



[Billing Code 4140-01-P]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods: Call for Nominations of High Throughput Screening (HTS) Assays for the Tox21 Initiative

AGENCY: Division of the National Toxicology Program (DNTP), National Institute of Environmental Health Sciences (NIEHS), National Institutes of Health (NIH).

ACTION: Call for Nominations.

SUMMARY: The multiagency Tox21 Initiative aims to improve hazard assessment of compounds potentially harmful to humans and the environment. This will be accomplished through the use of integrated high throughput screens that provide information on the ability of a substance to perturb biological pathways related to toxicity. On behalf of the Tox21 Consortium and its Assays and Pathways Working Group, the NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) is accepting nominations for HTS biochemical- or cell-based assays. Assays selected for further evaluation and found to be compatible with the HTS program will support Tox21 by providing data on endpoints that serve as markers for initiating or downstream events in toxicity pathways.

DATES: The nomination of HTS assays to Tox21 is an ongoing process and will continue to remain open. Periodic updates to this notice may be posted to reflect new focus areas of the Tox21 HTS program.

FOR FURTHER INFORMATION CONTACT: Nominations of assays should be submitted online at <http://iccvam.niehs.nih.gov/contact/Tox21-nomination.htm> (preferred means) or to Dr. Warren Casey, Deputy Director, NICEATM, NIEHS, P.O. Box 12233, Mail Stop: K2-16, Research Triangle Park, NC, 27709, (telephone) 919-541-2384, (fax) 919-541-0947, (email) niceatm@niehs.nih.gov. Courier address: NICEATM, NIEHS, Room 2034, 530 Davis Drive, Morrisville, NC 27560.

SUPPLEMENTARY INFORMATION:

Background

The Tox21 Consortium is a collaboration of the NIH Center for Translational Therapeutics (NCTT),¹ NIEHS/NTP,² U.S. Environmental Protection Agency (EPA),³ and U.S. Food and Drug Administration (FDA).⁴ The goal of Tox21 is to develop, validate, and translate innovative HTS methods to characterize the impact of chemicals on key steps in toxicity pathways and ultimately to provide tools to risk assessors to protect human health and the environment.

The Tox21 HTS Initiative aims to prioritize substances for in-depth toxicological evaluation, identify mechanisms of action for further investigation, and develop predictive models for *in vivo* biological responses using efficient, high throughput *in vitro* assays. Tox21 also aims to expand the ability to screen environmental compounds for organ-specific toxicity, focusing in particular on the liver, kidney, and nervous system.

The current Tox21 inventory of 10,000 chemicals covers a variety of classifications, including consumer products, food additives, human and veterinary drugs, manufacturing

¹ <http://nctt.nih.gov/27543703>

² <http://ntp.niehs.nih.gov/go/28213>

³ <http://www.epa.gov/ncct/Tox21/>

⁴ <http://www.fda.gov/>

intermediates, and pesticides. These 10,000 chemicals are being profiled using HTS assays designed to estimate toxicity potential and identify the specific perturbations they induce in biological pathways.

Request for Nominations of HTS Assays

NICEATM requests nominations of *in vitro* HTS toxicity assays that might be used in the Tox21 testing program. Tox21 intends to develop a systematic view of how chemicals interact with and affect biological systems using its collection of 10,000 chemicals. To achieve this goal, assays, which target all pathways relevant to toxicity, are needed to assess chemicals' effects. Nominated assays will be assessed for their overall applicability to the Tox21 HTS program in terms of biological relevance, cost, and potential for adaption to a HTS format. Suitable assays will then be prioritized for use by the NCTT. Protocol information and test data submitted in response to this notice may be incorporated into future NCTT and NICEATM reports and publications as appropriate.

Nominations should consider the following general criteria: (1) relevance to the goals of the Tox21 Initiative (<http://nctt.nih.gov/27543703>), (2) high throughput capability of the assay (96-well format or higher, with no obvious impediments to miniaturization to a 1536-well format), (3) evaluation of preliminary assay performance using appropriate reference compounds, (4) validation status of the assay, (5) availability of complete detailed protocols, and (6) efficiency and cost of the assay. A list of compatibility criteria for 1536-well biochemical and cell-based assays is available at <http://nctt.nih.gov/27545107>.

Assay nominations should be submitted electronically using the online form (<http://iccvam.niehs.nih.gov/contact/Tox21-nomination.htm>). When submitting HTS assay nominations and protocol information, please reference this **Federal Register** notice and provide

appropriate contact information (name, affiliation, mailing address, phone, fax, email, and sponsoring organization as applicable). NICEATM prefers submission of the nominations via the website identified above; however, submissions by mail, fax, or email are acceptable. Questions about the submission process should be directed to Dr. Warren Casey (see “FOR FURTHER INFORMATION CONTACT”).

Background Information on NICEATM

NICEATM was established in 1998 to administer and provide scientific support for the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM), which is composed of 15 member Federal agencies and includes the EPA, FDA, NIEHS, and NIH. The ICCVAM Authorization Act of 2000 (42 U.S.C. § 2851-2, 2851-5, available at <http://iccvam.niehs.nih.gov/about/PL106545.htm>) established ICCVAM as a permanent interagency committee of the NIEHS under NICEATM. NICEATM and ICCVAM conduct technical evaluations of new, revised, and alternative safety testing methods with regulatory applicability and promote the scientific validation and regulatory acceptance of safety-testing methods that more accurately assess the safety and hazards of chemicals and products and that will reduce, refine (enhance animal well-being and decrease or eliminate pain and distress), or replace animal use. NICEATM also conducts independent validation studies to assess the usefulness and limitations of new, revised, and alternative test methods and strategies applicable to the safety testing needs of Federal agencies. In 2012, NICEATM began providing support to Tox21 regarding HTS assay nomination and review.

NICEATM and ICCVAM welcome the public nomination of new, revised, and alternative test methods and strategies applicable to the needs of Federal agencies. Additional

information about NICEATM can be found on the NICEATM-ICCVAM website
(<http://iccvam.niehs.nih.gov>).

Dated: April 5, 2012

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[FR Doc. 2012-8942 Filed 04/12/2012 at 8:45 am; Publication Date: 04/13/2012]