



OCTOBER 2003

# UPDATE

National Toxicology Program

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

## Olden to Step Down as Director of NIEHS and NTP



On July 29, 2003, Kenneth Olden, Ph.D., Director of the National Institute of Environmental Health Services (NIEHS) and the National Toxicology Program (NTP), announced his intention to step down from both posts. He said he plans to remain in the positions until a replacement can be found.

Dr. Olden said, "I want to spend more time with my family and again become more directly involved in directing my research program," which he has continued while also directing the agencies. "Twelve years is enough as NIEHS/NTP director – the longest I have stayed in any position. That I have remained this long as director is the best indication of how much I have enjoyed the scientific and public health challenges of leading these great institutions."

While at Harvard University and the National Cancer Institute, Dr. Olden, a cell biologist and biochemist, was active in research into the properties of cell surface molecules and their roles in human cancer. In 1985, he became Director of the Howard University Cancer Center and Professor and Chair of the Howard Department of Oncology. During his tenure at Howard University, he was appointed to NIEHS.

At NIEHS/NTP, Dr. Olden proved to be an innovative scientific manager. He conducted *Town Meetings* around the country to convey his decisions regarding NIEHS' future research activities. He promoted the use of new genetic tools to determine how the environment helps or harms human health. He developed the NIEHS journal *Environmental Health Perspectives* as a monthly publication along with a new quarterly *Environmental Health Perspectives-Toxicogenomics* section. The *Report on Carcinogens*, under Dr. Olden, declared the safety of saccharin and announced the carcinogenicity of dioxin, of second-hand smoke and sun lamps and a number of industrial compounds. What he has called his mantra – the observation that human diseases are generally the product of a triangle of environment, genetics and age – has become widely accepted.

At the NTP, the first federal chemical screening using genetically modified rodents has begun. Dr. Olden believes this process will provide more safety with fewer animals and at less cost. The changes, he hopes, will also help bring needed products, such as new prescription drugs, to the market quicker.

Born in the eastern Tennessee farming community of Parrottsville, Dr. Olden rose to conduct frequently cited cancer-related studies and to become in 1991, the first African-American named to head an institute of the National Institutes of Health. He recalls that, as a child, he heard his great-grandmother, who was born in slavery, relate vivid accounts of those days. Dr. Olden said that his heritage has fueled his efforts to champion community-based research on health disparities and environmental justice.

Olden earned his B.S. at Knoxville College, an M.S. from the University of Michigan and, in 1970, a doctorate in biology from Temple University in Philadelphia. He did much of his doctoral research at the University of Rochester, where he was presented a second doctorate – the honorary degree of Doctor of Sciences – this past May 18<sup>th</sup>.

His honors include appointment by President George H.W. Bush to membership on the National Cancer Advisory Board, membership in the Institute of Medicine of the National Academy of Sciences; the Calver Award from the the American Public Health Association; the Health and Human Services (HHS) Secretary's Distinguished Service Award; the President's Meritorious and Distinguished Executive Awards, and the American College of Toxicology's First Distinguished Service Award.

Secretary of the HHS, Tommy Thompson said, "Dr. Olden has been the kind of federal scientific leader we are proud to have in this department. He is known for his vision and his outreach and communication efforts. He has been an articulate and compelling spokesperson on the need for better scientific information for making important public policy decisions."

(Source: Press Release NIEHS 03-10, 7/29/03)

## Postponement of the Draft NTP Technical Reports Peer Review Meeting

The meeting of the NTP Board of Scientific Counselors Technical Reports Review Subcommittee that was tentatively scheduled for November 5 and 6, 2003, has been postponed. The meeting will be rescheduled for the winter 2004.

The toxicology and carcinogenicity studies that will be peer reviewed are listed below with their CAS No. and include four dioxin/dioxin-like compounds, including dioxin, a polychlorinated biphenyl, a polychlorinated furan and a mixture of these compounds. The studies on the dioxin/dioxin-like compounds were designed to evaluate the relative toxic and carcinogenic effects between the individual chemicals and the mixture. Due to the need to ensure a consistent pathological diagnostic approach across all four studies, an

expanded evaluation of the liver pathology data is being conducted. Because of the expanded pathology review, the public comment period for these studies would have been insufficient if the meeting were held on the original dates.

The rescheduled Subcommittee meeting will be held in Research Triangle Park, NC. Once plans for the meeting are finalized, the NTP will publicize details about the meeting's date and location, deadlines for public comments and how to gain access to copies of the draft reports. This information will be made available through the Federal Register, the NTP's web site (<http://ntp-server.niehs.nih.gov>), its list-server (an electronic notification service), and its quarterly newsletter the NTP Update.

3,3',4,4',5-Pentachlorobiphenyl (PCB126) /57465-28-8  
2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) /1746-01-6  
2,3,4,7,8-Pentachlorodibenzo-furan (PeCDF) /57117-31-4  
A mixture of PCB 126, TCDD, and PeCDF  
Malachite Green /569-64-2 and Leucomalachite Green /129-73-7

Anthraquinone /84-65-1 (The draft NTP Technical Report on Anthraquinone was previously reviewed in May 1999. Subsequent to that peer review, the anthraquinone tested was found to contain a 0.1% contaminant. As a result, the NTP conducted additional mutagenicity and metabolism studies and the findings from those studies are being incorporated into a revised draft technical 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 the anthraquinone tested.)



## NTP Report on the Carcinogen Subcommittee to Meet in October

A meeting of the NTP Board of Scientific Counselors Report on Carcinogens Subcommittee, a standing subcommittee of the NTP Board of Scientific Counselors, is scheduled for October 14-15, 2003 at the Marriott at Metro Center, 775 12<sup>th</sup> St., N.W. in Washington, DC.

Scheduled for peer review is the 2<sup>nd</sup> set of nominations to the 11<sup>th</sup> Edition of the Report on Carcinogens. Listed in tentative order for review, they are:

- X-radiation and GAMMA-radiation
- Neutrons
- Lead and Lead Compounds
- Human Papillomaviruses (Genital Mucosal Types)
- Hepatitis B Virus
- Hepatitis C Virus
- Diazoaminobenzene

This meeting is open to the public and oral and written comments are welcome on any nomination. Meeting

plans are published in the Federal Register (August 8, 2003: Vol. 68, No. 153 pages 47346-47348) and posted on the NTP web site (<http://ntp-server.niehs.nih.gov> see What's New?) along with links to the background documents for these nominations and public comments received on them. Persons needing special assistance in order to attend are asked to contact the Dr. Mary Wolfe, Executive Secretary (T: 919-541-4253, e-mail: [wolfe@niehs.nih.gov](mailto:wolfe@niehs.nih.gov)) at least 7 business days prior to the meeting.

Background documents for nominations previously reviewed for nomination to the 11<sup>th</sup> RoC are also posted on the NTP web site (<http://ntpserver.niehs.nih.gov/newhomeroc/11RoCBkgrnd.html>) or available, as supply lasts, in hardcopy or CD from Dr. C. W. Jameson, Head, Report on Carcinogens (T: 919-541-4096 or [jameson@niehs.nih.gov](mailto:jameson@niehs.nih.gov)).

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

### Thyroid Workshop in April

CERHR sponsored a 2-day workshop "Thyroid Toxicants: Assessing Reproductive Health Effects" on April 28 and 29, 2003, in Alexandria, VA. The purpose of this workshop was two-fold:

- 1) To discuss appropriate designs of developmental and reproductive toxicity tests for detecting adverse effects resulting from thyroid dysfunction and
- 2) To discuss the relevance of thyroid-related adverse reproductive and developmental effects observed in rodents for predicting similar effects in humans.

The CERHR prepared a review document on the role of thyroid hormones in human and laboratory animal reproductive health, which it provided to the meeting participants. Based on discussions at the workshop and comments from participants, the document was revised and will be published in *Birth Defects Research*. A report of the workshop was submitted for publication in *Environmental Health Perspectives*.

### Monographs Available

Monographs are now available on CERHR evaluations of six phthalates [di-*n*-butyl phthalate (DBP), butyl benzyl phthalate (BBP), di-isodecyl phthalate (DIDP), di-isononyl phthalate (DINP), di-*n*-hexyl phthalate (DnHP), and di-*n*-octyl phthalate (DnOP)]. The report on di(2-ethylhexyl) phthalate (DEHP) is projected for publication in October 2003. Monographs are posted on the CERHR website: <http://cerhr.niehs.nih.gov>. Printed copies (limited number) or CDs of monographs are also available from CERHR. (See contact information below.)

The NTP CERHR monograph consists of three parts:

- 1) The NTP brief, which presents the NTP's interpretation of the available data and its conclusions on the potential for a chemical to cause adverse developmental and reproductive effects in humans. This brief utilizes information from the expert panel report, public comments, and studies published since the expert panel meeting to reach conclusions on human reproductive hazard.
- 2) The expert panel report.
- 3) All public comments on the expert panel report.

Monographs on methanol, 1-bromopropane, 2-bromopropane, ethylene glycol, and propylene glycol are in production and will be available soon. Public

comments on all expert panel reports are posted on the CERHR website.

### Fluoxetine Hydrochloride Evaluation

An expert panel evaluation of fluoxetine hydrochloride (Prozac®; Sarafem™; CASRN 54910-89-3) is planned for spring 2004. This antidepressant was selected for expert panel evaluation due to sufficient reproductive and developmental animal data, human exposure information, and public concern. Fluoxetine hydrochloride, under the name Sarafem™, is being prescribed to treat premenstrual dysphoric disorder (PMDD), potentially increasing the number of women exposed during childbearing age. The FDA recently approved its use in 7-17 year olds. CERHR is in the final stages of selecting the expert panel and preparation of the draft report is underway. A Federal Register announcement of meeting details and a request for public comments on the pre-meeting draft report will be released in November 2003.

### Acrylamide

Acrylamide (CASRN 79-06-1) is used in the production of polyacrylamide, which is used in water treatment, pulp and paper production, and mineral processing. It is used in the synthesis of dyes, adhesives, contact lenses, soil conditioners, and permanent press fabrics and in molecular biology procedures such as electrophoresis. Acrylamide is a neurotoxicant and in animal studies has been shown to be a carcinogen, germ cell mutagen, and reproductive toxicant. Acrylamide was selected for expert panel evaluation due to recent public concern for human exposure through its presence in starchy foods prepared at high temperatures, e.g., french fries, potato chips, and due to recent data on its occupational exposure, bioavailability, and reproductive toxicity. A CERHR expert panel evaluation of acrylamide is planned for 2004.

The CERHR invites chemical nominations for possible future evaluation from the public and other interested parties. Nominations can be made through the CERHR website, or by contacting Dr. Shelby, CERHR director.

*Contact Information: Dr. Michael Shelby, Director, CERHR, NIEHS, PO Box 12233, MD EC-32, 79 TW Alexander Drive, Research Triangle Park, NC 27709; T: 919-541-3455; shelby@niehs.nih.gov.*



### Upcoming Events\*

October 14-15, 2003	NTP Board of Scientific Counselors Report on Carcinogens Subcommittee Meeting Marriott Hotel at Metro Center, 775 12th Street, NW, Washington, DC
Postponed: Date to be announced	NTP Board of Scientific Counselors Technical Reports Review Subcommittee Meeting In Research Triangle Park, NC.

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

## Digitized Atlas of Rodent Kidney Lesions

The Laboratory of Experimental Pathology, Environmental Toxicology Program, NIEHS, announces the availability of a digitized atlas of rodent (rat and mouse) kidney lesions and lower urinary tract lesions. The purpose of this atlas is to familiarize pathologists and others with the spontaneous and chemically induced lesions seen in the kidneys of laboratory rodents. It contains a list of references on lesions of the rodent

kidney and lower urinary tract. This atlas is available on the NTP website at:

[http://ntp-server.niehs.nih.gov/main\\_pages/rodentmodlesions.html](http://ntp-server.niehs.nih.gov/main_pages/rodentmodlesions.html)

The web site also links to two additional atlases released previously: *A Digitized Atlas of Mouse Liver Lesions* and *Lesions of Genetically Altered Mice*.



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

### ICCVAM Revises Nomination and Submission Guidelines for New, Revised, and Alternative Test Methods

The Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) recently revised its guidelines entitled, "ICCVAM Guidelines for Nomination and Submission of New, Revised, and Alternative Test Methods" [NIH Publication 03-4508]. This information should be helpful to sponsors and

nominators of new or revised test methods. The document is available on the NICEATM/ ICCVAM web site (<http://iccvam.niehs.nih.gov>) or in hardcopy (limited number) from NICEATM.

*Contact Information:* Dr. William Stokes, Director, NICEATM, NIEHS/NIH 79 Alexander Drive, Rm. 3129, P. O. Box 12233, MD EC-17, Research Triangle Park, NC 27709, Phone: 919-541-2384; F: 919-541-0947; [stokes@niehs.nih.gov](mailto:stokes@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](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 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.

*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)