

Actions from Peer Review of the Draft Report on Carcinogens (RoC)
Monographs for *ortho*-Toluidine and Pentachlorophenol and By-products of its Synthesis

December 12 - 13, 2013

The NTP Monograph Peer-Review Panel (“the Panel”) was convened on December 12 - 13, 2013, to peer review the *Draft Report on Carcinogens Monograph for ortho-Toluidine* and the *Draft Report on Carcinogens Monograph for Pentachlorophenol and By-products of its Synthesis* (available at <http://ntp.niehs.nih.gov/go/38854>). A meeting report will be prepared and posted to the NTP website when completed. The Panel peer reviewed the draft monographs and provided its opinion on the NTP’s draft conclusions for the level of evidence for carcinogenicity from experimental animal studies and human cancer studies and the NTP’s preliminary listing decisions for *ortho*-toluidine and pentachlorophenol and by-products of its synthesis in the RoC. The NTP will consider the Panel’s peer-review comments in finalizing the monographs. When completed, the monographs will be published on the NTP website (<http://ntp.niehs.nih.gov/go/roc>).

***ortho*-Toluidine**

The Panel supported the statement that a significant number of persons in the United States are exposed to *ortho*-toluidine.

The Panel agreed unanimously (11 yes, 0 no, 0 abstentions) that the scientific information presented from studies in experimental animals supports the NTP’s level of evidence conclusion of *sufficient evidence of carcinogenicity* of *ortho*-toluidine. The basis is an increased incidence of tumors in two species and at several tissues sites: urinary bladder, connective tissue, subcutaneous tissue, mesothelium, blood vessel, or liver.

The Panel agreed unanimously (11 yes, 0 no, 0 abstentions) that the scientific information presented from human cancer studies supports the NTP’s level of evidence conclusion of *sufficient evidence of carcinogenicity* of *ortho*-toluidine. The basis is an increased risk of urinary bladder cancer among *ortho*-toluidine workers that is unlikely to be explained by chance, bias, or confounding.

The Panel agreed unanimously (11 yes, 0 no, 0 abstentions) with the NTP’s preliminary policy decision to list *ortho*-toluidine in the RoC as *known to be a human carcinogen* based on increased risks of urinary bladder cancer among *ortho*-toluidine exposed workers in concert with cancer studies in animals, including site concordance for urinary

bladder cancer in female and male rats and humans, and mechanistic data demonstrating biological plausibility in humans.

Pentachlorophenol

The Panel supported the statement that a significant number of persons in the United States are exposed to pentachlorophenol and by-products of its synthesis.

The Panel recommended changing the NTP's level of evidence conclusion in the draft monograph from *sufficient* to *limited* evidence of carcinogenicity of pentachlorophenol and by-products of its synthesis from studies in humans.

The Panel agreed unanimously (10 yes, 0 no, 0 abstentions) that the scientific information presented from human cancer studies supports the level of evidence conclusion of *limited evidence of carcinogenicity* of pentachlorophenol and by-products of its synthesis. The basis is limited evidence across studies in humans, which indicates a causal association between pentachlorophenol and by-products of its synthesis and non-Hodgkin lymphoma was credible, but alternative explanations such as chance, bias, or confounding factors could not be adequately excluded.

The Panel agreed unanimously (10 yes, 0 no, 0 abstentions) that the scientific information presented from studies in experimental animals supports the NTP's level of evidence conclusion of sufficient evidence of carcinogenicity of pentachlorophenol and by-products of its synthesis based on increased incidence of tumors in rats and mice at several tissue sites. The Panel also recommended (10 yes, 0 no, 0 abstentions) that there is *sufficient* evidence of carcinogenicity of pentachlorophenol itself based on studies in experimental animals. In reaching this recommendation, the panel considered the evidence from studies using two different purities (approximately 91% and 99%) of pentachlorophenol.

The Panel recommended changing the NTP's preliminary listing decision in the draft monograph from *known to be a human carcinogen* to *reasonably anticipated to be a human carcinogen*.

The Panel agreed unanimously (10 yes, 0 no, 0 abstentions) with the recommendation to list pentachlorophenol and by-products of its synthesis in the RoC as *reasonably anticipated to be a human carcinogen* based on limited evidence from studies in humans, sufficient evidence of carcinogenicity of pentachlorophenol, and pentachlorophenol and by-products of its synthesis, from studies in experimental animals, and supporting mechanistic evidence.