

## First two substances peer reviewed for listing in new Report on Carcinogens

By Robin Mackar

A [panel](http://ntp.niehs.nih.gov/NTP/About_NTP/MonoPeerRvw/2013/March/Roster20130322_508.pdf) ([http://ntp.niehs.nih.gov/NTP/About\\_NTP/MonoPeerRvw/2013/March/Roster20130322\\_508.pdf](http://ntp.niehs.nih.gov/NTP/About_NTP/MonoPeerRvw/2013/March/Roster20130322_508.pdf)) of experts concurred with the National Toxicology Program's preliminary decision to list [1-bromopropane](http://ntp.niehs.nih.gov/?objectid=950E6597-91E6-C65B-77056D66F665C475) (<http://ntp.niehs.nih.gov/?objectid=950E6597-91E6-C65B-77056D66F665C475>) and [cumene](http://ntp.niehs.nih.gov/?objectid=95006BFB-DE65-882D-C3F7B34AC113FBA8) (<http://ntp.niehs.nih.gov/?objectid=95006BFB-DE65-882D-C3F7B34AC113FBA8>) as reasonably anticipated human carcinogens, based on sufficient laboratory animal data.

These are the first two chemicals to be peer reviewed as part of a [new process](http://ntp.niehs.nih.gov/NTP/RoC/Thirteenth/Process/FinalRoCProcesswithFig.pdf) (<http://ntp.niehs.nih.gov/NTP/RoC/Thirteenth/Process/FinalRoCProcesswithFig.pdf>) for evaluating substances for the 13th Report on Carcinogens (RoC).

In an open meeting that was also webcast, the panel, which met March 21-22, was charged with reviewing the draft documents, referred to as monographs, and voting on whether the scientific evidence presented supports the NTP's listing decisions. The RoC can list substances in one of two categories — known to be human carcinogens or reasonably anticipated to be human carcinogens.

Each RoC monograph is comprised of a cancer evaluation component, which lays out all the information used to make a listing decision, and a substance profile, containing both the NTP's listing recommendation and a summary of the scientific information considered key to reaching that recommendation. The development of the draft monograph is one of the newer additions to the RoC evaluation process.

"We wanted to create a document that clearly illustrates how we came to our conclusions about listing a substance," said NTP Associate Director John Bucher, Ph.D.

The panel appeared to like the draft monographs. "This is about the third time I've served on a peer review committee for the NTP, and I must say you really hit your target in the way you are developing your documents and getting public input," said panel member Wayne Sanderson, Ph.D., of the University of Kentucky.

### Cumene

Ruth Lunn, Dr.P.H., director of the [Office of the Report on Carcinogens \(RoC\)](#), outlined the process for developing the documents. Next, Mary Wolfe, Ph.D., director of the NTP Office of Liaison Policy and Review, identified scientific issues in the written public comments on the substance, and asked the panel to carefully consider the public comments.

NTP health scientist Gloria Jahnke, D.V.M, gave the presentation on cumene. Cumene is a colorless liquid, primarily used to make other chemicals, including acetone and phenol. It is also found in fossil fuels, such as blended high octane gasoline and kerosene.

The panel spent time discussing whether or not a significant number of persons in the United States were exposed to cumene. Chair Lucy Anderson, Ph.D., summed up the panel conversations by saying the committee thinks that the occupational and environmental exposure data presented qualifies as significant.



Lunn provided an overview of the RoC process at the peer review panel meeting. (Photo courtesy of Steve McCaw)



U.S. Environmental Protection Agency senior scientist Stephen Nesnow, Ph.D., right, an organic chemist by training, and a well-known expert on chemical carcinogenesis, offered many thoughtful comments on both the cumene and 1-bromopropane draft monographs. Nesnow was seated next to Bucher. (Photo courtesy of Steve McCaw)

The panel voted to concur with NTP to list cumene as a reasonably anticipated human carcinogen. The panel's conclusions were based on tumors found in lung and liver, but, since there was not consensus about the renal tumors, the panel decided to recommend adding renal tumors as supporting evidence for the listing.

### 1-bromopropane

NTP health scientist Diane Spencer walked the panel through the science of 1-bromopropane, which is a solvent used as a cleaner to degrease electronics and metals, and may be used in some dry cleaning operations. The panel agreed that the chemical is significant to public health.

Because there were no human studies to consider, Spencer presented the animal data showing the substance caused skin tumors in male rats, large intestine tumors in male and female rats, and lung tumors in female mice.

Reviewer Terry Gordon, Ph.D., of the New York University Langone Medical Center, agreed with the data presented, saying he felt the rodent data were biologically relevant to humans, but remained puzzled by the different gender effects.

Although there were few mechanistic data available, the panel generally agreed with NTP conclusions on the genotoxicity data. They felt the overall evaluation was an effective synthesis of integrating the metabolic, genotoxic, and mechanistic data with the carcinogenicity results.

The panel also discussed the role that immunosuppression may play in tumor development in animals. "Immunosuppression needs to be mentioned and emphasized more in the document," said Paul White, Ph.D., of Health Canada, with concurrence from MaryJane Selgrade, Ph.D., of ICF International.

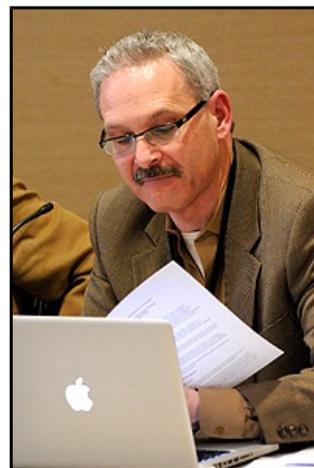
The panel unanimously voted to list 1-bromopropane as reasonably anticipated to be a human carcinogen, based on the animal studies presented by NTP.

The documents will be revised based on comments, placed on the public website, and shared at a public meeting with the NTP Board of Scientific Counselors.

(Robin Mackar is the news director in the NIEHS Office of Communications and Public Liaison, and a frequent contributor to the Environmental Factor.)



*Chairperson Anderson, left, consulted with Wolfe about the charge to the panel. (Photo courtesy of Steve McCaw)*



*Lawrence Lash, Ph.D., of the Wayne State University School of Medicine, reviewed his notes, while sharing his comments with fellow board members and NTP staff. (Photo courtesy of Steve McCaw)*



*Jahnke walked the panel through the cumene animal literature. (Photo courtesy of Steve McCaw)*



*Panel member Sanderson had many positive comments to make about the documents and the RoC process. (Photo courtesy of Steve McCaw)*



*While at NIEHS, Paul White also shared his expertise on chemical mixtures, during a separate talk hosted by NTP earlier in the week. (Photo courtesy of Steve McCaw)*



*Peer reviewer Michael Elwell, D.V.M., Ph.D., left, from Covance Laboratories Inc., and Gordon provided comments on the draft documents. (Photo courtesy of Steve McCaw)*



*Lunn, left, and Jahnke responded to questions from the panel about the cumene literature. Spencer joined Lunn the next day to present on 1-bromopropane. (Photo courtesy of Steve McCaw)*



*Wolfe, left, and Bucher were clearly pleased with the input they received from the public and the panel. (Photo courtesy of Steve McCaw)*

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