

Peer reviewers support NTP listing recommendation for TCE

By Robin Mackar

A panel of experts spent Aug. 12 peer reviewing an NTP draft monograph on trichloroethylene (TCE) (<http://ntp.niehs.nih.gov/pubhealth/roc/candidates/tce.html>), a chemical once prominently used as a degreaser for metal parts. The ten-member panel agreed with the NTP's preliminary decision to list TCE as a known human carcinogen in the [Report on Carcinogens](http://ntp.niehs.nih.gov/pubhealth/roc/index.html) (<http://ntp.niehs.nih.gov/pubhealth/roc/index.html>) (RoC), based on sufficient evidence of carcinogenicity from studies in humans.

The vote came after presentations and discussions by NTP and the reviewers focusing on evidence for cancer at three sites - kidney, liver, and non-Hodgkin lymphoma. An NTP-sponsored public [webinar](#) earlier in the year also helped provide information about TCE that was used in the evaluation of the human cancer studies.

An overview of the 30 major human studies used in the TCE evaluation was presented by Jennifer Ratcliffe, Ph.D., of ILS, a contractor supporting NTP. Ratcliffe went over the study selection and quality evaluation. Stanley Atwood, Ph.D., also of ILS, presented information about the metabolism and genetic effects of TCE.

Kidney cancer

Ruth Lunn, Dr.P.H., director of the [Office of the Report on Carcinogens](#), talked the panel through the human studies used by NTP when evaluating kidney cancer outcomes and TCE. She said the studies provide credible evidence of a causal association between increased cancer risk and exposure to TCE.

"The findings are consistent across the studies," Lunn said. "The highest risk for kidney cancer was found in studies where workers were exposed to higher levels of TCE."

Overall, the lead reviewers for the kidney cancer section of the draft had favorable comments. David Richardson, Ph.D., an epidemiologist from the University of North Carolina at Chapel Hill, and others called for more descriptive language to better characterize kidney and other cancers.

The mechanistic studies for kidney cancer were also presented. Reviewer George Douglas, Ph.D., scientist emeritus at Health Canada, did not feel there was strong evidence to show a clear mechanism of action of mutagenicity. "I'd call the evidence presumptive and supporting, but not strong."

John Bucher, Ph.D., NTP associate director reminded reviewers that epidemiological studies alone are enough to provide sufficient evidence of human carcinogenicity. He said identification of a mechanism is not required.

Non-Hodgkin lymphoma (NHL)

Ratcliffe presented human epidemiological studies on NHL, which is cancer that affects the body's white blood cells. The mechanistic studies were also presented. The panel agreed with NTP's assessment that there is limited evidence of a causal association between exposure to TCE and NHL from studies in humans.

Panel member Sarah Blossom, Ph.D., of Arkansas Children's Hospital Research Institute, commented on the studies focusing on immune effects of TCE that may be related to a mode of action for NHL. "We know it's immunotoxic, but we can't be sure it causes immune suppression."

The panel agreed with the preliminary evidence presented showing limited indication for a causal relationship between exposure to TCE and NHL from studies in humans.

Liver cancer

The human cancer and mechanistic studies were presented by Sanford Garner, Ph.D., also of ILS. Garner started out by saying that liver cancer is a relatively rare cancer and has a low survival rate.

"The data out there are basically inadequate to evaluate the relationship between liver cancer and exposure to TCE," Garner said. He pointed out that TCE-induced liver cancer is likely caused by complex mechanisms involving multiple pathways, including oxidative stress, genotoxicity, and more.

The panel agreed with NTP's preliminary conclusion that there is inadequate evidence of a causal relationship between exposure to TCE and liver cancer.



At the head table, from right, are Lunn; panel chair David Eastmond; Mary Wolfe, Ph.D., NTP deputy division director for policy; and NIEHS and NTP Director Linda Birnbaum, Ph.D. (Photo courtesy of Steve McCaw)



Panel members Douglas, left, and Marie-Elise Parent, Ph.D., provide valuable input on the TCE monograph. (Photo courtesy of Steve McCaw)



Peer reviewer Blossom, provided expertise on the immunological aspects of TCE. (Photo courtesy of Steve McCaw)

Overall listing recommendation and next steps

To wrap up the day, chair David Eastmond, Ph.D., of the University of California, Riverside, held a final vote on the preliminary listing decision for TCE.

The panel agreed with NTP that TCE is known to be a human carcinogen based on sufficient evidence of carcinogenicity from studies in humans. They went on to say that there are human epidemiological studies showing sufficient evidence for kidney cancer, as well as supporting evidence from toxicokinetic, toxicological, and mechanistic studies. They also agreed that there is limited evidence for TCE from studies of NHL in humans. Supporting evidence for the listing of TCE as a known human carcinogen is also found in animal studies.

NTP will carefully consider all comments made by the panel and the public, in revising the draft TCE monograph.

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



Reviewer Lawrence Lash, Ph.D., left, and David Richardson, Ph.D., listened carefully to presentations, and offered comments throughout the meeting. (Photo courtesy of Steve McCaw)



In the audience was Edward Murray, Ph.D., acting director of the Division of Toxicology and Human Health Services at the Centers for Disease Control and Prevention Agency for Toxic Substances and Disease Registry. (Photo courtesy of Steve McCaw)

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