



PENTACHLOROPHENOL  
AND SOME RELATED  
COMPOUNDS

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TO HUMANS

## GENERAL REMARKS

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This one-hundred-and-seventeenth volume of the *IARC Monographs* contains evaluations of the carcinogenic hazard to humans of pentachlorophenol, 2,4,6-trichlorophenol, 3,3',4,4'-tetrachloroazobenzene, aldrin, and dieldrin.

Pentachlorophenol, aldrin, and dieldrin are classified as persistent organic pollutants under the Stockholm Convention. Aldrin and dieldrin had been previously evaluated as *not classifiable as to their carcinogenicity to humans* (Group 3) in Supplement 7 ([IARC, 1987](#)), and combined exposures to polychlorophenols or to their sodium salts were evaluated as *possibly carcinogenic to humans* (Group 2B) in Volume 71 ([IARC, 1999](#)) of the *IARC Monographs*. 3,3',4,4'-Tetrachloroazobenzene was not previously evaluated by the *IARC Monographs* programme. A summary of the findings of this volume appears in *The Lancet Oncology* ([Guyton et al., 2016](#)).

### Pentachlorophenol

Impurities of chlorophenols include polychlorinated dibenzo-*para*-dioxins, as well as polychlorinated dibenzofurans, polychlorinated phenoxyphenols, polychlorinated diphenyl ethers, polychlorinated benzenes, and polychlorinated biphenyls. However, the pattern of excess cancers seen with pentachlorophenol differed from that observed in populations that are highly exposed to dioxins. In addition, the pattern of tumours in experimental animals

exposed to pentachlorophenol was similar across three test agents of different purity. Similarly, test agents varying in purity induced mechanistic effects that are different from those exhibited by dioxins. These mechanistic studies provided strong evidence of multiple key characteristics of carcinogens ([Smith et al., 2016](#)).

### 3,3',4,4'-Tetrachloroazobenzene

3,3',4,4'-Tetrachloroazobenzene is not manufactured commercially but is formed during the production and degradation of chloroanilide herbicides. 3,3',4,4'-Tetrachloroazobenzene bears structural similarity to dioxins and is highly lipophilic but is rapidly metabolized, with extensive azo reduction in the gut and liver to give 3,4-dichloroaniline metabolites that are readily eliminated. The spectrum of rodent tumours induced by 3,3',4,4'-tetrachloroazobenzene encompasses those observed with other aryl hydrocarbon receptor (AhR) agonists previously evaluated as *carcinogenic to humans* (Group 1) (e.g. dioxins, dioxin-like polychlorinated biphenyls, and 2,3,4,7,8-pentachlorodibenzofuran). In addition, 3,3',4,4'-tetrachloroazobenzene activates AhR and/or induces multiple non-neoplastic effects that are consistent with, or are

hallmarks of, AhR activation in various species, such as rodents, rabbits, chicken, and zebrafish (Poland et al., 1976; NTP, 1998, 2010; Xiao et al., 2016). 3,3',4,4'-Tetrachloroazobenzene was classified as *probably carcinogenic to humans* (Group 2A) because it belongs, based on mechanistic considerations, to a class of agents that activate AhR, and some members of this class have previously been evaluated as Group 1 or Group 2A.

## Aldrin and dieldrin

Aldrin and dieldrin each induced hepatocellular carcinomas in studies of carcinogenicity in experimental animals. For aldrin, epidemiological data were inadequate and mechanistic data were sparse. For dieldrin, epidemiological studies provided *limited evidence* in humans for breast cancer, whereas the evidence was *inadequate* for non-Hodgkin lymphoma and other cancers. Mechanistic studies provided moderate evidence for multiple key characteristics of carcinogens (Smith et al., 2016). Because aldrin rapidly converts to dieldrin in the body, exposure to aldrin inevitably entails internal exposure to dieldrin. Dieldrin is slowly excreted in humans, due to inefficient metabolism and sequestration in fat. Dieldrin, and aldrin metabolized to dieldrin, was evaluated as *probably carcinogenic to humans* (Group 2A).

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