



UPDATE

National Toxicology Program

JANUARY 2004

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

Toxicology in the 21st Century: The Role of the National Toxicology Program

The NTP Vision for the 21st Century is to move toxicology from a predominately observational science at the level of disease-specific models to a predominately predictive science focused upon a broad inclusion of target-specific, mechanism-based, biological observations.

Established in 1978, the National Toxicology Program coordinates toxicological testing programs within the Department of Health and Human Services, develops and validates improved testing methods, develops approaches and generates data to strengthen scientific knowledge about potentially hazardous substances, and communicates with stakeholders. In its 25 years of existence, NTP has become a world leader in providing scientific information that improves our nation's ability to evaluate potential human health effects from chemical and physical exposures. The program maintains a number of complex, interrelated research and testing programs that provide unique and critical information needed by health regulatory and research agencies to protect public health.

The last decade of the 20th century and the turn of the 21st century have produced dramatic technological advances in molecular biology and computer science. In an effort to determine how best to incorporate these new scientific technologies into its research and testing strategies and to broaden scientific knowledge linking mechanism and disease, the NTP has developed a vision. *The NTP Vision for the 21st Century is to move toxicology from a predominately observational science at the level of disease-specific models to a predominately predictive science focused upon a broad inclusion of target-specific, mechanism-based, biological observations.* The NTP plans to develop a roadmap or framework to guide the program in implementing its vision. The goal of the roadmap is to position the NTP strategically at the forefront of toxicology in providing scientific data and its interpretation for public health decision-making.

The NTP invites all interested stakeholders to comment on the NTP Vision and to help develop the roadmap. In developing the roadmap and milestones toward achieving the vision, the NTP seeks input on issues raised by the following questions:

1. What scientific information should the NTP be producing and what technical capabilities should the NTP have by 2008? By 2013?
2. How do you envision that the refinement/replacement of classical toxicological studies with mechanism-based assays will impact on the evaluation of public health hazards?
3. How can we best structure the NTP to provide this information and to ensure its optimal utilization in the protection of public health?
4. What resources will be needed to realize this vision and how long will it take?

Public Meeting Set to Discuss NTP Vision

The NTP will hold a public meeting on Thursday, January 29, 2004, to receive comment on the vision and input for developing a roadmap. This meeting will be held at the Lister Hill Center Auditorium (Building 38A), National Library of Medicine, National Institutes of Health, 9000 Rockville Pike, Bethesda, MD, 20892. It will begin at 9:00 a.m. and conclude by 5 p.m. or sooner, if public comments and discussion end earlier. Attendance at the meeting is limited only by the space available.

The NTP invites the public to submit written comments and/or present oral comments at the meeting. Persons

planning to submit written comments or give an oral presentation are asked to pre-register, if possible. Additional details about the meeting, including background information, agenda and the on-line registration form are posted at <http://ntp-server.niehs.nih.gov/> (select NTP Vision Public Meeting under What's New?). Registration will also be available on-site beginning at 8:30 a.m. on January 29th. Questions about the meeting can be directed to Nan Cushing, NTP Liaison and Scientific Review Office, T: (919) 541-0530, F: (919) 541-0295, e-mail: cushing1@niehs.nih.gov

Report on Carcinogens (RoC) Public Meeting

The NTP is holding a public meeting on January 27-28, 2004, to receive public comment on the current process for reviewing nominations for listing in or delisting from the RoC and on the current listing criteria used for evaluating the nominations. The purpose of this meeting is to obtain input and provide all interested parties the opportunity to express their views and/or to comment on the views expressed by others. All interested parties are invited to participate; attendance and participation are limited only by the space available. For planning purposes, persons attending the meeting are asked to pre-register on-line at <http://ntp-server.niehs.nih.gov> (see RoC Public Meeting *under* What's New?) or contact Anna Lee Sabella at the NIEHS (see contact information). Additional details about the meeting, including background information on the RoC, agenda, and security information are also available.

The meeting will be held, at the Lister Hill Center Auditorium (Bldg. 38A), National Library of Medicine, National Institutes of Health, 9000 Rockville Pike, Bethesda, Maryland, 20892. The meeting will begin at 9 a.m. on January 27th and will conclude by noon on January 28th or sooner if the public comments and discussion end earlier. On-site registration will begin at 8:30 a.m. on January 27th.

A panel to include NTP staff, representatives of the NTP Board of Scientific Counselors and the NTP Executive Committee will receive the public comments and participate in the discussion. Persons interested in providing oral comments are asked to pre-register on-line or contact Ms. Sabella. The time allotted per speaker depends upon the number of individuals registered to speak, although at least 10 minutes is

anticipated per presenter. Written comments are welcome and may be provided *in lieu* of an oral presentation or to supplement it. Comments received by January 15, 2004, will be distributed to the panel, posted on the NTP RoC web site prior to the meeting, and made available at the public meeting.

Persons needing special assistance in order to attend are asked to contact Ms. Anna Lee Sabella (contact information below) at least seven business days prior to the meeting.

Contact information: Ms. Anna Lee Sabella, Report on Carcinogens Group, NIEHS, P. O. Box 12233 MD EC-14, 79 T.W. Alexander Drive, Room 3123, Research Triangle Park, NC 27709; T: (919) 541-4982; F: (919) 541-0144; e-mail: sabella@niehs.nih.gov

NTP Requests Nominations for Future Evaluation for Listing/Delisting in the RoC

The NTP solicits and encourages the broadest participation from interested individuals or parties in nominating agents, substances, mixtures, or exposure circumstances for listing in or delisting from the RoC. Nominations should contain a rationale for the listing or delisting and appropriate supporting background information and relevant data (e.g., journal articles, NTP Technical Reports, Interagency Agency for Research on Cancer listings, exposure surveys, release inventories) when possible. Nominations should be directed to the address below.

Contact Information: Dr. C. W. Jameson, Head, Report on Carcinogens, NIEHS/NIH, 79 Alexander Dr., Room 3118, P. O. Box 12233, MD EC-14, Research Triangle Park, NC 27709; T: (919) 541-4096; F: (919) 541-0144, e-mail: jameson@niehs.nih.gov



Scientific Advisory Committee on Alternative Toxicological Methods (SACATM)

The next meeting of the SACATM will be held on March 10-11, 2004, at the Hyatt Regency Hotel, One Bethesda Metro Center, Bethesda, Maryland 20814. The meeting begins each day at 8:30 a.m. until adjournment and is open to the public with attendance limited only by space available. Individuals who plan to attend are asked to register with Dr. Kristina Thayer, Executive Secretary [NTP Liaison and Scientific Review Office, NIEHS, P. O. Box 12233, Research Triangle Park, NC 27709. T: (919) 541-5021, fax: (919) 541-0295, or e-mail: thayer@niehs.nih.gov].

Agenda and details of the meeting will be announced after the first of the year in the [Federal Register](#) and

posted on the NTP web site (<http://ntp-server@niehs.nih.gov> *select* What's New).

Chartered in January 2002, the SACATM replaced the Advisory Committee on Alternative Toxicological Methods. The SACATM advises the Director of the NIEHS, the Interagency Coordinating Committee on the Validation of Alternative Methods, and the NICEATM on priorities and directives related to the development, validation, scientific review, and regulatory acceptance of new or revised toxicological test methods and on ways to foster partnerships and communication with interested parties.

Review of Draft NTP Technical Reports Rescheduled

The NTP Board of Scientific Counselors Technical Reports Review Subcommittee has been rescheduled for February 17-18, 2004, in the Rodbell Auditorium, Rall Building at the National Institute of Environmental Health Sciences, 111 T. W. Alexander Drive, Research Triangle

Park, NC. The meeting will begin at 8:30 a.m. and is open to the public. The primary agenda topic is the peer review of seven draft NTP Technical Reports (see table below).

TR#	Chemical	Uses and Occurrence
494	Anthraquinone*	Intermediate in dye manufacture
520	3,3',4,4',5-Polychlorinated biphenyl 26 (PCB 126)	Insulating fluid for electronics
521	2,3,7,8, Tetrachloro- <i>p</i> -dibenzene dioxin (TCDD)	Byproduct of combustion and smelting
525	2,3,4,7,8-Pentachlorodibenzofuran ((PeCDF)	Byproduct of incineration and combustion
526	Dioxin mixture: (PCB 126, TCDD and PeCDF)	Insulator and combustion byproduct
527	Malachite Green & Leucomalachite Green	Dye; antifungal for fish
528	1,2,3-Trichloropropane 2,2-Bis(bromomethyl)- <i>p</i> -1,3-propanediol Nitromethane**	Paint and varnish remover Flame retardant Fuel additive, synthesis intermediate and solvent

* The Subcommittee reviewed the draft NTP Technical Report on Anthraquinone in May 1999. Subsequent to that peer review, the tested anthraquinone was found to contain a 0.1% contaminant. As a result, additional mutagenicity and metabolism studies were conducted and the findings from those studies are included in the revised draft report. The Subcommittee will evaluate the results from the follow-up studies, use that information to re-examine the carcinogenicity findings from the 2-year studies and make a recommendation on the carcinogenicity of anthraquinone.

** Studies of these compounds are being done in two species of fish (Medaka and Guppy)

Approximately seven weeks prior to the meeting, the draft NTP Technical Reports will be available for public review, free of charge, through ehponline (<http://ehp.niehs.nih.gov/>). Printed copies of the draft reports can be obtained, as available from Central Data Management [NIEHS, P. O. Box 12233, MD EC-03, Research Triangle Park, NC 27709; T:(919) 541-3419, e-mail: CDM@niehs.nih.gov].

The public is invited to submit written comments on any report and/or to attend the meeting and give oral comments. Additional details about the meeting, as available, will be posted on the NTP web site (<http://ntp-server.niehs.nih.gov> see What's New?). Persons needing special assistance in order to attend are asked to contact Dr. Barbara Shane, Executive Secretary [T: (919) 541-4253, e-mail: shane@niehs.nih.gov] at least seven business days prior the meeting.

The NTP conducts toxicology and carcinogenesis studies of agents of public health concern. Any scientist, organization, or member of the public may nominate a chemical for NTP testing. The results of short-term rodent toxicology studies are published in the NTP Toxicity Report series and from longer-term rodent carcinogenicity studies, generally two years, are published in the NTP Technical Report series. The NTP also has a new report series for reporting studies conducted in genetically modified models.

The Technical Reports Review Subcommittee is a standing subcommittee of the NTP Board of Scientific Counselors. Following the meeting, subcommittee actions and summary minutes will be posted on the NTP web site (<http://ntp-server.niehs.nih.gov>) or will be available in hardcopy from the NTP Executive Secretary.

Upcoming Events*

January 27-28, 2004	NTP Public Meeting on the Report on Carcinogens (see article page 2) Lister Hill Center Auditorium (Building 38A), National Library of Medicine, NIH, 9000 Rockville Pike, Bethesda, MD 20892
January 29, 2004	NTP Vision Public Meeting (see article page 1) Lister Hill Center Auditorium (Building 38A), National Library of Medicine, NIH, 9000 Rockville Pike, Bethesda, MD 20892
February 17-18, 2004	NTP Board of Scientific Counselors Technical Reports Review Subcommittee Meeting (see article page 3) Rodbell Auditorium, Rall Bldg. at the NIEHS, 111 T. W. Alexander Dr., Research Triangle Park, NC 27709
March 10-11, 2004	NTP Scientific Advisory Committee on Alternative Toxicological Methods (see article page 2) Hyatt Regency Hotel, One Bethesda Metro Center, Bethesda, MD 20814

* As available information about these meeting will be posted on the NTP web site (<http://ntp-server.niehs.nih.gov> see What's New?)

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

Updated ICCVAM Submission Guidelines

The NICEATM announces the availability of the publication, "ICCVAM Guidelines for Nomination and Submission of New, Revised, and Alternative Test Methods," September 2003, NIH Publication No. 03-4508. The guidelines are an updated version of guidelines published by the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) in 1999. The ICCVAM guidelines provide information to sponsors and nominators of new test methods on the framework for organizing the information and the mechanism by which ICCVAM evaluates the validation status of new, revised and/or alternative test methods proposed for regulatory testing use. This framework can also be used to organize information in support of test methods nominated for further evaluation, including proposals for validation studies. The updated ICCVAM guidelines are available electronically (PDF and HTML) on the NICEATM/ICCVAM web site at <http://iccvam.niehs.nih.gov/methods/udp.htm> and a limited number of printed guidelines are available from the NICEATM (see contact information).

Responses from Federal Agencies to ICCVAM Test Recommendations

The NICEATM announces the availability of Federal agencies' responses to ICCVAM test recommendations for 1) *in vitro* methods for assessing acute systemic toxicity and 2) the revised Up-and-Down Procedure (UDP) for determining acute toxicity. The responses and other current information relevant to these test recommendations are available electronically (PDF and HTML) on the NICEATM/ICCVAM web site (<http://iccvam.niehs.nih.gov>).

The ICCVAM Authorization Act of 2000 requires the agencies to review the test recommendations and notify the ICCVAM in writing of their findings, including the identification of relevant test methods for which the ICCVAM test recommendations may be added or substituted.

Contact Information: NICEATM, NIEHS/NIH, P. O. Box 12233, MD EC-17, Research Triangle Park, NC 27709; T: (919) 541-2384; F: (919) 541-0947; e-mail: niceatm@niehs.nih.gov



NTP Satellite Symposium on Hepatic Pathology

The NTP will sponsor a satellite symposium on Saturday, June 12, 2004, before the start of the Society of Toxicologic Pathology Annual Meeting. The annual meeting is scheduled for June 13-17, 2004. The format for the satellite symposium will be the same as the one held in Savannah in 2003.

Cases will be available on a web site prior to the meeting and audience response units (for audience voting and

instant display of the results) will be provided during the satellite symposium. The emphasis for the cases will be hepatic lesions although non-hepatic lesions will also be included.

Persons interested in attending can obtain information on-line at www.toxpath.org or send a message to stp@toxpath.org

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

Expert Panel Review of Fluoxetine

The CERHR will hold an expert panel meeting on fluoxetine on March 3-5, 2004, at the Holiday Inn Old Town Select, 480 King Street, Alexandria, VA 22314 [T:(703) 549-6080]. This meeting is open to the public with attendance limited only by available room space.

Sections 1-4 of the draft expert panel report on fluoxetine are available electronically on the CERHR web site (<http://cerhr.niehs.nih.gov>) or in hard copy by contacting Dr. Michael Shelby (see contact information). The CERHR invites interested parties to submit written comments on the draft expert panel report and/or give oral comments at the meeting.

Time is set-aside on March 3, 2004, for the presentation of oral public comments. To facilitate planning, persons wishing to make oral comments are asked to contact Dr. Shelby by February 25th and, if possible, to send a copy of the statement to him by that date. Seven minutes will be available for each speaker (one speaker per organization). Any written comments or statements received will be provided to the expert panel to assist them in identifying issues for discussion and will be noted in the meeting record. Registration for presentation of oral comments will also be available at the meeting on March 3 at 7:30-8:30 a.m. and in that case, public commentators are asked to bring 20 copies of their statement for distribution to the panel and for the record.)

NTP-CERHR Monograph on Methanol

The NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Methanol is now available. This monograph is the next in the NTP-CERHR series and is posted electronically on the CERHR website. A limited number of CDs and printed copies are available from the CERHR (see contact information)

Plans for Announcing Availability of Future Monographs

All future notifications about the availability of NTP-CERHR monographs will be provided through announcements from the NTP list-server and on the CERHR web site. Monographs are now completed for six phthalates [di-butyl phthalate, butyl benzyl phthalate, di-isodecyl phthalate, di-isononyl phthalate, di-*n*-hexyl phthalate, and di-*n*-octyl phthalate] and methanol. The monographs for di(2-ethylhexyl) phthalate, 1-bromopropane, 2-bromopropane, ethylene glycol, and propylene glycol are being drafted and the NTP will make them available as soon as they are completed.

Contact Information: Dr. Michael Shelby, Director CERHR, NIEHS, 79 T.W. Alexander Drive, Bldg. 4401, Room 103, P. O. Box 12233, MD EC-32, Research Triangle Park, NC 27709; T: (919) 541-3455; F: (919) 316-4511; e-mail: shelby@niehs.nih.gov

How to Subscribe to the NTP List-serve

The NTP Update is issued approximately 4 times each year. To subscribe to the "list-server" and receive the NTP Update as well as other NTP news and announcements electronically, register online at <http://ntp-server.niehs.nih.gov> or send e-mail to ntpmail-request@list.niehs.nih.gov with the word "subscribe" as the body of the message, or contact the NTP Liaison and Scientific Review Office. **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; F: (919) 541-0295; liaison@starbase.niehs.nih.gov

Additional information about the NTP along with announcements of meetings, publications, study results and its centers is available on the Internet at <http://ntp-server.niehs.nih.gov>

The ehpOnline maintains issues of the Report on Carcinogens and the library of NTP Technical Reports and NTP Toxicity Reports and adds new reports as available. The electronic PDF files of completed reports are available free-of-charge and printed reports can be purchased through ehpOnline. To gain access to these reports, go to <http://ehp.niehs.nih.gov> or call (866) 541-3841 or (919) 653-2595.