



UPDATE

National Toxicology Program

APRIL 2009

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

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NIEHS and NTP Formally Welcome Birnbaum as Director

Article by Eddy Ball, reprinted from *eFACTOR*, April 2009

NIEHS and the National Toxicology Program (NTP) formally welcomed their new leader, Director Linda Birnbaum, Ph.D., on March 13 with a morning installation ceremony and an "Afternoon of Science" of distinguished lecturers. Guests at the installation ceremony included NIH Acting Director Raynard Kington, M.D., Ph.D., and other NIH officials, U.S. Congressman David Price, Ph.D., NIEHS and NTP advisory and scientific board members, friends, family and Institute employees.

The ceremony was held in the Rodbell Auditorium at NIEHS, which was filled to capacity. It was by turns symbolic and inspirational, light-hearted and humorous, and profoundly moving.

The highlight of the day was the formal swearing-in of Birnbaum by Kington. However, as Birnbaum and the other speakers made clear, the ceremony was also deeply infused with symbolism — an event marking the appointment of the first woman and first toxicologist to hold the position of director in the Institute's 43-year history and a reassessment of the direction NIEHS will take in the months and years ahead.

The event was held as the vernal equinox approached, during Women's History Month and just before the annual meeting of the Society of Toxicology. With rain falling heavily outside, Birnbaum observed, "The drought here at NIEHS has ended." As she presented her vision for the Institute, Birnbaum pointed to new opportunities and the significant advances in environmental health science research and translation she hopes NIEHS and NTP will make.

After taking her oath of office, Birnbaum thanked her guests and introduced her family. "It is truly an honor to serve as the Director of the NIEHS and the NTP," she said. "This is a very special day for me, and it's even more special because so many of my family members, friends and colleagues are here to share this occasion with me." Seated in the audience were her mother, husband, David, two daughters, and a host of friends and colleagues from her careers at NIEHS, NTP and the U.S. Environmental Protection Agency.

Birnbaum spoke of her personal quest for equilibrium between the personal and professional — "I try to have some fun everyday" — and her optimism that America today is indeed experiencing the rise of "a national movement for positive and constructive change" in the nation's relationship with the environment. As she reminded the audience that "we all need to make the whole [of NIEHS and public health in general] bigger than the sum of the parts," she reiterated her dedication to comprehensive translational research, "open communication and transparency," and



Birnbaum and Kington joined NIH Associate Director for Management Colleen Barros during the reception that followed the installation ceremony. (Photo courtesy of Steve McCaw)



“empowering those who work for me and with me” at what she described as “the world’s premier environmental health research organization.”

“There is no better time than now,” Birnbaum said, to tease out “the more subtle actors” in disease processes and discover “more ways to share our science” nationally and globally. In her quest for inclusion, she promised to promote new and renewed relationships with sister institutes and centers at NIH, other governmental agencies, universities, advocates and the general public.

In their remarks, Kington, Price, and master of ceremonies and former NTP Associate Director and Environmental Health Perspectives Editor-in-Chief George Lucier, Ph.D., looked to Birnbaum’s past and future with comments about her qualifications for her leadership role. They also referred to her ability to balance her roles as a leader, mother, scientist, wife, citizen and grandmother — and the way her infectious humor helps put the gravitas of science and leadership into perspective.

The ceremony concluded with a performance by her daughter, New York actress Lisa Birnbaum. The young performer balanced her statement that “my mom is a role model for women and people everywhere” with a light-hearted little girl’s dedication — “This is for you, Mommy.” Relying solely on her vocal range, she then delivered an impressive rendition of the theme song from “The Man of La Mancha,” inspiring the audience “to dream the impossible dream” — and leaving several in the audience struggling to hold back their tears. ●

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NTP Board Peer Reviews Draft Cancer Reports

Article by Robin Mackar, reprinted from *eFACTOR*, April 2009

Report on Carcinogens (RoC)

National Toxicology Program (NTP) reports on five of the nine compounds being considered for listing in the 12th Report on Carcinogens (RoC) were for the first time peer reviewed by the NTP Board of Scientific Counselors (BSC) February 24 in Rodbell Auditorium. Four of the chemicals, including *ortho*-nitrotoluene, used in the synthesis of some dyes; aristolochic acids, a family of acids used in herbal medicine; captafol, previously used to control fungal diseases in fruits, vegetables and other plants; and riddelliine, a toxic plant component, underwent a thorough, but relatively quick review by the BSC. The majority of the day was spent discussing the weight of evidence presented in the styrene draft substance report.



Seated from left to right are NTP Associate Director John Bucher, Ph.D., Chair Raymond Novak, Ph.D., NIEHS/ NTP Director Linda Birnbaum, Ph.D., and NTP lead scientist for the technical reports, Michelle Hooth, Ph.D. (Photo courtesy of Steve McCaw)

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Upcoming Events

April 28-29, 2009

NICEATM/ICCVAM Independent Scientific Peer Review Panel on the Murine Local Lymph Node Assay

Natcher Conference Center
National Institutes of Health
45 Center Drive, Bethesda, MD

May 19-21, 2009

NICEATM/ICCVAM Independent Scientific Peer Review Panel on Alternative Ocular Safety Testing Methods

U.S. Consumer Products Safety Commission Headquarters
4330 East West Highway
Bethesda, MD

June 9-10, 2009

Report on Carcinogens Expert Panel Meeting: Scientific Review of Certain Glass Wool Fibers

Chapel Hill Sheraton Hotel
One Europa Drive, Chapel Hill, NC

June 25-26, 2009

Scientific Advisory Committee on Alternative Toxicological Methods (SACATM) Meeting

Hilton Arlington
950 North Stafford Street
Arlington, VA

July 23-24, 2009

NTP Board of Scientific Counselors Meeting

NIEHS
111 TW Alexander Drive
Research Triangle Park, NC

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

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Styrene is a highly flammable liquid used worldwide in the production of polymers that are incorporated into products such as rubber, plastic, insulation, fiberglass, pipes, automobile parts, food containers and carpet backing. The NTP's preliminary policy decision for listing styrene is that *styrene is reasonably anticipated to be a human carcinogen* based on limited evidence in humans, sufficient evidence of carcinogenicity in experimental animals and supporting mechanistic data.

“This is the first time we’re bringing draft substance profiles from the RoC for peer review to the Board,” said Mary Wolfe, Ph.D., director of the NTP Office of Liaison, Policy and Review, during her presentation to the BSC. She outlined the new multi-step scientific review process for the **RoC** and presented the board’s charge, which is to determine whether the scientific information cited in each draft substance report is technically correct, clearly stated and supports the NTP’s preliminary decision regarding its listing in the RoC. She explained the status of the remaining four RoC candidate substances — cobalt-tungsten carbide powders and hard metals, metalworking fluids, certain glass wool fibers, and formaldehyde — and told the board they would likely be peer reviewing those substances in the next year.

Wolfe also highlighted the multiple opportunities for public input into the process, which was evident at the board meeting. Eight public commenters were provided ample opportunity to offer oral remarks or make presentations regarding the styrene draft substance profile, in addition to providing written comments for the record. Board members also had an opportunity to discuss and deliberate the comments with the public presenters.

The public comments followed a scientific presentation on each compound made by NTP staff. In the case of styrene, RoC Director Ruth Lunn, Dr. P.H., discussed the critical papers and data used by the NTP to recommend listing styrene as *reasonably anticipated to be a human carcinogen*. Her analysis included human, animal and mechanistic data.

The NTP recommended listing aristolochic acids as *known to be human carcinogens* based on sufficient evidence from studies in humans and supporting mechanistic data. Captafol, o-nitrotoluene, and riddelliine are recommended to be listed as *reasonably anticipated to be human carcinogens*.

Each compound reviewed had two to six lead BSC or ad hoc reviewers. Other BSC members also participated in the discussion of each profile. Overall, the BSC provided editorial and thoughtful comments and input on each draft report that the NTP will use to finalize its policy decision regarding the compound’s listing in the RoC. The BSC meeting was chaired by Kenneth Portier, Ph.D.

Technical Reports on NTP 2-Year Cancer Bioassays

The following day, the NTP BSC Technical Reports Review Subcommittee completed its independent public peer review of six draft NTP technical reports. These reports are used by regulatory authorities worldwide for developing risk assessments and regulations to establish “safe” levels of chemicals in the environment.

The agents studied included goldenseal root powder, a dietary supplement ingredient; androstendione, a dietary supplement banned in 2004 for over-the-counter sales; β -myrcene, an ingredient used in the production of scents and flavorings; 2,3',4,4',5-pentachlorobiphenyl (PCB 118), a dioxin-like compound evaluated as part of NTP's program on dioxins; 3,3',4,4'-tetrachloroazobenzene, a contaminant found in herbicides; and tetralin, an industrial solvent. An overview of each report was presented by an NTP study scientist, followed by the committee's peer review. An additional presentation by NTP pathologist Mark Cesta, D.V.M., following the overview of the β -myrcene report provided more detail about the histopathologic features of the non-neoplastic renal diseases that were seen in the rat studies. All of the agents presented were found to have carcinogenic activity in the rodent models. The draft reports are available [online](#). The technical report reviews were chaired by Raymond Novak, Ph.D. ●

For information regarding the meeting: <http://ntp.niehs.nih.gov/go/15849>

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Institute Enjoys a Banner Year at SOT

Article by Eddy Ball, reprinted from *eFACTOR*, April 2009

It was a record-setting year at the Society of Toxicology (SOT) 48th Annual Meeting in Baltimore March 15-19 – both for SOT itself and for NIEHS and top-level sponsor the National Toxicology Program (NTP). NIEHS and NTP rolled out their largest exhibit ever and showcased new Director Linda Birnbaum, Ph.D., a major NTP initiative and a range of continuing and American Recovery and Reinvestment Act (ARRA) funding opportunities.

SOT reports that first day registrations hit a record of 6,671 participants for the five days that included an unprecedented 27 symposia, 19 workshops, 14 roundtables, and six keynote and named lectures — many of them featuring scientists and students with ties to NIEHS programs. The SOT Annual Meeting is the major professional development forum for the scientists of NIEHS and the NTP, as well as for Superfund Basic Research Program (SBRP) and other extramural program grantees worldwide. One of those NIEHS grantees, SOT President Ken Ramos, Ph.D., who served as chair of this year's meeting, is also a member of the NIEHS National Advisory Environmental Health Sciences Council.

Current and former NIEHS grantees received awards at the meeting. SBRP trainee Courtney Kozul and NTP Postdoctoral Fellow Scott Auerbach, Ph.D. were also honored.

A “Meet the NIEHS Director” session drew a capacity audience to hear Birnbaum speak on March 18, as the new NIEHS and NTP leader — a toxicologist and former president of SOT — outlined her vision for the Institute in a time of great challenges and opportunities. Toxicologists were naturally eager to hear how one of their own will guide NIEHS research and funding priorities in the months and years ahead.

NTP scientists Paul Foster, Ph.D., and Dori Germolec, Ph.D., were featured speakers for the March 17 NTP Exhibitor Hosted Session “[NTP Criteria for Hazard Identification in Non-Cancer Studies](#).” They explained how NTP plans to predict developmental, reproductive and immune system challenges of chemicals with more subtle, but significant functional and biological pathway effects — offering the public and regulatory agencies a clearer and more comprehensive estimate of the health risks they may pose.

Two events were of special interest to current and potential grantees — an NIH Brown Bag Lunch on March 17 and two full days of walk-in and appointment opportunities for one-on-one discussions with NIEHS grant administrators. Staff from the NIH Center for Scientific Review joined NIEHS grant administrators at the lunch on March 17 to field questions about the review process and grant opportunities, including those newly available through the ARRA.

NTP Deputy Program Director for Science Nigel Walker, Ph.D., entered the nanotechnology fray as the SOT scientific delegate at the annual debate on March 16 arguing the proposition “Nanotoxicology Is NOT Much Ado About Nothing” with European Societies of Toxicology (EUROTOX) delegate Kai Savolainen, Ph.D., of the Finnish Institute of Occupational Healthreceives. Walker and Savolainen will give an encore performance of their encounter at the 46th Congress of EUROTOX in Dresden, Germany September 13–16.

NIEHS and NTP investigators and program officers led no fewer than 24 sessions, ranging from educational and career development to platform and symposium sessions. Nearly 60 poster displays featured the research of NIEHS and NTP senior scientists and trainees.

Along with her own luncheon session and posters, Birnbaum also had a chance to see the fruits of her labors as a mentor. On March 18, Birnbaum was recognized as the sponsor of trainee Michele La Merrill (see related [story](#)), who received the Award for Best Manuscript at the Meeting from the Occupational and Public Health Specialty Section (OPHSS).

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NTP's Cunningham Selected as a Fellow of the ATS



NTP Host Susceptibility Branch Michael Cunningham, Ph.D., DABT, has been selected as a Fellow of the Academy of Toxicological Sciences (ATS). The vision of the ATS is to be recognized as the leading international organization that certifies toxicologists based on their education, professional experience, demonstrated achievement, proven ability and scientific expertise. Certification, which is recognized by the title of Fellow, is based on peer review by ATS Fellows who serve on the Board of Directors. ATS certifies toxicologists not only to recognize their professional achievement but also to assure that toxicology professionals, who participate in research and testing, determine safety, risk and risk-benefit, and who make regulatory decisions that impact public health and the environment, exercise sound scientific judgment, free of bias, based on the scientific data.

NTP's Auerbach Wins Prestigious SOT Poster Award



NTP Toxicology Branch Fellow Scott Auerbach won the SOT Risk Assessment Specialty Section Perry J. Gehring Best Postdoc Abstract Award. Auerbach submitted an extended description of the data presented in his poster "Independent validation of gene expression based hepatocarcinogenicity prediction models," which detailed the research observations and their relevance to hazard characterization. This poster was part of the Bioinformatics and Prediction of Toxicity Poster Session on March 17. The award is funded by an endowment to honor the legacy of Perry J. Gehring, D.V.M., Ph.D., who served as SOT president in 1980-1981. It consists of a \$500 check to Auerbach and achievement plaques for him and his advisor, NTP Senior Toxicologist Richard D. Irwin, Ph.D. ●

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NTP Board of Scientific Counselors

The next NTP Board of Scientific Counselors meeting will be held on July 23-24, 2009, at the NIEHS, 111 T.W. Alexander Drive, Research Triangle Park, NC. Preliminary agenda items include NTP nominations and concepts, a report on the recommendations from the NTP Technical Reports Review Subcommittee meeting with FDA/NCTR and NIOSH, contract concept reviews for: (1) investigative absorption, distribution, metabolism, and excretion (ADME) studies of toxicants in NTP animal model systems and (2) toxicology and carcinogenicity studies, and presentations on studies being conducted under NIEHS/NTP interagency agreements.

NTP Board of Scientific Counselors Technical Reports Review Subcommittee

The subcommittee met on February 25, 2009, at the NIEHS, Research Triangle Park, NC to peer review the findings and conclusions from draft NTP technical reports using conventional rodent models. The Subcommittee made the recommendations recorded below regarding the findings and conclusions of the draft reports. These findings will be reported to the NTP Board of Scientific Counselors at its meeting on July 23-24, 2009. Additional details about the meeting are available on the NTP website at <http://ntp.niehs.nih.gov/go/165>.

Goldenseal Root Powder (TR 562)

The subcommittee accepted unanimously (8 yes, 0 no) the conclusions as written, *clear evidence of carcinogenic activity* of goldenseal root powder in male and female F344/N rats, *some evidence of carcinogenic activity* in male B6C3F1 mice, and *no evidence of carcinogenic activity* in female B6C3F1 mice.

Androstenedione (TR 560)

The subcommittee accepted unanimously (8 yes, 0 no) the conclusions, *equivocal evidence of carcinogenic activity* of androstenedione in male and female F344/N rats, and *clear evidence of carcinogenic activity* in male and female B6C3F1 mice. The subcommittee recommended that the specific types of liver neoplasms in male B6C3F1 mice that increased with treatment be reported in the conclusions.

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2,3,4,4',5 -Pentachlorobiphenyl [PCB 118] (TR 559)

The subcommittee accepted (7 yes, 1 no) the conclusions as written, *clear evidence of carcinogenic activity* of PCB 118 in female Harlan Sprague-Dawley rats.

3,3',4,4' -Tetrachloroazobenzene [TCAB] (TR 558)

The subcommittee accepted unanimously (8 yes, 0 no) the conclusions, *clear evidence of carcinogenic activity* of TCAB in male and female Harlan Sprague-Dawley rats, and *clear evidence of carcinogenic activity* in male B6C3F1 mice. The Subcommittee recommended the conclusion, *clear evidence of carcinogenic activity* in female B6C3F1 mice based upon increased incidences of fibrosarcoma and fibrosarcoma or malignant schwannoma (combined) of the skin.

β-Myrcene (TR 557)

The subcommittee accepted unanimously (8 yes, 0 no) the conclusions, *clear evidence of carcinogenic activity* of β-myrcene in male F344/N rats, *equivocal evidence of carcinogenic activity* in female F344/N rats, *clear evidence of carcinogenic activity* in male B6C3F1 mice, and *equivocal evidence of carcinogenic activity* in female mice. The subcommittee recommended that the specific types of liver neoplasms in B6C3F1 mice that increased with treatment be reported in the conclusions.

Tetralin (TR 561)

The subcommittee accepted (7 yes, 1 no) the conclusions, *some evidence of carcinogenic activity* of tetralin in male and female F344/N rats, *no evidence of carcinogenic activity* in male B6C3F1 mice, and *equivocal evidence of carcinogenic activity* in female B6C3F1 mice. The subcommittee recommended that the specific types of hepatocellular neoplasms in female F344/N rats that increased with treatment be reported in the conclusions. ●

Contact Information: Dr. Barbara Shane, Executive Secretary, NTP Office of Liaison, Policy, and Review, NIH/NIEHS, P.O. Box 12233, MD K2-03, Research Triangle Park, North Carolina 27709; T: (919) 541-4253; FAX: (919) 541-0295; shane@niehs.nih.gov

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Report on Carcinogens Center

Scientific Review of Certain Glass Wool Fibers June 9-10, 2009

Availability of Draft Background Document and Request for Public Comment

The expert panel meeting for the scientific review of certain glass wool fibers is scheduled for June 9-10, 2009, at the Chapel Hill Sheraton Hotel, Chapel Hill, NC. At this public meeting, the expert panel will (1) peer review the draft background document on certain glass wool fibers and (2) provide a recommendation and scientific justification for the listing status of certain glass wool fibers in the 12th Report on Carcinogens (RoC). Public comments on the draft background document can be made in writing to the RoC Center or in person at the public meeting. Meeting information and the RoC draft background document on certain glass wool fibers is available on the RoC website (<http://ntp.niehs.nih.gov/go/29679>) or by contacting the RoC Center (see contact information below).

Availability of the Final RoC Background Document on Cobalt Tungsten Carbide: Powders and Hard Metals and Expert Panel Recommendation on its Listing Status in the 12th RoC

The public meeting for the scientific review of cobalt tungsten carbide powders and hard metals took place on December 9-10, 2008, at the Chapel Hill Sheraton Hotel, Chapel Hill, NC. At this meeting, the expert panel peer reviewed the draft background document and made a recommendations regarding the listing status of cobalt tungsten carbide: powders and hard metals in the 12th Report on Carcinogens. The final RoC background document, peer review comments on the document, and recommendation and scientific justification for listing status are posted on the RoC website (<http://ntp.niehs.nih.gov/go/29682>) and are also available in hardcopy or on CD from the RoC Center (contact information below). ●

Contact Information: Dr. Ruth M. Lunn, 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 Center for the Evaluation of Risks to Human Reproduction (CERHR)

Genistein and Soy Formula Update Evaluation

Planning continues for a second expert panel to consider the new literature and to review and update the conclusions drawn by the previous expert panel on the reproductive and developmental toxicity of genistein (Birth Defects Research (Part B) 77:485-638, 2006) and soy infant formula (Birth Defects Research (Part B) 77:280-397, 2006). Preparation of the initial updated draft report is underway and a public meeting of the expert panel is anticipated to occur in the late fall of 2009. A Federal Register notice [Vol. 73, No. 192, pp 57360-1] was published October 2, 2008, requesting public comment on the proposed review as well as nominations of expert panel members.



Hydroxyurea and Bisphenol A Monographs

Printed copies of the NTP-CERHR Monographs on Hydroxyurea and Bisphenol A are now available (see contact information below). The monographs are also available on CERHR website at

<http://cerhr.niehs.nih.gov/reports/index.html#reports> ●

Contact Information: Dr. Michael D. Shelby, Director CERHR, NIH/NIEHS, P.O. Box 12233, MD K2-04, Research Triangle Park, NC 27709, T: (919) 541-3455; FAX: (919) 316-4511; shelby@niehs.nih.gov

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

NICEATM Announces Peer Review Panel Meeting on the Murine Local Lymph Node Assay and Availability of Revised Draft Background Review Documents and Draft ICCVAM Test Method Recommendations



NICEATM, in collaboration with the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM), will convene an independent scientific peer review panel to evaluate updated information on three non-radioactive modified versions and new applications for the Murine Local Lymph Node Assay (LLNA). The panel meeting will take place April 28-29, 2009, at the Natcher Conference Center, National Institutes of Health, Bethesda, MD, and is open to the public.

The LLNA is a test method used to determine the allergic contact dermatitis potential of chemicals and products for regulatory hazard classification and labeling purposes. As an accepted alternative to traditional guinea pig tests, the LLNA uses fewer animals and eliminates pain and distress. The proposed applications could expand the range of substances and products that can be tested in the LLNA, while the proposed new versions may allow for broader use of the LLNA and also avoid the need for radioactive markers.

Meeting information is available at <http://iccvam.niehs.nih.gov/meetings/LLNAPanelMtg09/LLNAPanelMtg09.htm>. The draft ICCVAM test method recommendations and draft background review documents are available at: http://iccvam.niehs.nih.gov/methods/immunotox/llna_PeerPanel.htm.

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NICEATM Announces Peer Review Panel Meeting on Alternative Methods for Ocular Safety Assessments and the Availability of Draft Background Review Documents and Draft ICCVAM Test Method Recommendations

NICEATM, in collaboration with ICCVAM, will convene an independent scientific peer review panel to evaluate several alternative ocular toxicity testing methods and approaches. The panel will evaluate a proposal for the routine use of topical anesthetics, systemic analgesics, and humane endpoints to avoid or minimize pain and distress during *in vivo* ocular irritation safety testing. Methods to be reviewed by the panel include a testing strategy using *in vitro* test methods to assess the eye irritation potential of antimicrobial cleaning products and the validation status of four test methods for identifying moderate and mild irritants and products that do not require labeling for eye hazards. The panel will also consider the validation status of the *in vivo* low volume eye test. The meeting will take place May 19-21, 2009, at the U.S. Consumer Products Safety Commission Headquarters, Bethesda Towers Building, 4330 East West Highway, Bethesda, MD and is open to the public.

Persons wishing to attend the meeting should register by May 5, 2009 at http://iccvam.niehs.nih.gov/contact/reg_form_OcuPanel.htm. Additional information about the meeting and materials are available at <http://iccvam.niehs.nih.gov/methods/ocutox/PeerPanel09.htm>.

New Page on NICEATM-ICCVAM Website Summarizes Test Method Evaluation Activities

NICEATM has added a new page to its website that provides a summary of the status of ongoing and completed NICEATM-ICCVAM alternative test method evaluation projects, as well as updates on collaborative projects with other validation organizations.

The page provides a graphic representation of the progress towards evaluation and acceptance milestones. Links from this list link to more details for each project milestone including peer review reports, other publications, and national and international regulatory acceptance consideration and decisions. There are also links to relevant documents or pages on the NICEATM-ICCVAM website. This page should serve as a useful resource for current information on the status of specific projects.

Visit the new webpage at: <http://iccvam.niehs.nih.gov/methods/milestones.htm>. Information on the status of projects that have led to U.S. regulatory acceptance of alternative test methods is available at: <http://iccvam.niehs.nih.gov/methods/milestones-US.htm>.

Agency Responses to *In Vitro* Pyrogenicity Test Method Recommendations

NICEATM, on behalf of ICCVAM, forwarded the ICCVAM Test Method Evaluation Report: Validation Status of Five *In Vitro* Test Methods Proposed for Assessing Potential Pyrogenicity of Pharmaceuticals and Other Products (NIH Publication Number 08-6392) to U.S. Federal agencies in November 2008 for regulatory consideration. The report includes ICCVAM recommendations regarding the usefulness and limitations of the five test methods based on their current validation status. ICCVAM recommended that these and other *in vitro* alternative test methods should be considered prior to conducting *in vivo* pyrogenicity testing, and should be used where determined appropriate for specific testing situations.

Federal agency responses to the ICCVAM recommendations are posted as they are received on the NICEATM-ICCVAM website at <http://iccvam.niehs.nih.gov/methods/pyrogen/pyrogen.htm>. ●

Contact Information: Dr. William S. Stokes, Director, NICEATM, NIH/NIEHS, P.O. Box 12233, MD K2-16, Research Triangle Park, NC 27709; T: 919-541-2384; FAX: (919) 316-0947; niceatm@niehs.nih.gov

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NTP Publications October-December 2008

Auerbach, S. S., J. Mahler, G. S. Travlos and R. D. Irwin. A comparative 90-day toxicity study of allyl acetate, allyl alcohol and acrolein. *Toxicology* (2008) v. 253 (1-3): pp. 79-88

PubMed: <http://www.ncbi.nlm.nih.gov/pubmed/18817840>

DOI: <http://dx.doi.org/10.1016/j.tox.2008.08.014>

Beseler, C. L., L. Stallones, J. A. Hoppin, M. C. R. Alavanja, A. Blair, T. Keefe and F. Kamel. Depression and Pesticide Exposures among Private Pesticide Applicators Enrolled in the Agricultural Health Study. *Environmental Health Perspectives* (2008) v. 116 (12): pp. 1713-1719

PubMed: <http://www.ncbi.nlm.nih.gov/pubmed/19079725>

DOI: <http://dx.doi.org/10.1289/ehp.11091>

Hermon, T. L., A. B. Moore, L. Yu, G. E. Kissling, F. J. Castora and D. Dixon. Estrogen receptor alpha (ERalpha) phospho-serine-118 is highly expressed in human uterine leiomyomas compared to matched myometrium. *Virchows Arch* (2008) v. 453 (6): pp. 557-69

PubMed: <http://www.ncbi.nlm.nih.gov/pubmed/18853184>

DOI: <http://dx.doi.org/10.1007/s00428-008-0679-5>

Hotchkiss, A. K., C. V. Rider, C. R. Blystone, V. S. Wilson, P. C. Hartig, G. T. Ankley, P. M. Foster, C. L. Gray and L. E. Gray. Fifteen years after "Wingspread" - Environmental endocrine disrupters and human and wildlife health: Where we are today and where we need to go. *Toxicological Sciences* (2008) v. 105 (2): pp. 235-259

PubMed: <http://www.ncbi.nlm.nih.gov/18281716>

DOI: <http://dx.doi.org/10.1093/toxsci/kfn030>

Kamel, F. Organophosphate Insecticides and Neurologic Dysfunction in the Agricultural Health Study. *Epidemiology* (2008) v. 19 (6): pp. S80-S80

PubMed: Not Available

DOI: Not Available

Karlsson, A., J. Ungerback, A. Rasmussen, J. E. French and P. Soderkvist. Notch1 is a frequent mutational target in chemically induced lymphoma in mouse. *International Journal of Cancer* (2008) v. 123 (11): pp. 2720-2724

PubMed: <http://www.ncbi.nlm.nih.gov/pubmed/18798262>

DOI: <http://dx.doi.org/10.1002/ijc.23832>

Koujitani, T., T. V. Ton, S. A. Lahousse, H. H. Hong, N. Wakamatsu and R. C. Sills. K-ras cancer gene mutations in lung tumors from female Swiss (CD-1) mice exposed transplacentally to 3'-azido-3'-deoxythymidine.

Environ Mol Mutagen (2008) v. 49 (9): pp. 720-6

PubMed: <http://www.ncbi.nlm.nih.gov/pubmed/18800350>

DOI: <http://dx.doi.org/10.1002/em.20420>

Mattie, M. D., M. K. McElwee and J. H. Freedman. Mechanism of Copper-Activated Transcription: Activation of AP-1, and the JNK/SAPK and p38 Signal Transduction Pathways. *Journal of Molecular Biology* (2008) v. 383 (5): pp. 1008-1018

PubMed: <http://www.ncbi.nlm.nih.gov/pubmed/18793645>

DOI: <http://dx.doi.org/10.1016/j.jmb.2008.08.080>

Morgan, D. L., G. P. Flake, P. J. Kirby and S. M. Palmer. Comments on respiratory toxicity of diacetyl in C57Bl/6 mice – Response. *Toxicological Sciences* (2008) v. 105 (2): pp. 433-434

PubMed: Not Available

DOI: Not Available



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