



UPDATE

National Toxicology Program

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Headquartered at the
National Institute of Environmental
Health Sciences NIH-HHS

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Highlights of the 49th Annual SOT Meeting

Article by Ed Kang reprinted from *eFACTOR*, April 2010

Leading toxicologists and environmental health scientists shared their latest findings, discussed funding and training opportunities, received input on future research priorities, and more at this year's Society of Toxicology (SOT) meeting in Salt Lake City. NIEHS and NTP led the way at the 49th annual SOT conference with investigators and program officers hosting more than 30 sessions and 60 posters.

Among the highlights of this year's conference were the [Live Updates](#) provided by attendees. NIEHS and NTP representatives, including Director Linda Birnbaum, Ph.D., and guests, such as Cheryl Walker, Ph.D., outgoing president of SOT and an NIEHS [grantee](#), posted nearly 100 real-time updates. These unscripted postings, viewable in a day-by-day account, gave web viewers a unique "behind the scenes" perspective of the conference.

Next year's meeting is the Society's 50th and will be held in Washington, D.C. It promises to be a spectacular event with more of what makes this gathering of the toxicology community such an amazing experience.

Some of the highlights about NIEHS scientists at the 2010 conference:

- [A View from the Top](#) Birnbaum recapped the Institute's successes for the past year and her thoughts for the future. She talked about the link between environmental health and prevention, and the connection between bench, policy and public health.
- [Promises, Pitfalls and the Potential of High Throughput Technologies](#) Sri Nadadur, Ph.D., co-chaired a discussion of technologies to better understand toxic responses and for generating global molecular profiles.
- [The Best of Toxicology](#) [SOT] recognized some of the very best in our profession: Mike Waalkes, Ph.D. was elected to the SOT Council, and Rick Paules, Ph.D., was awarded the Leading Edge in Basic Science Award for his contributions to understanding fundamental mechanisms of toxicology.



- [The Future of Toxicology](#) Students were able to enjoy an opportunity to network with professionals. A panel of experts including NTP Toxicologist Michelle Hooth, Ph.D., spoke to 200 students about opportunities, successes and lessons-learned. Hooth also co-chaired a collaborative informational [session](#) on tungsten and tungsten alloys.



NIEHS/NTP PROVIDING
**LIVE
UPDATES**
AT THE SOCIETY OF TOXICOLOGY
CONFERENCE IN SALT LAKE CITY
(March 7-11)

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- [Herbals and Women's Health Discussion](#) Nigel Walker, Ph.D., of NTP, reviewed dietary supplements, with Retha Newbold, recently retired from NIEHS, speaking on developmental exposure, and Mark Cline, D.V.M., Ph.D., of Wake Forest University speaking on adult exposure to soy.
- [Immunotox Specialty Section Celebrates Its Silver Jubilee](#) The Immunotox Specialty Section celebrated 25 years at SOT. The highlight of the event was the "Paper of the Year" award won by a project funded by an NTP-NIOSH interagency agreement.
- [Organize It and They Will Come](#) Ray Tice, Ph.D., of NTP, and Bob Kavlock, Ph.D., of EPA, organized "The Tox21 Community and the Future of Toxicology." Related presentations included efforts to develop a 10,000 compound library for testing by Cynthia Smith, Ph.D., and insights into the future of toxicology from Linda Birnbaum.

These and many other updates are available through the end of April at www.niehs.nih.gov/LiveatSOT. ●

(Ed Kang is a public affairs specialist in the Office of Communications and Public Liaison and a regular contributor to the Environmental Factor.)

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The Way Forward

From AltTox.org, December 4, 2009



In December 2008, the Proctor & Gamble Company and the Humane Society of the United States recognized the Tox21 program with the North American Alternative Award for outstanding scientific contributions to advance viable alternatives to animal testing. (see NTP Update January 2009). The Tox21 program winners included Christopher Austin of the

NIH Chemical Genomics Center (NCGC), Raymond Tice of the NTP, and Robert Kavlock of the Environmental Protection Agency. The award, which included a \$25,000 grant to support the ongoing alternative methodologies efforts, was used to partially fund a post-doctoral fellow working on the Tox21 program at the NCGC. The post-doctoral fellow – Dr. Sunita Shukla – recently contributed the essay, A New Perspective on the Past, Present and Future of Toxicity Testing (<http://alttox.org/ttrc/overarching-challenges/way-forward/shukla/>) to The Way Forward series in the AltTox newsletter. The essay provides her perspective as a young scientist contributing to the transformation of toxicology as it moves into the 21st century. ●

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Upcoming Events

May 10, 2010

NTP Board of Scientific Counselors
NIEHS
111 TW Alexander Drive
Research Triangle Park, NC

June 17-18, 2010

Scientific Advisory Committee on
Alternative Toxicological Methods
U.S. Environmental Protection Agency
109 TW Alexander Drive
Research Triangle Park, NC

June 21-22, 2010

NTP Board of Scientific Counselors
NIEHS
111 TW Alexander Drive
Research Triangle Park, NC

September 14-16, 2010

International Workshop on Alternative
Methods to Reduce, Refine, and
Replace the Use of Animals in
Vaccine Potency and Safety Testing
Sponsor: NICEATM-ICCVAM
NIH Natcher Conference Center
Bethesda, MD

October 12-13, 2010

NTP Board of Scientific Counselors
Technical Reports Review
Subcommittee
NIEHS
111 TW Alexander Drive
Research Triangle Park, NC

December 6-7, 2010

NTP Board of Scientific Counselors
NIEHS
111 TW Alexander Drive
Research Triangle Park, NC

<http://ntp.niehs.nih.gov/go/calendar>



NTP Board of Scientific Counselors

May 10, 2010 Meeting

The first of several meetings in 2010 for the NTP Board of Scientific Counselors (BSC) is scheduled for May 10 at the NIEHS, 111 TW Alexander Drive, Research Triangle Park, NC. The preliminary agenda topics for this meeting are (1) peer review of the draft NTP Brief on Soy Infant Formula (http://cerhr.niehs.nih.gov/chemicals/genistein-soy/SoyFormulaUpdt/DraftNTPBriefSoyFormula16Mar2010_508.pdf), (2) the research concept for NTP studies on isoflavones in soy infant formula, (3) a concept on the approach for the Center for the Evaluation of Risks to Human Reproduction evaluation of low-level lead (A concept for the evaluation of low-level lead was discussed by the BSC at a meeting in December 2007; minutes available at <http://ntp.niehs.nih.gov/go/9741>), and (4) Technical Reports Review Subcommittee report for the meeting held November 19, 2009.

The preliminary agenda, background materials, public comments, and any additional information, when available, will be posted on the BSC meeting website (<http://ntp.niehs.nih.gov/go/165>). The deadline for submission of written comments is April 26, 2010, and for pre-registration to attend the meeting, including registering to present oral comments, is May 3, 2010. The opportunity for making oral public comments will be available both in-person at the meeting or via conference line.

June 21-22, 2010 Meeting

Planning is underway for a meeting of the NTP BSC in June. Although the agenda is not yet final, preliminary topics include (1) peer review of draft substance profiles for the Report on Carcinogens, (2) research concepts for nominations to the NTP testing program, and (3) a concept for a proposed evaluation activity by the Center for the Evaluation of Risks to Human Reproduction. Information about the meeting will be announced in the Federal Register and as available posted to the NTP website (<http://ntp.niehs.nih.gov/go/165>). ●

Contact Information: Dr. Lori White, Designated Federal Officer, NTP Office of Liaison, Policy and Review, NIH/NIEHS, P.O. Box 12233, MD K2-03, Research Triangle Park, NC 27709; T: (919) 541-9834; FAX: (919) 541-0295; whiteld@niehs.nih.gov

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Report on Carcinogens (RoC) Center

The NTP is nearing completion of the evaluation of the final set of candidate substances under review for the 12th Report on Carcinogens. Peer review of the draft substances profiles for cobalt-tungsten carbide: hard metals and powders, glass wool fibers, and formaldehyde will be conducted by the NTP Board of Scientific Counselors at a meeting scheduled for June 21-22, 2010. Each draft substance profile will contain the NTP's preliminary listing recommendation for the candidate substance and the science supporting that recommendation. The draft substance profiles will be available by April 21, 2010, at <http://ntp.niehs.nih.gov/go/165>. Notice of their availability, request for public comment, and further information about the meeting will be announced in the Federal Register and communicated via the NTP listserv. Notice about the last set of candidate substances for the 12th RoC will also be forthcoming in the Federal Register notice. ●

Contact Information: Dr. Ruth M. Lunn, Director, Report on Carcinogens Center, NIH/NIEHS, P.O. Box 12233, MD K2-14, Research Triangle Park, NC 27709; T: (919) 316-4637; FAX: (919) 541-0144; lunn@niehs.nih.gov

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NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM)

International Workshop on Alternative Methods for Vaccine Potency and Safety Testing



Regulatory authorities require potency and safety testing during the production of human and veterinary vaccines to ensure their effectiveness and minimize adverse health effects. For some vaccines, these assessments require the use of laboratory animals for studies such as immunization and immunization-challenge procedures. A public workshop will be held on September 14-16, 2010, at the William H. Natcher Conference Center at the National Institutes of Health in Bethesda, MD. This workshop will bring together international experts to review currently available alternatives and identify research, development, and validation activities needed to advance the use of alternative methods that may further reduce, refine (less pain and distress), and replace the use of animals for vaccine potency and safety testing. NICEATM and the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) are organizing the workshop in cooperation with the European

Centre for the Validation of Alternative Methods, the Japanese Center for the Validation of Alternative Methods, and Health Canada. Information about the workshop is available on the NICEATM-ICCVAM website at:

<http://iccvam.niehs.nih.gov/meetings/BiologicsWksp-2010/BiologicsWksp.htm>

NICEATM and ICCVAM Proposals for International Test Guidelines Approved

The Test Guidelines Programme National Coordinators for the 30 member countries of the Organisation for Economic Co-operation and Development (OECD) met on March 23-25, 2010. The Coordinators approved several new international test guidelines and a guidance document developed by NICEATM and ICCVAM in cooperation with their partners in the International Cooperation on Alternative Test Methods (ICATM). The test guidelines and guidance document include the following alternative methods evaluated and recommended by ICCVAM:

- An updated Test Guideline 429 for using the murine local lymph node assay (LLNA) to assess if chemicals and products may cause allergic contact dermatitis. The revised test guideline provides an updated protocol that reduces animal use by 20% compared to the previous version of the guideline, and also incorporates an optional reduced LLNA procedure that allows for an additional 40% reduction in animal use.
- A new test guideline for the LLNA: BrdU-ELISA. This non-radioactive version of the LLNA uses the nucleotide analog bromodeoxyuridine (BrdU) to assess lymph node cell proliferation instead of radiolabeled substances.
- A new test guideline for the LLNA: DA. This version of the LLNA measures adenosine triphosphate content to assess lymph node cell proliferation instead of radiolabelled markers.
- A guidance document on using cytotoxicity tests to estimate starting doses for acute oral systemic toxicity tests. The approach uses an IC_{50} value from an *in vitro* basal cytotoxicity test to estimate the *in vivo* LD_{50} value. The estimated LD_{50} value can then be used as a starting dose for assessing acute oral systemic toxicity using the up-and-down procedure, the acute toxic class test method, or the fixed dose procedure. This approach can reduce animal use as much as 50% for some substances. The guidance document is based on the results of a NICEATM international validation study and ICCVAM recommendations that were endorsed by U.S. Federal agencies in 2008.
- A new test guideline on *in vitro* test methods for skin irritation. These test methods are based on multilayered, highly differentiated three-dimensional reconstructed epidermis models comprised of cultured primary human-derived epidermal keratinocytes. Following topical application of test substances, relative cell viability is measured to identify substances that may have the potential to cause substantial irritation to human skin without using animals.



The National Coordinators will communicate their recommendations to the Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology, the policy body that oversees the OECD Chemicals Programme. The test guidelines and guidance documents will be made available on the OECD website after their adoption is announced formally at the joint meeting, which is scheduled for fall of 2010.

Information about the OECD Test Guidelines Programme and links to adopted Test Guidelines and Guidance Documents can be found on the OECD website at http://www.oecd.org/document/40/0,3343,en_2649_34377_37051368_1_1_1_1,00.html.

NICEATM-ICCVAM Society of Toxicology Posters Now Available

NICEATM and ICCVAM presented eight posters at the annual meeting of the Society of Toxicology in Salt Lake City, Utah on March 7-11, 2010. The topics discussed in the posters included:

- Four posters presenting recommendations and findings from the ICCVAM evaluation of the LLNA:
 - Recommendations on the LLNA applicability domain
 - Evaluation of the use of the LLNA for assessing skin sensitizer potency
 - Analysis supporting sample size recommendations for the LLNA
 - Assessment of the use of various mouse strains in the LLNA
- ICCVAM recommendations that reduce or eliminate pain and distress during *in vivo* ocular toxicity testing
- Progress in international cooperation and harmonization in the evaluation of alternative test methods
- An Implementation Plan to achieve the goals presented in the NICEATM-ICCVAM Five-Year Plan
- An update on an ongoing validation study of a test method to identify potential endocrine disruptors

Copies of the posters and their abstracts are available at <http://iccvam.niehs.nih.gov/meetings/SOT10/sotablst.htm>.



Former ICCVAM Chair Receives SOT Award

During the Society of Toxicology (SOT) meeting, Dr. Leonard Schechtman, former ICCVAM chair, received the Enhancement of Animal Welfare Award. This award honors a Society of Toxicology member whose scientific accomplishments have led to a marked reduction in the use of experimental animals for research. The presentation of this award to Dr. Schechtman recognized his outstanding contributions to the advancement of toxicology through the development of methods that reduce, refine, and replace the use of experimental animals

in research, education, and regulatory safety testing.

Dr. Schechtman, who retired from the Food and Drug Administration in 2006, served as the agency's principal agency representative to ICCVAM from 1999 – 2006 and was chair of ICCVAM from 2002 - 2006. Some notable accomplishments by ICCVAM under Dr. Schechtman's leadership include:

- Development of guidelines for nomination and submission of alternative test methods for consideration by ICCVAM.
- Definition and implementation of test method performance standards to expedite validation.
- Enhanced cooperation with international validation organizations.
- Evaluation and transmittal of recommendations to U.S. Federal agencies on the use of alternative test methods for assessment of dermal corrosion, acute systemic toxicity, ocular toxicity, and pyrogenicity.

Dr. Schechtman has also contributed significantly to the development and adoption of internationally harmonized guidance on the validation and use of novel safety evaluation methods. ●

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The NTP website offers electronic files of the Report on Carcinogens and the library of NTP Technical Reports and NTP Toxicity Reports. The PDF files of these reports are available free-of-charge through the NTP website at <http://ntp.niehs.nih.gov> (see Resources).

Contact Information: NTP Office of Liaison, Policy and Review, NIEHS, P.O. Box 12233, MD K2-03, Research Triangle Park, NC 27709; T: (919) 541-0530; FAX: (919) 541-0295; CDM@niehs.nih.gov

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