



UPDATE

National Toxicology Program

October 2007

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

What's Inside:

Calendar – Page 2

NTP Board of Scientific
Counselors
Page 2

CERHR
Page 3

Staff Publications
Pages 4-5

NICEATM
Pages 6

Subscribe to the
NTP Listserv
Page 6

Recent Publications
Page 6

Melnick Earns Rall Award for Work in Health Advocacy

Reprinted from
The Nation's Health, September 2007

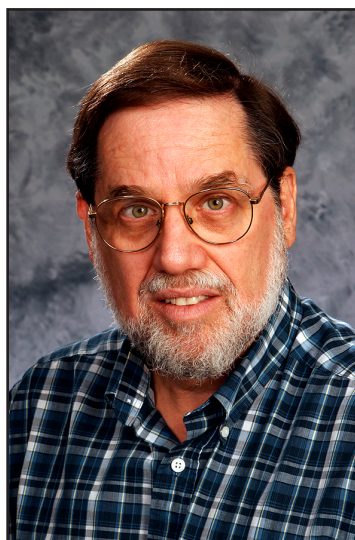
For his outstanding contributions to public health through science-based advocacy, Ronald L. Melnick, Ph.D, will receive the 2007 David P. Rall Award for Advocacy in Public Health at American Public Health Association's (APHA) 135th Annual Meeting in Washington, D.C.

Melnick is senior toxicologist and director of special programs in the Environmental Toxicology Program at the National Institute of Environmental Health Sciences. He is heralded by his colleagues for standing up to those who propose weakening chemical exposure standards based on inadequate evidence.

"He has devoted his entire professional life to improving our knowledge and understanding of issues concerning public health, working constantly with both a vision of the future and a tight grasp on the daily tasks of getting there," said APHA member Jennifer Sass, Ph.D, in a letter nominating Melnick.

She described Melnick as a "committed workhorse and public servant, laying the scientific foundation for sound policies that protect public and environmental health."

Melnick's research has advanced the understanding of the toxicity of widely used industrial chemicals such as



butadiene, isoprene and glycol esters as well as drinking water disinfection by-products such as chloroform. He has testified about the cancer-causing potential of DEHP, a chemical contained in medical devices such as intravenous tubing and dialysis machines, and the gasoline additive known as MTBE.

He has worked at the National Institute of Environmental Health

Sciences since 1980, where he has been involved in toxicity and carcinogenesis studies, as well as research on the health effects of environmental and occupational agents. He spent a year as an agency representative to the White House Office of Science and Technology Policy to work on interagency assessments of health risks of environmental agents and on risk assessment research needs in the federal government.

The author or co-author of more than 140 journal articles, book chapters and technical reports related to the health effects of environmental agents, Melnick has organized several symposiums and workshops on health risks associated with exposure to toxins. He has served on numerous scientific review boards and advisory panels, including those of the North Carolina Department of Environment and Natural Resources and the U.S. Environmental Protection Agency. ♦

(Photo courtesy of Steve McCaw)



Upcoming Events

October 15-16, 2007

RoC Expert Panel Meeting on Captafol and *ortho*-Nitrotoluene
Chapel Hill Sheraton Hotel
One Europa Drive
Chapel Hill, NC 27514

December 6, 2007

NTP Board of Scientific Counselors
National Institute of Environmental Health Sciences
111 T.W. Alexander Drive
Research Triangle Park, NC 27709

February 27-28, 2008

NTP Board of Scientific Counselors Technical Reports Review Subcommittee
National Institute of Environmental Health Sciences
111 T.W. Alexander Drive
Research Triangle Park, NC 27709

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

NTP Board of Scientific Counselors

The next NTP Board of Scientific Counselors (BSC) Meeting will be held on December 6, 2007, at NIEHS. Preliminary agenda items include: review of NTP study nominations, a report from a workshop on mold and review of a contract concept to study mold, actions from the May 2007 NTP peer review of 7 draft technical reports by the BSC Technical Reports Review Subcommittee, nominations to the Center for the Evaluation of Risks to Human Reproduction, the process and timeline for the 12th Report on Carcinogens, and implementation of recommendations from recent NTP workshops and October 2006 retreat.

Details about the meeting will be announced in the Federal Register and posted on the NTP web site <http://ntp.niehs.nih.gov> (select *Advisory Board & Committees*) or can be obtained by contacting the Executive Secretary, Dr. Barbara Shane. The BSC meeting is open to the public and public comment, both written and oral, is welcome on any topic. ♦

Contact Information: Dr. Barbara Shane, Executive Secretary, NTP Liaison and Scientific Review Office, NIH/NIEHS, P.O. Box 12233, MD A3-01, Research Triangle Park, NC 27709; T: 919- 541-4253; shane@niehs.nih.gov

The NTP Board of Scientific Counselors Technical Reports Review Subcommittee

The NTP Board of Scientific Counselors Technical Reports Review Subcommittee will meet in a public forum on February 27-28, 2008, at the NIEHS, 111 TW Alexander Drive, Research Triangle Park, NC. The subcommittee will peer review the findings and conclusions from 7 draft NTP Technical Reports on studies performed in conventional rats and mice and an additional draft report on the photocarcinogenicity of aloe vera performed in the SKH-1 mouse. A 90-day NTP Toxicity Report on estragole (TOX 82) will also be reviewed.

The draft reports tentatively scheduled for review are:

TR 544 Dibromoacetonitrile
TR 549 Bromochloroacetic acid
TR 551 Isoeugenol
TR 553 Photocarcinogenicity study of aloe vera
TR 554 5-(Hydroxymethyl)-2-furfural
TR 555 1,2-Dibromo-2,4-dicyanobutane
TR 556 Chromium picolinate monohydrate
TR 557 β -Myrcene
TOX 82 Estragole

This meeting will be announced in the Federal Register and details posted on the NTP web site <http://ntp.niehs.nih.gov> (select *Advisory Board & Committees*) or can be obtained by contacting the Executive Secretary, Dr. Barbara Shane. Public comment, both written and oral, is welcome on any report. ♦

Contact Information: Dr. Barbara Shane, Executive Secretary, NTP Liaison and Scientific Review Office, NIH/NIEHS, P.O. Box 12233, MD A3-01, Research Triangle Park, NC 27709; T: 919- 541-4253; shane@niehs.nih.gov



NTP Center for the Evaluation of Risks to Human Reproduction (CERHR)

Bisphenol A Second Expert Panel Meeting

CERHR convened a second meeting of the independent, 12-member scientific panel on August 6-8, 2007, in Alexandria, VA to complete its evaluation of bisphenol A (BPA). At this meeting, the expert panel evaluated information on human exposure and the reproductive and developmental toxicities of BPA. BPA is a high-production-volume chemical used to produce epoxy resins, polyester resins, polysulfone resins, polyacrylate resins, polycarbonate plastics, and flame retardants.

In brief, the panel's greatest level of concern was directed towards possible neural and behavioral effects caused by BPA exposure during infancy and childhood. The members expressed "some" concern for these types of effects, which is a moderate level of concern. The panel expressed "minimal" concern that exposure to BPA during infancy and childhood causes reproductive effects, such as accelerations in puberty. A summary of the August meeting can be found at: <http://cerhr.niehs.nih.gov/chemicals/bisphenol/bisphenol-mtg.html>

The final expert panel report is in preparation and will be released for public comment this fall. Availability of the final report will be announced in the Federal Register and public comment on the report will be solicited. The report will be posted on the CERHR web site <http://cerhr.niehs.nih.gov> and made available in hardcopy or on CD from CERHR (contact information at the end of article).

Audit of Bisphenol A Draft Expert Panel Reports

In March 2007, the NTP announced that it would review services provided to CERHR for the BPA review by the Sciences International, Inc. contract. This review included an audit of the (1) selection of literature on BPA relevant to the expert panel's evaluation and (2) incorporation of input from expert panel members into draft reports. The NTP completed this audit in July 2007 and concluded that the draft expert panel reports included consideration of all



relevant references and reliably included changes requested by the expert panel members. Thus, the draft expert panel reports are useful for the CERHR evaluation of bisphenol A. For the audit report, see <http://cerhr.niehs.nih.gov/chemicals/bisphenol/Slauditreviewreportv12072407.pdf> ♦

Contact Information: Dr. Michael D. Shelby, Director, CERHR, NIH/NIEHS, P.O. Box 12233, MD EC-32, Research Triangle Park, NC 27709, T: (919) 541-3455; shelby@niehs.nih.gov

Report on Carcinogens

Captafol and *ortho*-Nitrotoluene Expert Panel Meeting

Scientific review of candidate substances under consideration for the 12th Report on Carcinogens (RoC) will begin with an expert panel meeting on captafol and *ortho*-nitrotoluene. This public meeting will take place on October 15-16, 2007, at the Chapel Hill Sheraton Hotel, One Europa Drive, Chapel Hill, NC. Details about the meeting, including registration, submission of public comments, and access to the background documents on these candidate substances, were announced in the Federal Register (72FR41755) and are available on the RoC web site <http://ntp.niehs.nih.gov/go/29679> or by contacting C. W. Jameson. ♦

Contact Information: Dr. C.W. Jameson, Director, Report on Carcinogens, NIH/NIEHS, P.O. Box 12233, MD EC-14, Research Triangle Park, NC 27709, T: (919) 541-4096 jameson@niehs.nih.gov



NTP Staff Publications: June - August 2007

The names of NIEHS/NTP staff are identified in bold. The URL to the article is provided although in some incidences, access may require a subscription to the journal.

Chan, S. S., J. H. Santos, J. N. Meyer, B. S. Mandavilli, D. L. Cook, Jr., C. L. McCash, **G. E. Kissling**, A. Nyska, **J. F. Foley**, B. van Houten, W. C. Copeland, V. E. Walker, **K. L. Witt** and **J. B. Bishop** (2007). "Mitochondrial toxicity in hearts of CD-1 mice following perinatal exposure to AZT, 3TC, or AZT/3TC in combination." *Environmental and Molecular Mutagenesis* 48(3-4): 190-200.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16395692

Delclos, K. B., C. C. Weis and **R. R. Newbold** (2007). "Reproductive and developmental toxicity of phytoestrogens." *Birth Defects Research Part a-Clinical and Molecular Teratology* 79(5): 402-402.

<http://gateway.isiknowledge.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=CustomerName&SrcApp=CustomerName&DestLinkType=FullRecord&DestApp=WOS&KeyUT=ISI:000246425800092>

Dobrovolsky, V. N., J. G. Shaddock, R. A. Mittelstaedt, M. E. Bishop, S. M. Lewis, F. W. Lee, A. Aidoo, **J. E. A. Leakey**, **J. K. Dunnick** and R. H. Heflich (2007). "Frequency of Hprt mutant lymphocytes and micronucleated erythrocytes in p53-haplodeficient mice treated perinatally with AZT and AZT in combination with 3TC." *Environmental and Molecular Mutagenesis* 48(3-4): 270-282.

<http://gateway.isiknowledge.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=CustomerName&SrcApp=CustomerName&DestLinkType=FullRecord&DestApp=WOS&KeyUT=ISI:000245318100013>

Doi, A. M., G. Hill, J. Seely, J. R. Hailey, **G. Kissling** and **J. R. Bucher** (2007). " α 2u-globulin nephropathy and renal tumors in national toxicology program studies." *Toxicologic Pathology* 35(4): 533-540.

<http://www.scopus.com/scopus/inward/record.url?eid=2-s2.0-34247224061&partnerID=40&rel=R6.5.0>

Dunnick, J. K., K. A. Thayer and G. S. Travlos (2007). "Inclusion of Biomarkers for Detecting Perturbations in the Heart and Lung and Lipid/Carbohydrate Metabolism in National Toxicology Program Studies." *Toxicol Science*

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=17490986

Golomb, E., A. Schneider, E. Houminer, **J. Dunnick**, **G. Kissling**, J. B. Borman, A. Nyska and H. Schwalb (2007). "Occult cardiotoxicity: Subtoxic dosage of bis(2-chloroethoxy)methane impairs cardiac response to simulated ischemic injury." *Toxicologic Pathology* 35(3): 383-387.

<http://gateway.isiknowledge.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=CustomerName&SrcApp=CustomerName&DestLinkType=FullRecord&DestApp=WOS&KeyUT=ISI:000245117300007>

Hong, H. H., J. Dunnick, R. Herbert, T. R. Devereux, **Y. Kim** and **R. C. Sills** (2007). "Genetic alterations in K-ras and p53 cancer genes in lung neoplasms from Swiss (CD-1) male mice exposed transplacentally to AZT." *Environmental and Molecular Mutagenesis* 48(3-4): 299-306.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16395694

(Continued on page 5)



(Continued from page 4)

Huff, J., **R. M. Lunn**, M. P. Waalkes, L. Tomatis and P. F. Infante (2007). "Cadmium-induced cancers in animals and in humans." *International Journal of Occupational and Environmental Health* 13(2): 202-212.

<http://gateway.isiknowledge.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=CustomerName&SrcApp=CustomerName&DestLinkType=FullRecord&DestApp=WOS&KeyUT=ISI:000247494000009>

Jefferson, W. N., E. Padilla-Banks and **R. R. Newbold** (2007). "Disruption of the female reproductive system by the phytoestrogen genistein." *Reprod Toxicol* 23(3): 308-16.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=17250991

Meyer, J. N., **W. A. Boyd**, G. A. Azzam, A. C. Haugen, **J. H. Freedman** and B. Van Houten (2007). "Decline of nucleotide excision repair capacity in aging *Caenorhabditis elegans*." *Genome Biology* 8(5):

<http://gateway.isiknowledge.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=CustomerName&SrcApp=CustomerName&DestLinkType=FullRecord&DestApp=WOS&KeyUT=ISI:000246983100008>

Newbold, R. R., E. Padilla-Banks, R. J. Snyder, T. M. Phillips and **W. N. Jefferson** (2007).

"Developmental exposure to endocrine disruptors and the obesity epidemic." *Reprod Toxicol* 23(3): 290-6.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=17321108

Pacyniak, E. K., X. Cheng, **M. L. Cunningham**, K. Crofton, C. D. Klaassen and G. L. Guo (2007).

"The flame retardants, polybrominated diphenyl ethers, are pregnane X receptor activators."

Toxicological Sciences 97(1): 94-102.

<http://www.scopus.com/scopus/inward/record.url?eid=2-s2.0-34347263448&partnerID=40&rel=R6.5.0>

Ramot, Y., D. A. Lewis, T. L. Ortel, M. Streicker, G. Moser, **S. Elmore**, S. M. Ward, **S. Peddada** and A. Nyska (2007). "Age and dose sensitivities in the 2-butoxyethanol F344 rat model of hemolytic anemia and disseminated thrombosis." *Experimental and Toxicologic Pathology* 58(5): 311-322.

<http://gateway.isiknowledge.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=CustomerName&SrcApp=CustomerName&DestLinkType=FullRecord&DestApp=WOS&KeyUT=ISI:000246294600005>

Walker, D. M., **D. E. Malarkey**, S. K. Seilkop, F. A. Ruecker, K. A. Funk, M. J. Wolfe, C. P. Treanor, **J. F. Foley**, F. F. Hahn, J. F. Hardisty and V. E. Walker (2007). "Transplacental carcinogenicity of 3'-azido-3'-deoxythymidine in B6C3F1 mice and f344 rats." *Environmental and Molecular Mutagenesis* 48(3-4): 283-298.

<http://gateway.isiknowledge.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=CustomerName&SrcApp=CustomerName&DestLinkType=FullRecord&DestApp=WOS&KeyUT=ISI:000245318100014>

Witt, K. L., C. K. Cunningham, K. B. Patterson, **G. E. Kissling**, S. D. Dertinger, E. Livingston and **J. B. Bishop** (2007). "Elevated frequencies of micronucleated erythrocytes in infants exposed to zidovudine *in utero* and postpartum to prevent mother-to-child transmission of HIV."

Environmental and Molecular Mutagenesis 48(3-4): 322-9.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=17358032



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The NTP web site 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 web site at <http://ntp.niehs.nih.gov> (see Resources).

Contact Information: NTP Liaison and Scientific Review Office, NIEHS, P.O. Box 12233, MD A3-01, Research Triangle Park, NC 27709; T: (919) 541-0530; FAX: (919) 541-0295; CDM@niehs.nih.gov

Recent NTP Publications

NTP Technical Report:

TOX 75 *Toxicity Studies of Dimethylaminopropyl Chloride*

Available at:

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

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



Draft Performance Standards for Murine LLNA

NICEATM and the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) invite public comments on draft performance standards for the murine Local Lymph Node Assay (LLNA). In January 2007,

the Consumer Product Safety Commission submitted a nomination to NICEATM and ICCVAM requesting an assessment of the validation status of (1) the LLNA as a stand-alone assay for potency determination for hazard classification purposes; (2) modified LLNA protocols; (3) the LLNA limit test; (4) the use of LLNA to test mixtures, aqueous solutions, and metals; and (5) the applicability domain for LLNA. ICCVAM has now prepared draft

performance standards for the LLNA and recently announced their availability in the Federal Register (72FR52130) and invited public comments on them. The draft performance standards and on-line submission of public comments are available on the NICEATM-ICCVAM website at: <http://iccvam.niehs.nih.gov/methods/immunotox/immunotox.htm>

6th World Congress on Alternatives & Animal Use in the Life Sciences

Scientists from NICEATM and ICCVAM attended the World Congress in Tokyo, Japan on August 21-25, 2007, and were represented on the program through oral presentations, poster presentations, and as chairs of various sessions at the meeting. Copies of the abstracts and poster presentations are available at: <http://iccvam.niehs.nih.gov/meetings/6thWC/6WCablst.htm> ♦

Contact Information: Dr. William S. Stokes, Director, NICEATM, NIH/NIEHS, P.O. Box 12233, MD EC-17, Research Triangle Park, NC 27709; T: (919) 541-2384; iccvam@niehs.nih.gov