



## *Public Meeting on Hexavalent Chromium*

Based upon concern by a number of California legislators, the California Environmental Protection Agency, and the California Health and Human Services Agency, the National Toxicology Program (NTP) will study the carcinogenic potential of hexavalent chromium in drinking water. Hexavalent chromium is an established human carcinogen in certain occupational settings from inhalation exposure. There is uncertainty, however, regarding the long-term consequences of exposure to hexavalent chromium in water sources.

The NTP will hold an open public meeting starting at 8:30 a.m. on July 24, 2002, at the National Institute of Environmental Health Sciences (NIEHS), Rall Building, 111 TW Alexander Drive, Research Triangle Park, North Carolina. It was announced recently in the *Federal Register* (May 24, 2002: Vol. 67, No. 101, pages 36620-36621).

The primary focus of this meeting is to review and discuss 1) data from studies designed to assess the absorption of chromium by rats, mice, and guinea pigs receiving hexavalent chromium as sodium dichromate dihydrate in drinking water; 2) the design and data from 90-day oral toxicity studies in rats and mice receiving hexavalent chromium in drinking water; and 3) a proposed design for 2-year rodent cancer studies of hexavalent chromium in drinking water. The NIEHS has invited scientific experts to participate in this review and there is also time set aside for oral public comments.

Additional information about this meeting, including the tentative agenda, roster of scientific experts, study protocols and data from completed studies is available on the NTP web site (<http://ntp-server.niehs.nih.gov>, see What's New) or by contacting the NTP Liaison and Scientific Review Office (contact information on page 7).

Oral and written public comments are welcome. Seven minutes will be allowed per oral public presentation, and if time permits, may be extended up to 10 minutes. Each organization is allowed one time slot for an oral presentation. Speakers are requested to provide, if possible, a written copy of the statement by July 15, 2002. On-site registration for oral presentations will be available. If registering on-site to speak, the speaker is requested to provide 15 copies of the statement. Written comments can be submitted in lieu of an oral presentation or to supplement one and should be received by July 15, 2002, in order to allow time for review by the scientific experts and NTP staff. Registration to present oral comments, submission of written comments, and questions about this meeting should be directed to Dr. Mary S. Wolfe, NTP Executive Secretary, NTP Liaison and Scientific Review Office.

If possible, persons attending this meeting are asked to pre-register. New procedures for accessing the NIEHS campus by the public are now in place. Specific directions are given on page 3.

***New Procedures for Accessing the NIEHS Campus, see page 3...***

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## Upcoming NTP Board of Scientific Counselors' Meetings

### Technical Reports Review Subcommittee

The Technical Reports Review Subcommittee ("the Subcommittee") provides independent scientific peer review of draft technical reports of NTP long-term toxicology and carcinogenesis studies.

The Subcommittee is scheduled to meet September 5-6, 2002, at the National Institute of Environmental Health Sciences (NIEHS), Rodbell Conference Center, Rall Building, 111 TW Alexander Drive, Research Triangle Park, North Carolina. The meeting is tentatively scheduled to begin at 8:30 a.m. each day. This peer review is open to the public. Plans are also underway for making this meeting available for viewing on the Internet (<http://www.niehs.nih.gov/external/video.htm>). The technical reports (TR) scheduled for review are:

- **Cinnamaldehyde (TR 514)** – flavoring and fragrance ingredient; the primary component of cinnamon oil.
- **Decalin (TR 513)** – industrial solvent for fats, resins, oils, waxes, and naphthalene; a substitute for turpentine; a constituent of motor fuels and lubricants.
- **Dipropylene glycol (TR 511)** – component of air and room fresheners, household cleansers, cosmetic formulations, auto paints, and antifreeze.
- **Elmiron (TR 512)** – used in treatment of thrombosis and hyperlipidemia and for relief of urinary bladder pain associated with interstitial cystitis.
- **Pentaerythritol triacrylate (TR 517)** – representative multifunctional acrylate used in photocurable inks and coatings and as an ingredient of acrylic glues, adhesives, and sealants.
- **Trimethylolpropane triacrylate (TR 516)** – representative multifunctional acrylate used in photocurable inks and coatings, acrylic glues, paper and wood impregnates, wire and cable extrusion, and polymerconcrete composites.
- **Urethane + ethanol (TR 510)** – Urethane is a by-product of fermentation and occurs in breads and alcoholic beverages. The effect of urethane was studied in combination with alcohol (ethanol).

Oral and written public comments are welcome on any of the reports scheduled for review (for information about providing comments see page 3). All written comments should be received by August 28, 2002, to allow time for their review by the Subcommittee and NTP staff prior to the meeting.

Information about this meeting, including the tentative agenda and Subcommittee roster, will be posted on the NTP web site (<http://ntp-server.niehs.nih.gov>, see What's New) or available by contacting the NTP Liaison and Scientific Review Office (see page 7 for contact information). Prior to the meeting, draft reports will be available for public review on the Internet through *Environmental Health Perspectives* at <http://ehp.niehs.nih.gov>. Printed copies of the reports can be obtained, as available, from Central Data Management, NIEHS, P.O. Box 12233, EC-03, Research Triangle Park, NC 27709; T: 919-541-3419; F: 919-541-3687; [cdm@niehs.nih.gov](mailto:cdm@niehs.nih.gov).

### Board of Scientific Counselors

The NTP Board of Scientific Counselors ("the Board") is composed of scientists from the public and private sectors and provides primary scientific oversight to the NTP.

The Board is scheduled to meet on September 17-18, 2002, in Research Triangle Park, North Carolina. The exact times and location of the meeting are not yet set. As details for this meeting, including the agenda and location, are finalized, they will be posted on the NTP web site (<http://ntp-server.niehs.nih.gov>), announced in the *Federal Register*, and available by contacting the NTP Liaison and Scientific Review Office (see page 7 for contact information). This meeting will be open to the public and written and oral comments will be welcome on any agenda topic (see page 3 for information about submitting public comments).



## The Report on Carcinogens Subcommittee

The Report on Carcinogens Subcommittee (“the RoC Subcommittee”) provides independent scientific peer review of substances (including agents, mixtures, and exposure circumstances) nominated for listing in or delisting (removal) from the RoC (see page 4 for additional information about the RoC).

The RoC Subcommittee is scheduled to meet on November 19-20, 2002, in Washington, DC. This meeting will be open to the public. The exact times and location of the meeting are not yet set. As details for this meeting are finalized, they will be posted on the NTP web site (<http://ntp-server.niehs.nih.gov>), announced in the *Federal Register*, and available by contacting the NTP Liaison and Scientific Review Office (see page 7 for contact information). Oral and written public comments will be welcome on any nomination reviewed at this meeting (see below for information about providing public comments).

The Subcommittee will be reviewing nominations being considered for the 11<sup>th</sup> edition of the RoC. Tentatively planned for review are:

- **1-Amino-2,4-dibromo-anthraquinone**
- **Cobalt sulfate heptahydrate**
- **Diethanolamine**
- **High Risk Human papilloma viruses (HPV)**
- **Naphthalene**
- **Nitrobenzene**
- **Nitromethane**
- **4,4'-Thiodianiline**

As completed, the background documents for these nominations are being posted on the NTP web site (<http://ntp-server.niehs.nih.gov>, see Report on Carcinogens; a related article about nominations to the 11<sup>th</sup> RoC is on page 5). At least 8 weeks prior to the meeting, all background documents will be available on the NTP web site or in hard copy by contacting Dr. C.W. Jameson (see page 4 for contact information).

### **Public Comments at NTP Board of Scientific Counselors' Meetings**

The NTP invites written and oral comments at all meetings of the NTP Board of Scientific Counselors and its two subcommittees (Technical Reports Review Subcommittee and Report on Carcinogens Subcommittee). Seven minutes are allowed for each oral public presentation, and if time permits, may be extended up to 10 minutes. Each organization is allowed one time slot for an oral presentation per agenda item (i.e. per technical report, per nomination to the RoC, etc.). Speakers are requested to provide, if possible, a written copy of their statement prior to the meeting electronically or by mail or fax. Persons can register on-site to give oral comments. If registering on-site to speak, the presenter is requested to provide 25 copies of the statement. Written comments can supplement or be submitted in lieu of an oral presentation and should be received by published deadlines to allow time for review by committee members and NTP staff. Registration to present oral comments, submission of written comments, and questions about NTP Board meetings should be directed to Dr. Mary S. Wolfe, Executive Secretary, NTP Liaison and Scientific Review Office (see page 7 for contact information). Additional information about public comments, meetings, and deadlines are posted through notices on the NTP web site (<http://ntp-server.niehs.nih.gov>) and in the *Federal Register*.

## *New Procedures for Accessing the NIEHS Campus*

The National Institute of Environmental Health Sciences (NIEHS) has moved to a higher level of security awareness. In an attempt to make everyone's visit to the campus safe, more stringent requirements for access to NIEHS' campus have been implemented. Any individual seeking



access to the NIEHS campus to attend a conference/seminar must show 2 forms of identification (i.e., driver's license plus one of the following: e.g., company ID, government ID or university ID) and provide pertinent information about the conference/seminar (i.e., name of the speaker, host of the conference/seminar or title of the conference/seminar).

## The Report on Carcinogens



Prepared by the NTP, the *Report on Carcinogens* (RoC) is an informational scientific and public health document that identifies and discusses substances (including agents, mixtures, or exposure circumstances) that may

pose a carcinogenic hazard to human health. It serves as a meaningful and useful compilation of data on (1) the carcinogenicity, genotoxicity, and biologic mechanisms of the listings in humans and/or animals; (2) the potential for exposure to them, and (3) the regulations promulgated by Federal agencies to limit exposures.

The NTP follows a formal process for the review of nominations that includes multiple phases of scientific peer review and several opportunities for public comments. The criteria, a description of the RoC review process, background documents, public comments received on nominations, and information about how to nominate a substance to the RoC are available on the NTP homepage (<http://ntp-server.niehs.nih.gov>, see Report on Carcinogens) or by contacting Dr. C.W. Jameson (see contact information on this page).

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 removal from the RoC. Nominations should contain a rationale for the listing or delisting (removal) 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.

### 10<sup>th</sup> Edition of the RoC

The scientific review of nominations to the 10<sup>th</sup> RoC is complete and publication is anticipated in 2002. A list of the nominations to the 10<sup>th</sup> RoC was published in the March 2002 NTP Update. The recommendations from the three scientific peer review committees for listing these nominations in the 10<sup>th</sup> RoC, all public comments on these nominations, the background documents in PDF format, and the criteria and process used for review of these nominations can be accessed through the NTP

home page or by contacting Dr. Jameson.

#### **Talc (Asbestiform and Non-asbestiform)**

*The NTP conducted a review of the nomination of talc containing asbestiform fibers and not containing asbestiform fibers. The NTP's review of talc found that there has been considerable confusion over the mineral nature and consequences of exposure to talc, both containing asbestiform fibers and not containing asbestiform fibers. It is very evident that the literature on both forms of talc, with few exceptions, provides an inadequate characterization of the actual minerals under study to enable one to reach definitive conclusions concerning the specific substances responsible for the range of adverse health outcomes reported. This confusion was clearly reflected in the deliberations during the December 14, 2000, public review of the talc nomination by the NTP's Board of Scientific Counselors RoC Subcommittee. Because of this, the NTP has decided to defer consideration of the listing of talc, both containing and not containing asbestiform fibers, in the RoC. The NTP plans to carefully review the literature on these materials to determine if a clear definition of the agent or agents could be developed for a RoC review and if additional research to investigate potential carcinogenic hazards of these materials would be appropriate at this time. (Additional information about the talc review is available on the NTP web site: <http://ntp-server.niehs.nih.gov>)*

### 11<sup>th</sup> Edition of the RoC

The NTP has identified the nominations under consideration for listing in the 11<sup>th</sup> RoC (*Federal Register*: July 24, 2001: Vol. 66, No. 142, pages 38430-38432 and March 28, 2002: Vol. 67, No. 60, page 14957). A list of these nominations was published in the March 2002 NTP Update and is available on the NTP web site (<http://ntp-server.niehs.nih.gov>, see Report on Carcinogens) or by contacting Dr. Jameson. The 11<sup>th</sup> RoC is scheduled for publication in 2004.

The NTP has announced availability of background documents for 4 substances nominated (cobalt sulfate, diethanolamine, nitromethane, and 4,4'-thiodianiline) for listing in the RoC (*Federal Register* May 24, 2002: Vol. 87, No. 101, pages 36621-36620). These documents are available on the NTP web site or in hardcopy by contacting Dr. Jameson. All future notifications about the availability of background documents for other nominations to the 11<sup>th</sup> RoC will be provided through NTP list-server announcements (see page 7 for information about how to subscribe to the NTP list-server). Individuals who have already subscribed do not need to do so again.

*Contact information:* Dr. C.W. Jameson, Head, Report on Carcinogens, NIEHS, 79 TW Alexander Drive, Rm. 3118, P.O. Box 12233, MD EC-14, Research Triangle Park, NC 27709; T: 919-541-4096; F: 919-541-0144; [jameson@niehs.nih.gov](mailto:jameson@niehs.nih.gov)



## NTP Testing Program

### New Nominations for NTP Study

The NTP Interagency Committee for Chemical Evaluation and Coordination (ICCEC) evaluated 19 substances nominated to the NTP for testing at its meeting in April 2002. The ICCEC makes testing recommendations on nominated substances and serves as the first level of review in the NTP's formal chemical nomination and selection process.

Testing recommendations for these nominations are available on-line and were announced in the *Federal Register* (June 12, 2002: Vol. 67, No. 113, pages 40329-40333). Public comments on the nominations and ICCEC recommendations are being solicited through August 12. Further information, including supporting documents for each nomination, is available on the NTP web site at <http://ntp-server.niehs.nih.gov/NomPage/noms.html>

*The 14 substances for which one or more types of toxicological studies are recommended:*

- **Abrasive blasting agents** – 5 different industrial materials used as alternatives to sand.
- **5-Amino-o-cresol** – permanent hair dye ingredient.
- **tert-Butyl hydroperoxide** – high production volume industrial catalyst.
- **Chloramine-T and p-Toluenesulfonamide** – active ingredient and metabolite of therapeutic used in aquaculture to control bacterial infections.
- **Cobalt metal dust** – important industrial material linked to lung problems in workers.
- **Ephedrine alkaloid dietary supplements** – widely used in herbal dietary supplements with numerous reports of adverse effects.
- **Ethanone, 1-(1,2,3,4,5,6,7,8-octahydro-2,3,8,8-tetramethyl-2-naphthalenyl)-(Iso-E-Super)** – high-production-volume fragrance material.
- **Hexafluorosilicic acid and Sodium hexafluorosilicate** – primary agents used to fluoridate public drinking water supplies.
- **Ketamine hydrochloride** – approved anesthetic drug that causes brain lesions in developing rats.
- **Mercury, ((o-carboxyphenyl)thio)ethyl-, sodium salt (Thimerosal)** – organomercuryl-based preservative used in vaccines and other biological products.

- **Nitrogen trifluoride** – cleaning and etching agent in the semiconductor industry.
- **Sodium metasilicate** – industrial cleaning agent.
- **Turpentine** – high-production-volume industrial solvent and raw material.
- **Welding fumes** – variable composition mixture responsible for respiratory and other adverse effects in exposed workers.

*The 5 nominations for which no studies are recommended at this time:*

- **1,3-Hexachlorobutadiene** – industrial by-product and persistent environmental contaminant.
- **Infrasound** – low frequency acoustic energy present at low levels in community and occupational settings.
- **Magnesium oxide** – high-production-volume chemical with numerous industrial uses.
- **Methylolurea** – starting material for and impurity in urea-formaldehyde resins.
- **4-Methylquinoline** – environmental pollutant structurally related to the carcinogen quinoline.

The NTP continually solicits nominations of chemicals and other agents for toxicological studies from all sources including academia, industry, labor unions, federal and state agencies, and the general public. All nominations should be accompanied by a rationale for study (e.g., 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 Chemical Abstract Service (CAS) number. Nominations and comments regarding nominations or testing initiatives should be sent to the Office of Chemical Nomination and Selection.

*Contact information:* Dr. Scott Masten, Office of Chemical Nomination and Selection, NIEHS, P.O. Box 12233, MD A3-07, Research Triangle Park, NC 27709; T: 919-541-5710; [masten@niehs.nih.gov](mailto:masten@niehs.nih.gov)

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

The CERHR serves as an environmental health information resource. It provides 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.



The CERHR conducts reviews on man-made or naturally occurring chemicals or chemical mixtures and welcomes the nomination of chemicals for future evaluations from all interested individuals and groups. Nominations should include the chemical's name, Chemical Abstract Service registry (CAS) number (if known), and a justification for the nomination. As possible, information on the chemical and its potential reproductive or developmental toxicity is also requested. Nominations can be submitted through the CERHR web site (choose Nominate a Chemical) or directly to the CERHR. The CERHR also invites submission, at any time, of recent, relevant toxicology or human exposure studies for chemicals under evaluation.

### **Expert Panel Report on Methanol**

The CERHR Methanol Expert Panel met in October 2001 to conduct its evaluation of methanol. Methanol is a commercially important, high-production-volume chemical (10.54 billion pounds, US production, 1993) that has a potential for substantial occupational, consumer, and environmental exposure. The CERHR announced availability of the *Expert Panel Report on the Developmental and Reproductive Toxicity of Methanol* through the *Federal Register* (May 8, 2002: Vol. 67, No. 89, pages 30942-30943). It contains summaries and conclusions of the expert panel's evaluation of the scientific data for potential reproductive and/or developmental hazards associated with exposure to methanol. The report is available electronically on the CERHR web site at <http://cerhr.niehs.nih.gov> and in printed copy by contacting the CERHR (see this page for contact information).

### **Bromopropane Expert Panel Reports**

A 10-member expert panel composed of scientists from academia, industry, and state and federal government agencies met in December 2001 to conduct an evaluation of the reproductive and developmental toxicities of 1-bromopropane and 2-bromopropane. 1-Bromopropane is used as a solvent for fats, waxes, or resins; as an intermediate in the synthesis of pharmaceuticals, insecticides, quaternary ammonium compounds, flavors, or fragrances; as a vehicle in spray adhesives; and as a cold bath degreaser. It is estimated that approximately 4.3 million pounds of 1-bromopropane are produced in or imported into the U.S. annually. 2-Bromopropane is used as an intermediate in the synthesis of pharmaceuticals, dyes, and other compounds; the extent of these uses and associated human exposures is unknown. 2-Bromopropane is also present as a contaminant in 1-bromopropane. Bromopropanes are being considered as replacement chemicals for ozone-depleting chemicals such as hydrochlorofluorocarbons and chlorinated solvents.

The CERHR announced availability of the *Expert Panel Report on the Developmental and Reproductive Toxicity of 1-Bromopropane* and the *Expert Panel Report on the Developmental and Reproductive Toxicity of 2-Bromopropane* through the *Federal Register* (March 8, 2002: Vol. 67, No. 46, pages 10734-10735). They contain summaries and conclusions of the expert panel's evaluation of the scientific data for potential reproductive and/or developmental hazards associated with exposures to 1-bromopropane and 2-bromopropane. The two reports are available electronically on the CERHR web site and in printed copy by contacting the CERHR.

*Contact information:* Dr. Michael Shelby, Director, CERHR, NIEHS, P.O. Box 12233, MD EC-32, 79 TW Alexander Drive, Research Triangle Park, NC 27709; T: 919-541-3455; [shelby@niehs.nih.gov](mailto:shelby@niehs.nih.gov)

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



The NICEATM and the Interagency Coordinating Committee for the Validation of Alternative Methods (ICCVAM) collaborate to facilitate development, validation, scientific review, and regulatory acceptance of

new and improved test methods, including methods that will reduce, refine, or replace animal use.

### **NIEHS Establishes the SACATM**

In response to the ICCVAM Authorization Act of 2000, the NIEHS has established a new federally chartered advisory committee, the Scientific Advisory Committee on Alternative Toxicological Methods (SACATM) (*Federal Register* March 13, 2002: Vol. 67, No. 49, page 11358). This committee will provide advice on the statutorily mandated activities of the ICCVAM and on activities of the NICEATM, including ways to foster partnerships and communication with interested parties. A copy of the charter is posted on the NICEATM/ICCVAM web site (<http://iccvam.niehs.nih.gov>) or available from the NTP Liaison and Scientific

Review Office (contact information bottom of page). The NIEHS is in the process of preparing a membership slate for this new committee. Meetings of this committee will be announced in the *Federal Register* and posted on the NICEATM/ICCVAM web site.

### **Endocrine Disruptor Screening Assays**

The NICEATM in conjunction with the ICCVAM recently held an expert panel meeting, May 21-22, 2002, to assess the validation status of several *in vitro* assays, including estrogen receptor (ER) and androgen receptor (AR) binding assays and ER and AR transcriptional activation assays, proposed for use in the U.S. Environmental Protection Agency's Endocrine Disruptor Screening Program (see NTP Update, March 2002). Background review documents on these assays and details about the meeting are available on the NICEATM/ICCVAM web site (see Test Methods) or by contacting the NICEATM.

*Contact information:* Dr. William Stokes, Director, NICEATM, NIEHS, P.O. Box 12233, MD EC-17, 79 TW Alexander Dr., Research Triangle Park, NC 27709; T: 919-541-2384; [niceatm@niehs.nih.gov](mailto:niceatm@niehs.nih.gov)



## *Atlas of Mouse Liver Lesions*

The Laboratory of Experimental Pathology of the Environmental Toxicology Program, NIEHS has prepared a digitized atlas of mouse liver lesions. The purpose of this atlas is

to familiarize pathologists with the spontaneous and chemically induced lesions seen in livers of B6C3F1 mice. Persons interested in receiving a copy of this CD should contact Dr. Robert Maronpot ([maronpot@niehs.nih.gov](mailto:maronpot@niehs.nih.gov)).

### **How to Subscribe to the NTP List-server**

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>, send email to [ntpmail-request@list.niehs.nih.gov](mailto: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.

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 Environmental Health Perspectives (EHP) maintains issues of the Report on Carcinogens and the library of NTP Technical Reports and NTP Toxicity Reports and adds new reports as available. To gain access to these reports, contact EHP online at <http://ehp.niehs.nih.gov> or call 1-800-315-3010 or 919-541-3841.

*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](mailto:liaison@starbase.niehs.nih.gov)