



National Toxicology Program

U.S. Department of Health and Human Services

Office of the Report on Carcinogens
Public Webinar (via Adobe® Acrobat® Connect™)

**Human cancer studies on exposure to pentachlorophenol (PCP):
Differentiating potential cancer effects of PCP exposure from
effects
due to occupational co-exposures or PCP contaminants**

April 11, 2013, 12:30 to 5:00 PM

ABSTRACTS

Presentation 1. *Overview of occupational exposures to pentachlorophenol: Components, contaminants, and common co-exposures*

Kevin Dunn, M.S., National Institute for Occupational Safety and Health (NIOSH)

Pentachlorophenol (PCP) was produced in the United States from 1936 to 2006. The PCP manufacturing process results in a product that contains several di-benzo-p-dioxins and di-benzo furans. PCP has been classified as a possible human carcinogen by the International Agency for Research on Cancer. This presentation will describe the manufacturing and finishing processes for technical grade PCP, as well as the formation and identification of contaminants. Routes of exposure and reported exposure profiles from the PCP manufacturing workers and wood preservative workers will also be presented, in addition to common co-exposures encountered in these industries.

Presentation 2. *Occupational exposure to PCP and other agents: Issues to consider in evaluating human epidemiology studies*

Avima Ruder, Ph.D., NIOSH

Pentachlorophenol (PCP) manufacturing workers, sawmill workers, and end-users of PCP-treated lumber are the three major PCP-exposed occupational groups. North American PCP manufacturing workers were not exposed to 2,3,7,8-tetrachloro-dibenzo-p-dioxin (TCDD) contaminants in the manufacturing process, but they were exposed to other dioxins and furans of varying potency. In addition, in the plants where they worked there were a multitude of co-exposures, particularly if they did not work exclusively in a PCP production department. Sawmill workers may be exposed to chlorophenols as well as wood dust, and some continue to be exposed to creosote, still used as a wood preservative. End-users of treated lumber including, in the past, residential construction workers and, currently, workers repairing or constructing railroad ties and wooden docks, and hazardous waste disposal workers may be exposed to PCP. Telephone poles may be treated with PCP and PCP has been found in the urine of electrical utility linemen, who are also

exposed to sunlight and electrical and magnetic fields. Such co-exposures can affect study findings, particularly if the co-exposure and PCP are associated with the same health outcome. These study issues will be considered in the context of the recently completed mortality study of U.S. PCP production workers. The possible effect on study findings and ways in which researchers have tried to or should try to control for this confounding will be discussed.

Presentation 3. *Biomonitoring and epidemiologic studies of PCP producers*

Jim Collins, Ph.D., The Dow Chemical Company

We examine data from fourteen published epidemiology studies of nine pentachlorophenol (PCP) producers in the United States, China, England and Wales, the Czech Republic, Russia, and the Netherlands [1-14]. We summarize how these studies developed exposure assessment and dealt with potential confounders. While the data is limited, exposure to PCP appears higher in manufacture than in wood preserving and saw mills and the population case control appear to have the lowest overall exposures [15-18]. Exposure assessment for PCP is difficult for several reasons. First, impurities in commercial grade PCP typically make up 10% of the product [19]. The impurities include dioxins [16]. Most of the studies of PCP manufacture use duration of exposure as an indicator of level of exposure or a combination of subjective and quantitative results. Also, since PCP has several impurities and PCP is made at sites which often make other pesticides, exposures are to mixtures of substances. Approaches for dealing with mixtures are discussed. Second, PCP has a relatively short half life in the human body and thus exposure assessment through biomonitoring is impractical [20]. Some studies have used biomonitoring of dioxins in PCP as an indicator of exposure [10, 11, 14]. Since some dioxins are relatively long lived in the body, past exposures can be estimated with more precision. The dioxins also offer a biologic based method for dealing with dioxin mixtures [10]. We examine several other issues including exposure modeling, reducing biases and dealing with potential confounders. We also discuss the results of the Dow Midland, Michigan pentachlorophenol study in the context of other studies [9, 10].

References

1. Jirasek, J., J. Kalensky, and K. Kubec, *Occurrence of acne chlorina and porphyria cutanea tarda during the production of herbicides*. Ceskoslovenska Dermatologie, 1973. 48(5): p. 306-317.
2. Jirasek, L., et al., *Chloracne, porphyria cutanea tarda, and other poisonings due to herbicides*. Hautarzt, 1976. 27(7): p. 328-333.
3. O'Malley, M.A., et al., *Chloracne Associated with Employment in the Production of Pentachlorophenol*. Am J Ind Med, 1990. 17: p. 411-421.
4. Cheng, W.N., et al., *A health survey of workers in the pentachlorophenol section of a chemical manufacturing plant*. Amer J Ind Med, 1993. 24: p. 81-92.

5. Bueno de Mesquita, H.B., et al., *Occupational exposure to phenoxy herbicides and chlorophenols and cancer mortality in The Netherlands*. Am J Ind Med, 1993. 23(2): p. 289-300.
6. Baxter, R.A., *Biochemical Study of Pentachlorophenol Workers*. Ann Occup Hyg, 1984. 28(4): p. 429-438.
7. Revich, B., et al., *Dioxin Exposure and Public Health in Chapaevsk, Russia*. Chemosphere, 2001. 43: p. 951-966.
8. Hryhorczuk, D.O., et al., *A Morbidity Study of Former Pentachlorophenol Production Workers*. Environ Health Perspect, 1998. 106(7): p. 401-408.
9. Ramlow, J.M., et al., *Mortality in a cohort of pentachlorophenol manufacturing workers, 1940-1989*. J Occup Med, 1996. 30: p. 180-194.
10. Collins, J.J., et al., *Mortality rates among workers exposed to dioxins in the manufacture of pentachlorophenol*. J Occup Environ Med, 2009. 51: p. 1212-1219.
11. Boers, D., et al., *Cause-specific mortality of Dutch chlorophenoxy herbicide manufacturing workers*. Occup Environ Med, 2010. 67(1): p. 24-31.
12. Ruder, A.M. and J.H. Yiin, *Mortality of US pentachlorophenol production workers through 2005*. Chemosphere, 2011. 83: p. 851-861.
13. Kogevinas, M., et al., *Cancer Mortality in Workers Exposed to Phenoxy Herbicides, Chlorophenols, and Dioxins*. Am J Epidemiol, 1997. 145(12): p. 1061-1075.
14. Flesch-Janys, D., et al., *Estimation of the cumulated exposure to polychlorinated dibenzo-p-dioxins / furans and standardized mortality ratio analysis of cancer mortality by dose in an occupationally exposed cohort*. Environmental Health Perspective, 1998. 106 (suppl.2): p. 665-672.
15. Schecter, A., et al., *Comparison of dibenzodioxin levels in blood and milk in agricultural workers and other following pentachlorophenol exposure in China*. Chemosphere, 1994. 29(9-11): p. 2371-2380.
16. Collins, J.J., et al., *Serum concentrations of chlorinated dibenzo-p-dioxins and dibenzofurans among former Michigan trichlorophenol and pentachlorophenol workers*. J Exp Sci Environ Epidemiol, 2007. 17: p. 541-548.
17. McLean, D., et al., *Morbidity in former sawmill workers exposed to pentachlorophenol (PCP): a cross-sectional study in New Zealand*. Am J Ind Med, 2009. 52(4): p. 271-81.
18. Hardell, L., et al., *Adipose tissue concentrations of dioxins and dibenzofurans, titers of antibodies to Epstein-Barr virus early antigen and the risk for non-Hodgkin's lymphoma*. Environmental Research, 2001. Section A 87: p. 99-107.
19. Cooper, G.S. and S. Jones, *Pentachlorophenol and cancer risk: focusing the lens on specific chlorophenols and contaminants*. Environ Health Perspect, 2008. 116(8): p. 1001-8.
20. Plimmer, J.R., *Technical pentachlorophenol: Origin and analysis of base-insoluble contaminants*. Environ Health Persp, 1973. September: p. 41-48.

Presentation 4. *Epidemiologic studies of PCP users*

Paul Demers, Ph.D., Occupational Cancer Research Centre, Cancer Care Ontario;
Professor, Dalla Lana School of Public Health, University of Toronto

Pentachlorophenol (PCP) is primarily used as a fungicide to preserve wood products, such as utility poles, railroad ties, foundation pilings, bridge timbers and ties, and fence posts. Historically, it was also used extensively to treat freshly cut lumber until it was replaced with less toxic products in most countries 20-30 years ago. The risk of cancer among pentachlorophenol users has been studied through a number of case-control and cohort studies, which were primarily, conducted in regions with a large forest industry, such as the Nordic countries, the northwest coast of North America, and New Zealand. The strongest evidence has been for an increased risk of non-Hodgkin's lymphoma, with positive associations observed in both case-control and cohort studies. There is also evidence of an excess risk of multiple myeloma and soft tissue sarcoma, although the evidence is somewhat less consistent, and much more limited evidence for other sites. Challenges in interpreting this literature are ruling out the role of co-exposures and contaminants and assessing the quality of the exposure assessments performed, which is made more difficult because there have been changes in exposure over time.