate improved test methods, NICEATM also conducts independent validation studies for promising alternative test methods. The overall goal of NICEATM and ICCVAM is to promote the development, validation, and use of alternative and other new testing methods and strategies that are more predictive of human health, animal health, and ecological effects than currently available methods and strategies. NICEATM and ICCVAM contribute to the mission and vision of NIEHS and NTP by advancing improved safety assessment tools that will protect, promote, and advance the health of people, animals, and the environment.

Background on Current Contract

NICEATM is currently comprised of three Federal employees (Director, Deputy Director, and Special Assistant), and therefore relies heavily on contract staff to perform activities necessary to carry out its mission. The current contract provides ICCVAM and ICCVAM Interagency Working Group (WG) committee management assistance to NICEATM, which includes arranging for meetings, drafting meeting minutes, and preparing draft background review documents and analyses for consideration by ICCVAM and ICCVAM WGs. The contractor maintains the NICEATM-ICCVAM restricted and public websites, and prepares and provides other written communications for ICCVAM, ICCVAM WGs, and all other NICEATM and ICCVAM activities. The contractor provides technical and scientific support to evaluate the scientific validity of proposed new test methods, and prepares reports and analyses

necessary for ICCVAM working groups, peer review panels, expert panels, workshops, and NICEATM validation studies. The contractor assists in organizing committee-related activities such as peer reviews and workshops for test methods of interest to U.S. Federal agencies. The contractor supports the coordination of independent validation studies for high-priority alternative test methods that may reduce, refine (enhance animal well-being and lessen or avoid pain and distress), or replace animal use for regulatory safety testing. This includes the receipt and statistical analysis of data to evaluate the relevance and intra- and inter-laboratory reproducibility of test methods. The contractor compiles reference data generated using accepted test methods to assess the performance of new and revised test methods.

Proposed Changes to the Current Statement of Work

The statement of work for this recompetition reflects the projected support needed to achieve goals identified in the draft NICEATM-ICCVAM 2013-2017 Five Year Plan.[3] This document outlines how, consistent with ICCVAM's statutory duties and purposes, NICEATM and ICCVAM will contribute to the transformation of safety testing by fostering and promoting the incorporation of scientific advances and innovative technologies into new improved test methods and integrated testing and decision strategies. The new support contract will mirror the changing nature of toxicology by providing NICEATM-ICCVAM with increased expertise in the areas of bioinformatics and computational toxicology, while still maintaining a high level of expertise in traditional areas such as ocular, reproductive, and acute oral/dermal toxicity. Reducing animal use by vaccine manufactures (efficacy/potency testing) will continue to be a focus area.

Background on NICEATM and ICCVAM

In 1994, the Director of the National Institute of Environmental Health Sciences (NIEHS) created an *ad hoc* Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) to respond to directives in the National Institutes of Health (NIH) Revitalization Act of 1993 (42 U.S.C. 285*l*-1 and 42 U.S.C. 283*e*).[1] This Act required NIEHS to establish criteria for the validation and regulatory acceptance of alternative test methods and to develop a process through which alternative methods could be accepted for regulatory use once their usefulness and limitations for a specific proposed purpose was demonstrated through appropriate validation studies. The *ad hoc* ICCVAM committee consisted of representatives from the 15 U.S. Federal agencies represented on ICCVAM today. In 1997, the *ad hoc* ICCVAM committee published its final report, *Validation and Regulatory Acceptance of Toxicological Test Methods* (ICCVAM 1997). The same year, NIEHS, in conjunction with the 14 other Federal agencies, established a standing ICCVAM committee to (1) implement a process to evaluate new test methods of agency interest and (2) coordinate agency interactions related to the development, validation, acceptance, and national and international harmonization of toxicological test methods.

The ICCVAM Authorization Act of 2000 established ICCVAM as a permanent interagency committee of NIEHS under NICEATM. The ICCVAM Authorization Act was enacted to establish, wherever feasible, guidelines, recommendations, and regulations that promote the regulatory acceptance of new or revised scientifically valid toxicological tests that protect human and animal health and the environment while reducing, refining, or replacing animal tests and ensuring human safety and product effectiveness.

The Act states that the purposes of ICCVAM are to:

- Increase the efficiency and effectiveness of Federal agency test method review
- Eliminate unnecessary duplicative efforts and share experiences between Federal regulatory agencies
- Optimize utilization of scientific expertise outside the Federal government
- Ensure that new and revised test methods are validated to meet the needs of Federal agencies
- Reduce, refine, and replace the use of animals in testing, where feasible

ICCVAM consist of members representing 15 U.S. Federal regulatory and research agencies that use, generate, or disseminate toxicological information used to determine the safety or potential adverse health effects of chemicals and products to which workers and consumers may be exposed. ICCVAM's mission is to promote the development, validation, and regulatory acceptance of new, revised, and alternative regulatory safety testing methods. Emphasis is on alternative methods that will reduce, refine (less pain and distress), and replace the use of animals in testing while maintaining and promoting scientific quality and the protection of human health, animal health, and the environment. NICEATM provides scientific and operational support for ICCVAM and works closely with ICCVAM to carry out test method evaluations, sponsor test method validation studies, organize workshops and peer reviews, and communicate with ICCVAM stakeholders. NICEATM, in collaboration with ICCVAM, conducts technical reviews of alternative safety testing methods and forwards recommendations on behalf of the ICCVAM regarding their scientific validity through the Secretary of Health and Human Services.

NICEATM solicits and receives test method nominations and submissions for ICCVAM to consider and review. Test methods can be nominated for validation studies or technical reviews. The ICCVAM evaluation process involves an initial assessment by NICEATM of the adequacy and completeness of the test method nomination or submission and a determination by ICCVAM of the priority of the proposed method for technical evaluation or validation studies. Once a proposed test method is accepted for evaluation or validation, ICCVAM convenes an interagency working group with appropriate scientific and regulatory expertise to collaborate with NICEATM on the validation or evaluation process. Depending on the validation status of the proposed test method, ICCVAM, with NICEATM technical support, develops recommendations and priorities for appropriate evaluation activities. Such efforts might include an expert

workshop, an expert panel meeting, a peer panel meeting, an expedited peer review process, or a validation study.

Information on the status and results of NICEATM and ICCVAM activities, including meeting reports and background documents, is available on the NICEATM-ICCVAM website. Since ICCVAM was established, NICEATM, ICCVAM, and the ICCVAM member agencies have contributed to the regulatory acceptance of over 50 alternative methods to protect the health of people, animals, and the environment while reducing, refining, and replacing animal use[2].

NICEATM collaborates extensively with its international partner organizations on joint validation studies, independent peer reviews and workshops, and development of harmonized test method recommendations. In 2009, the United States, together with the European Union, Canada, and Japan, signed a Memorandum of Cooperation to establish the International Cooperation on Alternative Test Methods (ICATM). In 2011, Korea also signed the MOC. The agreement seeks to promote enhanced international cooperation and coordination among the five national validation organizations.

NICEATM prepares, reviews, and contributes to the development of internationally harmonized test method documents by the Test Guidelines Programme of the Organisation for Economic Co-operation and Development (OECD) and its 34 member countries. Documents include new test guidelines or proposals for new test guidelines, revisions of existing test guidelines, and guidance documents for alternative test methods. NICEATM contributed to the development of 18 such documents in 2010 and 2011. OECD test guidelines represent internationally agreed-upon testing methods that can be used by government, industry, and independent laboratories to determine the safety of chemicals and chemical preparations.

Additional information on NICEATM and ICCVAM and their activities and accomplishments, including biennial reports, can be found on their web site at: http://iccvam.niehs.nih.gov/.

References

1. ICCVAM Authorization Act. 2000. 42 U.S.C. 285*l*-3. Public Law 105-545. Available: http://iccvam.niehs.nih.gov/docs/about_docs/PL106545.pdf.

2. ICCVAM. 2012. Biennial Progress Report 2010-2011: Interagency Coordinating Committee on the Validation of Alternative Methods. NIH Publication No. 12-7873. Research Triangle Park, NC: National Institute of Environmental Health Sciences. Available: http://iccvam.niehs.nih.gov/about/ICCVAMrpts.htm.

3. The NICEATM-ICCVAM Five-Year Plan (2013-2017), A plan to advance innovative test methods of high scientific quality to protect and improve the health of people, animals, and the environment. DRAFT: May 14, 2012. Available: http://iccvam.niehs.nih.gov/docs/5yrPlan/2013-5YP-14May2012-draft.pdf.