



# NTP UPDATE

NATIONAL TOXICOLOGY PROGRAM

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Department of Health &  
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*We are pleased to provide the information included in this bulletin to update our readers on NTP programs and initiatives, as well as to highlight upcoming meetings. We invite public input and participation in all aspects of our*

## ***NIEHS Sessions at SOT***

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### **The Role of the Environment in Parkinson's Disease**

A special session sponsored by the National Institute of Environmental Health Sciences (NIEHS) on the role of the environment in Parkinson's Disease, will be presented at 1:30 p.m. March 29 at the annual Society of Toxicology (SOT) meeting, room 310, Moscone Convention Center, San Francisco, CA.

The cause(s) of Parkinson's Disease is unknown. Like many diseases with an unknown etiology there is evidence of interaction between environmental exposures and genetic susceptibility. During this session, invited speakers will present the most recent experimental and epidemiological evidence for this interaction, and in doing so, will provide a unique perspective on the potential for toxic exposures to cause a human neurological disorder. This research effort demonstrates how the fields of toxicology, genetics, molecular biology, epidemiology, exposure assessment and clinical medicine can work collaboratively in pursuit of an unknown etiology.

### **Environmental Health Burdens of Poor Communities**

The NIEHS will sponsor a workshop beginning at noon March 29 at the annual SOT meeting that provides an orientation on environmental justice and health disparities issues, an overview of existing research, communication and research efforts, and an opportunity for in-depth discussion of issues. The session will be held in room 135 of the Moscone Convention Center, San Francisco, CA.

Exposure to environmental and occupational hazards falls mostly on low income communities and communities of color and their working people. The workshop is aimed at people interested in translating this observation, as well as recent basic research and epidemiology, into public health action among community groups, including Hispanics,

African Americans, Laotians and Native Americans. Case studies of successful community-university interactions and research partnerships will be highlighted, and elements essential for development of such collaborations will be presented.

## ***NTP Publishes 500<sup>th</sup> Report***

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The NTP has published its 500<sup>th</sup> two-year toxicology and carcinogenesis study. This 500<sup>th</sup> report is a landmark in a series that has influenced what is allowed in your drugs, your water, your foods and your air, as these reports have often formed the foundation for regulatory actions. In 1997 and 1998 alone, nine of these studies were the basis for regulatory decisions by the EPA, FDA and Occupational Safety and Health Administration

The 500<sup>th</sup> report is on naphthalene, the chemical that gives mothballs that strong, familiar scent. The most widely known use of naphthalene is in mothballs and bathroom deodorizers, but it also has a number of chemical manufacturing uses and is used in veterinary medicine to control lice and as a disinfectant for lesions and incisions. The two-year study showed clear evidence of causing cancer in male and female laboratory rats. The rats in the study were exposed by inhalation, just as most people are, in doses comparable to some human consumer and workplace exposures.

*An abstract the NTP Technical Report on Naphthalene can be viewed on the NTP web site at <http://ntp-server.niehs.nih.gov/htdocs/LT-studies/tr500.html>. Hardcopies and PDF files of the NTP Technical Report on Naphthalene as well as other Technical Reports can be obtained by contacting the Environmental Health Information Service, 1-800-315-3010 or <http://ehis.niehs.nih.gov/ntp/docs/ntp.html>. The entire list of study abstracts for NTP Technical Reports and the results of each can be viewed at the NTP web site: [http://ntp-server.niehs.nih.gov/main\\_pages/NTP\\_ALL\\_STDY\\_PG.html](http://ntp-server.niehs.nih.gov/main_pages/NTP_ALL_STDY_PG.html) under Abstracts.*

## NTP Boards

### NTP Board of Scientific Counselors to Meet May 2001

A meeting of the NTP Board of Scientific Counselors is scheduled for May 25, 2001 at the Rodbell Auditorium, Building 101, National Institute of Environmental Health Sciences, 111 T.W. Alexander Drive, Research Triangle Park, North Carolina. The Board, composed of scientists from the public and private sectors, provides primary scientific oversight to the NTP. This one-day meeting is tentatively scheduled to begin at 8:30 a.m. The entire meeting is open to the public and time will be available for public comments.

Primary agenda topics include:

- A discussion of the draft guidelines for the NTP Center for the Evaluation of Risks to Human Reproduction expert panels.
- Review of chemical nominations under consideration for future NTP toxicology testing (see page 6, NTP Chemical Testing Nominations, for a list of these chemicals).
- A presentation about chemical disposition and toxicokinetics studies and their application to toxicokinetic modeling.
- Updates on NTP activities including the *Report on Carcinogens* and peer review of NTP Technical Reports.

*For additional information, to obtain a draft agenda, or to register to present oral public comments contact Dr. Mary S. Wolfe, NTP Executive Secretary at 919-541-3971 or [wolfe@niehs.nih.gov](mailto:wolfe@niehs.nih.gov).*

### 2001 NTP Technical Report Reviews

#### May 3, 2001

The NTP Board of Scientific Counselors Technical Reports Review Subcommittee will meet May 3, 2001 at the Rodbell Auditorium, Building 101, National Institute of Environmental Health Sciences, 111 T.W. Alexander Drive, Research Triangle Park, North Carolina. This subcommittee provides independent scientific peer review of draft technical reports of NTP long-term toxicology and carcinogenesis studies. The candidate technical

reports for this review include acrylonitrile, citral, methacrylonitrile, *o*-nitrotoluene, and *p*-nitrotoluene. It is anticipated that the meeting will begin around 8:30 a.m. The peer review is open to the public and time will be available for public comment on the reports.

- **Acrylonitrile** is used widely in the production of acrylic fibers, elastomers, resins, and a variety of chemical intermediates; annual production is in the millions of tons.
- **Citral** is used as a lemon flavoring in foods and beverages and as a lemon fragrance in detergents, perfumes, and toiletries.
- **Methacrylonitrile** is used in the production of polymers, elastomers, and plastics including those used in beverage containers.
- The two major isomers, ***o*-nitrotoluene** and ***p*-nitrotoluene**, were studied separately to compare their toxicologic profiles. Nitrotoluene usually occurs as a mixture of three isomers, with 55% to 60% *o*-nitrotoluene, 35% to 40% *p*-nitrotoluene, and 3% to 4% *m*-toluene. The nitrotoluenes are widely used in synthesis of agricultural and rubber chemicals and of a variety of dyes.

*Approximately one month prior to the meeting, draft reports for these chemicals will be available on the Internet for public review through the Environmental Health Information Service (EHIS) at <http://ehis.niehs.nih.gov>. Printed copies can be obtained, as available, from: Central Data Management, NIEHS, P.O. Box 12233, MD E1-02, Research Triangle Park, NC 27709; T: 919-541-3419; F: 919-541-3687; [cdm@niehs.nih.gov](mailto:cdm@niehs.nih.gov).*

*For additional information, to obtain a draft agenda, or to register to present public comments contact Dr. Mary S. Wolfe, NTP Executive Secretary at 919-541-3971 or [wolfe@niehs.nih.gov](mailto:wolfe@niehs.nih.gov).*

#### October 18, 2001

A second meeting of the Technical Reports Review Subcommittee is scheduled for October 18, 2001 at NIEHS. The reports tentatively planned for this second review are:

- vanadium pentoxide
- riddelliine
- 2,4-hexadienal
- urethane, ethanol and combinations of urethane with ethanol

*Draft reports will be available approximately one month prior to the meeting. Questions or additional information can be obtained from Dr. Mary S. Wolfe, NTP Executive Secretary (see above).*

## **Report on Carcinogens**

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### **9<sup>th</sup> Edition - TCDD/Dioxin Addendum**

Prepared by the NTP, the *Report on Carcinogens (RoC)* identifies substances -- such as metals, pesticides, drugs, and natural and synthetic chemicals -- mixtures or exposure circumstances that are "known" or are "reasonably anticipated" to be human carcinogens, and to which a significant number of Americans are exposed.

The 9<sup>th</sup> Edition of the *RoC* is the most recent and was published in May 2000. An addendum to the 9<sup>th</sup> *RoC* was published in January 2001 and issued to change the listing of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin CAS No. 1746-01-6, also known as "TCDD" or "Dioxin," to a "known to be human carcinogen," from its previous listing as "reasonably anticipated to be a human carcinogen." Publication of the addendum followed the ruling by the US Court of Appeals for the District of Columbia Circuit denying the request for an injunction to prevent the listing of TCDD as a "known human carcinogen" in the 9<sup>th</sup> Report, pending appeal of the district court's decision upholding the listing. The proposal to list TCDD as a "known human carcinogen" was reviewed in the same way and at the same time as the other new listings for the Ninth *RoC*. The review procedure is outlined in Section V of the 9<sup>th</sup> *RoC*.

*The revised 9<sup>th</sup> RoC that contains all addendum materials is available on the Internet from the NTP web page at <http://ntp-server.niehs.nih.gov/NewHomeRoC/AboutRoC.html> or by contacting Dr. C.W. Jameson, Head, Report on Carcinogens (contact information below).*

### **10<sup>th</sup> Edition of the Report on Carcinogens**

#### **First Group of Nominations**

Scientific review of the first group of nominations being considered for inclusion in the 10<sup>th</sup> edition of the *RoC* has been completed. This group of nominations includes the following:

- **Beryllium and Beryllium Compounds**  
Used in fiber optics and cellular network communications systems, aerospace, defense and other industry applications. Reviewed for possible upgrading to a known human carcinogen in the 10<sup>th</sup> Report.
- **2,3-Dibromo-1-propanol**  
Used as a flame retardant, as an intermediate in the preparation of the flame-retardant tris(2,3-dibromopropyl) phosphate, and as an intermediate in the manufacture of pesticides and pharmaceutical preparations.
- **2,2-Bis-(Bromomethyl) –1,3-propanediol**  
Used as a fire retardant in unsaturated polyester resins, in molded products, and in rigid polyurethane foam.
- **Dyes Metabolized to 3,3 -Dimethoxybenzidine (Dimethoxybenzidine Dyes as a Class)**  
Dyes formerly widely used for leather, paper, plastics, rubber, and textile industries.
- **Dyes Metabolized to 3,3-Dimethylbenzidine (Dimethylbenzidine Dyes as a Class)**  
Dyes formerly widely used for leather, paper, plastics, rubber, and textile industries.
- **IQ (2-Amino-3-methylimidazo[4,5-f]quinoline)**  
Found in cooked meat and fish.
- **Styrene-7,8-oxide**  
Used mainly in the preparation of fragrances and in some epoxy resin formulations.
- **Vinyl Bromide**  
Used commercially since 1968, primarily in the manufacture of flame retardant synthetic fibers.
- **Vinyl Fluoride**  
Used commercially since the 1960's, in the production of polyvinylfluoride that is used for plastics.

The NTP will review the recommendations from all review committees, including the Federal interagency NTP Executive Committee, and consider all public comments received throughout the process in making decisions regarding the NTP recommendations to the Secretary, Department of Health and Human Services (DHHS), for listing of the nominated substances in the 10<sup>th</sup> *RoC*.

*Final public comments for this set of nominations have also been received. A table of the recommendations for these nominations from the three scientific peer review committees for listing in the 10<sup>th</sup> RoC can be accessed through the NTP home page on the web at: <http://ntp-server.niehs.nih.gov/> or by contacting Dr. C. W. Jameson at the address provided below. All public comments as well as the background documents provided to the review committees and the public are available on the web in PDF format through the web address above. Hard copies of these documents are also available upon request.*

### **Second Group of Nominations - NTP Solicits Final Public Comment**

The second group of nominations for possible listing in the 10<sup>th</sup> RoC completed scientific review in 2000. These nominations include:

- **Broad Spectrum UV Radiation and UVA and UVB and UVC**  
Solar and artificial sources of ultraviolet radiation.
- **Chloramphenicol**  
Used widely as an antibiotic since the 1950s. Veterinary use of chloramphenicol has resulted in the occurrence of residues in animal-derived food.
- **Estrogens, Steroidal**  
Estrogens are widely used in oral contraceptives and in post-menopausal therapy for women.
- **Methyleugenol**  
Flavoring agent used in jellies, baked goods, nonalcoholic beverages, candy, and ice cream. Also used as a fragrance for many perfumes and soaps.
- **Nickel (metallic) & Certain Nickel Alloys**  
Widely used in commercial applications for over 100 years.
- **Talc (Containing Asbestiform Fibers and not Containing Asbestiform Fibers)**  
Both asbestiform talc (i.e. talc containing asbestiform fibers) and non-asbestiform talc (i.e. talc not containing asbestiform fibers) occur in various geological settings around the world. Occupational exposure to both forms occurs during mining, milling, and processing. Exposure to non-asbestiform talc by the general population occurs through the use of products such as cosmetics.
- **Trichloroethylene**  
Trichloroethylene is widely used as a solvent with 80-90% used worldwide for degreasing metals.

- **Wood Dust**

It is estimated that at least two million people are routinely exposed occupationally to wood dust worldwide. Non-occupational exposure also occurs. The highest exposures have generally been reported in wood furniture and cabinet manufacture, especially during machine sanding and similar operations.

To date, the review of these nominations has included two Federal (the NIEHS/NTP review group and the NTP Executive Committee Interagency Working Group) and one non-government (NTP Board of Scientific Counselors Report on Carcinogens Subcommittee) scientific peer reviews and public comment and review. As with the first set of nominations, the three scientific review committees evaluated all available data relevant to the criteria for inclusion of candidate nominations in the Report. The NTP is now soliciting final public comment on this set of nominations to supplement any previously submitted comments or to provide comments for the first time. Comments should be directed to Dr. C. W. Jameson at the address listed below. Following the final public comment period, the NTP Executive Committee will review the nominations and comments. The NTP will review the recommendations from each review committee and consider all public comments received throughout the process in making decisions regarding its recommendations to the Secretary, DHHS, for listing or upgrading the listing of the nominated substances in the 10<sup>th</sup> RoC.

*The criteria, a description of the RoC review process, and a list of the review groups' recommendations can be obtained through the NTP homepage: <http://ntp-server.niehs.nih.gov/>, see Report on Carcinogens, or by contacting Dr. Jameson (see below). All public comments received to date and the background documents provided to the review committees and the public for these nominations are available on the web in PDF format at the web address above. Hard copies of these documents are also available upon request.*

## 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, IARC listings, exposure surveys, release inventories) when possible. Nominations should be directed to Dr. Jameson at the following address.

*Dr. C.W. Jameson, Head, Report on Carcinogens, NIEHS/NIH, 79 Alexander Drive, Rm. 3118, P.O. Box 12233, MD EC-14, Research Triangle Park, NC 27709; T: 919-541-4906; F: 919-541-0144, [jameson@niehs.nih.gov](mailto:jameson@niehs.nih.gov)*

## NTP TESTING PROGRAM

### NTP Chemical Testing Nominations

The NTP Interagency Committee for Chemical Evaluation and Coordination (ICCEC) recently evaluated a group of substances nominated to the NTP for toxicology and carcinogenicity testing. This committee makes testing recommendations on the nominated substances and serves as the first level of review in the NTP's formal chemical nomination and selection process. Notice of this meeting including a request for public comment on these nominations and the ICCEC's testing recommendations was published in the *Federal Register* December 4, 2000 (65FR75727).

The nominated substances under consideration include several drinking water contaminants, drugs and dietary supplements. The substances for which the ICCEC recommends one or more types of toxicity testing are:

- Aluminum complexes found in drinking water
- Bilberry fruit extract
- Black cohosh
- Blue-Green algae dietary supplements
- Cefuroxime
- Clarithromycin
- D&C Red No. 27 and D&C Red No. 28

- N,N-Dimethyl-*p*-toluidine
- Lemon Oil and Lime Oil
- Local anesthetics that metabolize to 2,6-xylidine or *o*-toluidine
- Microcystin-LR
- Organotins occurring in drinking water
- All-*trans*-retinyl palmitate
- S-Adenosylmethionine
- Senna

The nominated substances for which a testing recommendation is deferred pending the receipt and consideration of additional information are:

- 1,3-Dichloropropane, 2,2-Dichloropropane, and 1,1-Dichloropropene
- Hydergine
- Yohimbe bark extract and Yohimbine

*Additional opportunity for public comment will be provided at the NTP Board of Scientific Counselors meeting May 25, 2001 (see page 3). Following this review by the NTP Board, the NTP Executive Committee will review and approve the testing recommendations before NTP studies are designed and implemented. Further information is available on the web at:*

[http://ntp-server.niehs.nih.gov/htdocs/liason/ICCE\\_C102700finalFR.html](http://ntp-server.niehs.nih.gov/htdocs/liason/ICCE_C102700finalFR.html)

### NTP Solicits Input and Nominations of Agents for Study

The nomination and selection process is integral to the effective operation and success of the NTP's testing program with respect to its testing of chemicals of greatest public health concern. The NTP solicits nominations of new chemicals and agents for study from all sources including academia, industry, labor unions, Federal and State agencies and the general public.

NTP studies include research and testing of selected chemicals and agents in order to characterize their toxicity and determine possible adverse effects that may be associated with human and environmental exposure. Health-related effects addressed include subchronic toxicity, genetic toxicity, chronic toxicity and carcinogenicity, as well as effects on reproduction and development and the immune, respiratory and central nervous systems. Studies are also designed to address specific data gaps for priority substances such as biological fate, mechanisms of toxicity and other adverse effects

that may be of human health concern. Data generated from NTP studies are critical to strengthening the science base used by regulatory agencies for assessments of human health hazards associated with exposure to those chemicals and agents studied. The NTP also supports an active program to develop and validate new and improved assays for chemical toxicity and test methods and systems that eliminate or minimize the use of laboratory animals.

Each nomination is considered carefully in order to maximize the use of available resources. Chemicals or other agents for which a significant portion of the population are known to be exposed and for which there is a lack of available adequate toxicological information are the best candidates for study.

The NTP invites the submission of nominations. All nominations should be accompanied by a rationale for study, i.e. populations exposed, source of exposure, any known adverse health effects, etc. When possible, nominations should also be accompanied by available information describing production and use, possible adverse effects associated with exposure, as well as a chemical name, structure and CAS number. The NTP considers each nomination as it is received and conducts a literature search to supplement any supporting documentation on the nomination prior to its review and prioritization for future evaluation. The nominator is informed of the status of the nomination as it moves through the review, selection and testing process.

In addition to formal nominations for study, comments on testing directions and priorities are welcome. Some current testing initiatives include the study of botanical dietary supplements, drinking water contaminants, occupational exposures and mixtures, and DNA-based therapeutic agents. It is important, however, to emphasize that the NTP seeks the broadest participation in the nomination process and nominations need not be limited to any of these areas.

*Nominations and inquires regarding nominations or testing initiatives should be addressed to:*  
*Dr. Scott Masten, NIEHS, P.O. Box 12233, MD B3-10, Research Triangle Park, NC 27709*  
*Email: [masten@niehs.nih.gov](mailto:masten@niehs.nih.gov).*

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

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The NTP and the NIEHS established CERHR in June 1998. The purpose of the Center is to provide timely and unbiased, scientifically sound evaluations of human and experimental evidence for adverse effects on reproduction, including development, which may be caused by agents to which humans are exposed.

### **Review of Phthalate Esters Nears Completion**

The Phthalate Expert Panel completed its evaluation of seven phthalate esters for potential reproductive and developmental toxicity in July 2000. The seven phthalates evaluated were:

- butyl benzyl phthalate
- di(2-ethylhexyl) phthalate
- di-isodecyl phthalate
- di-isononyl phthalate
- di-n-butyl phthalate
- di-n-hexyl phthalate
- di-n-octyl phthalate

Phthalate esters are used as plasticizers in a wide range of polyvinyl chloride-based consumer products. These phthalate esters were selected for evaluation based on their high production volume, extent of human exposures, use in children's products, or published evidence of reproductive or developmental toxicity.

The panel's deliberations focused on the amount and quality of data available in two primary areas, human exposures to these phthalates and experimental evidence for their reproductive and developmental toxicity. Working over a 15-months period, the panel assigned "low, minimal, or negligible concern" for five of the agents [di-isononyl phthalate, di-n-butyl phthalate, butyl benzyl phthalate, di-n-octyl phthalate, di-isodecyl phthalate] and higher concern for only one, di(2-ethylhexyl) phthalate. The Panel concluded that too few data were available on di-n-hexyl phthalate to reach any conclusions.

*The Expert Panel Reports for the individual phthalate esters are available electronically on the CERHR's web site, <http://cerhr.niehs.nih.gov> or in hardcopy by contacting the Center (contact information provided below).*

The CERHR is in the process of preparing its Center Report on Phthalates. The NTP Center Report will include background information on the selection of phthalates for evaluation; the evaluation process; the Expert Panel Reports; public comments received; summaries of relevant studies available since the Panel Reports were finalized, comments on how these new data might impact the conclusions of the Expert Panel and the critical data needs they identified; and the NTP's position on the potential for adverse effects from phthalates in humans. Finally, the NTP Center Report will discuss the critical data needs identified by the Expert Panel and any plans for studies to address them. The NTP Center Report on Phthalates is expected to be completed in summer 2001 and will be transmitted to interested government agencies and available to all other interested groups and individuals.

### **CERHR to Review Methanol**

The next CERHR Expert Panel Review will examine methanol and is scheduled for summer 2001 in Alexandria, VA. Methanol is a commercially important, high production volume chemical (10.54 billion pounds, US production, 1993) that has a high potential for occupational, consumer, and environmental exposure. This meeting will be open to the public and time will be available for oral public comments. A 60-day period for written public comment is anticipated prior to the meeting.

*Further information on this meeting will be provided through the Federal Register and posted on the CERHR web site. Questions and requests for additional information should be directed to Dr. Michael Shelby, Director CERHR (see contact information below).*

### **Future Reviews**

Ethylene glycol and 1- and 2-bromopropane are currently under consideration for future CERHR reviews.

### **CERHR Prepares Guidelines for Expert Panels and Seeks Public Comment**

CERHR is preparing guidelines for use by its expert panels in the conduct of their reviews. These guidelines will aid in preparation of the Expert Panel Reports, promote understanding among panel members regarding the evaluation process, and help facilitate consistency among reports. The draft guidelines are nearing completion and will be available for public review in the near future. Once completed, they will be posted on the CERHR web site and a notice for public comment will be published in the *Federal Register*. The guidelines will be reviewed at the upcoming meeting, May 25<sup>th</sup>, of the NTP Board of Scientific Counselors (see page 3). This meeting will include opportunity for oral public comment.

### **CERHR Solicits Nominations**

The CERHR conducts reviews on man-made or naturally occurring chemicals or chemical mixtures and welcomes the nomination of chemicals for future evaluations. Nominations are welcome from all interested individuals and groups. Nominations should include the chemical's name, Chemical Abstract Service registry number (if known), justification for the nomination, and as possible, references or articles on the chemical and its potential reproductive or developmental toxicity.

*Nominations can be submitted through the CERHR web site, choose Nominate a Chemical, or directly to: Dr. Michael Shelby, Director, CERHR, NIEHS, P.O. Box 12233, MD EC-32, Research Triangle Park, NC 27709; T: 919-541-3455; F: 919-541-4636; [shelby@niehs.nih.gov](mailto:shelby@niehs.nih.gov).*



## **CERHR Web Site Expanded to Include a Section on Common Pregnancy Concerns**

A new section, *Common Concerns and Exposures*, has been added to the CERHR web site. This section includes information and links to other sites dealing with numerous exposure topics and medical information relating to fertility, pregnancy, and the health of unborn children. This section is available through the CERHR homepage:

<http://cerhr.niehs.nih.gov>

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

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NICEATM and the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) collaborate to develop, validate, and achieve regulatory acceptance of new and improved test methods.

### **ICCVAM Authorization Act of 2000 Signed into Law**

ICCVAM, first convened in 1997, was established as a permanent committee under NICEATM by the ICCVAM Authorization Act of 2000 (Public Law 106-545) signed on December 19, 2000. The law also establishes a Scientific Advisory Committee and it requires agencies to determine that alternative test methods are valid. Currently, the Advisory Committee on Alternative Toxicological Methods provides advice to the NTP on NICEATM's and ICCVAM's activities and priorities.

The objective of the law is to establish, wherever feasible, guidelines, recommendations, and regulations that promote the regulatory acceptance of new and revised toxicological tests that protect human and animal health and the environment while reducing, refining, or replacing animal tests and ensuring human safety and product effectiveness. The law establishes ICCVAM as a permanent committee consisting of the heads of 15 federal agencies or their designees. The purposes of the ICCVAM will be to:

- Increase the efficiency and effectiveness of federal agency test method review.
- Eliminate unnecessary duplicative efforts and share experiences between federal regulatory agencies.
- Optimize utilization of scientific expertise outside the federal government.
- Ensure that new and revised test methods are validated to meet the needs of federal agencies.
- Reduce, refine, or replace the use of animals in testing, where feasible.

*Public Law 106-545 will be published on the Government Printing Office (GPO) web site under the Catalog of Public Laws for the 106<sup>th</sup> Congress at <http://www.access.gpo.gov/nara/publaw/106publ.html>*

### **NICEATM Solicits Data and the Nomination of Experts for Independent Peer Review of Endocrine Disruptor Screening Assays**

At the request of the U.S. Environmental Protection Agency (EPA), ICCVAM and NICEATM are planning an Independent Peer Review Panel meeting in early 2002 to assess the validation status of several *in vitro* assays proposed for use in the EPA's Endocrine Disruptor Screening Program (EDSP). The proposed assays are estrogen receptor (ER) and androgen receptor (AR) binding and transcriptional activation assays. They are relevant for screening purposes in the EDSP because a number of chemical substances may alter natural endocrine processes in the body by binding with estrogen and/or androgen receptors and either initiating or inhibiting sex hormone-dependent gene activation.

NICEATM is currently preparing background review documents on *in vitro* estrogen receptor and androgen receptor binding and transcriptional activation assays. These documents will provide comprehensive reviews of available data and related information necessary to evaluate the validation states of these assays.

*NICEATM welcomes data and information from completed, ongoing, or planned studies using or evaluating ER and AR binding and/or transcriptional activation assays. Study information should be sent to Dr. Stokes (address provided below).*

The nomination of scientists with relevant knowledge and experience who might be considered for the Independent Peer Review Panel is also invited. Areas of expertise that may be relevant include, but are not limited to, endocrinology, reproductive toxicology, cellular biology, molecular genetics and biostatistics.

*For each expert suggested, his/her name, affiliation, contact information (i.e., mailing address, telephone and fax numbers, and e-mail address), and a brief summary of relevant experience and qualifications should be provided. Nominations should be sent to Dr. Stokes (see below).*

### **Test Methods under Review**

ICCVAM has reviewed the following alternative test methods:

- Murine Local Lymph Node Assay (LLNA)
- Corrositex® Assay
- Frog Embryo Teratogenesis Assay - *Xenopus*
- Up-and-Down Procedure
- *In Vitro* Methods for Assessing Acute Systemic Toxicity

*Additional information about the reviews of these methods is available from the ICCVAM/NICEATM web site <http://iccvam.niehs.nih.gov> see Methods under Review, or by contacting NICEATM directly (contact information provided below).*

### **NTP Advisory Committee for Alternative Toxicological Methods (ACATM)**

ACATM, established by the Department of Health and Human Services, meets biannually to provide ICCVAM and NICEATM advice on activities and priorities and on ways to foster partnerships and productive interactions among stakeholders. At its meeting November 28, 2000, in Bethesda, MD, the Committee discussed recent ICCVAM/NICEATM test method meetings and proposed future activities. Minutes from this and previous meetings are posted on the ICCVAM/NICEATM web site (<http://iccvam.niehs.nih.gov>).

*For information contact: Dr. William S. Stokes, Director, NICEATM, NIEHS/NTP, P.O. Box 12233, MD EC-17, Research Triangle Park, NC 27709; T: 919-541-3398; F: 919-541-0947; [iccvam@niehs.nih.gov](mailto:iccvam@niehs.nih.gov)*

## **NIEHS National Center for Toxicogenomics**

The National Institute of Environmental Health Sciences (NIEHS) recently established the National Center for Toxicogenomics (NCT) to coordinate an international research effort for developing the field of toxicogenomics. Toxicogenomics is a new scientific field that elucidates how the entire genome is involved in biological responses of organisms exposed to environmental toxicants/stressors. It combines information from studies of genomic-scale mRNA profiling (by microarray analysis), cell-wide or tissue-wide protein profiling (proteomics), genetic susceptibility, and computational models to understand the roles of gene-environment interactions in disease.

A coordinated, multi-disciplinary research program, the NCT will provide a unified strategy, create a public database, and develop the informatics infrastructure necessary to promote development of this field. The NIEHS will pay special attention to toxicogenomics as applied to the prevention of environmentally related diseases. The overarching goal of the NCT is to use the methodologies and information of genomics science to improve significantly the understanding of basic biological responses to environmental stressors/toxicants. Specific goals of the NCT are to:

- Facilitate further development of gene expression methodology.
- Create a public database relating environmental stressors to biological responses.
- Collect information relating environmental exposures to disease.
- Develop an improved paradigm for use of computational mathematics for understanding responses to environmental stressors.
- Identify biomarkers of disease or exposure to enhance environmental health.

The NCT will accomplish its goals through a combination of financial support to scientists at academic and other research institutions, in-house research, and collaborations with public agencies, private healthcare, and biotechnology companies.

For additional information about the NCT visit its new web site at:

<http://www.niehs.nih.gov/nct/home.htm> or contact Dr. Raymond W. Tennant, Director, NCT, NIEHS, P.O. Box 12233, MD F1-05, Research Triangle Park, NC 27709; T: 919-541-4141.

## **UPCOMING WORKSHOP**

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### **Assessment of the Potential Allergenicity of Genetically Modified Foods**

The general public and the scientific community are increasingly concerned regarding the potential toxicity of genetically modified (GM) foods. Of specific interest is the ability of GM proteins to illicit potentially harmful immunologic responses including hypersensitivity and/or autoimmunity.

The lack of information on the potential toxicity of these products has created a considerable backlash against the producers and users of these crops. To address these issues, the NTP along with the EPA and FDA is sponsoring a workshop on the safety assessment of GM foods, to be held on September 24-26, 2001 in Research Triangle Park, NC. The goals of this meeting are to examine the current state of knowledge in this area, identify the critical issues regarding GM materials, and develop testing strategies for examining the toxicity of these compounds. Participants will include experts in food allergy, GM crops, and the regulatory aspects of these products.

*Additional information can be obtained by contacting Dr. Dori Germolec, NIEHS at [germolec@niehs.nih.gov](mailto:germolec@niehs.nih.gov) or 919-541-3230.*

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***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>.***

***Environmental Health Information Service (EHIS) maintains the library of NTP Technical Reports and adds new reports as available. To gain access to these reports, contact EHIS online at: <http://ehis.niehs.nih.gov> or call 1-800-315-3010 or 919-541-3841.***