Canadian Tissue Residue Guidelines for the Protection of Wildlife Consumers of Aquatic Biota

TOXAPHENE

Toxaphene (CAS 8001-35-2) is the common name for a complex mixture of chlorinated camphenes and bornane derivatives resulting from the chlorination of camphene (ATSDR 1994). More than two-thirds of the isomers contain 7 to 9 chlorine atoms (CCREM 1987), the molecular weight averaging 414 $g \cdot mol^{-1}$ (Eisler and Jacknow 1985). Toxaphene, also known as campheclor, chlorocamphene, or polychlorocamphene (PCC), is typically an amber-coloured waxy solid with a pine or terpene odour (Brooks 1974; Budavari et al. 1989).

Toxaphene was developed in 1946 and used as a contact insecticide to control infestations of agricultural crops including cereal grains, fruits, nuts, oil-seeds, vegetables, and cotton (WHO 1984; ATDSR 1994). Toxaphene has also been used in herbicides and to control ectoparasites on livestock (WHO 1984; ATSDR 1994). Toxaphene, or mixtures of toxaphene and rotenone, were commonly applied during the 1950s and 1960s to lakes and streams to eliminate undesirable fish, lamprey, and invertebrate communities, particularly in Canada and the northern United States (Lockhart et al. 1992; Miskimmin and Schindler 1994; Stern et al. 1996).

Chromatography has been used to identify between 177 and 670 compounds in the toxaphene mixture (Vetter 1993). In theory, 197 bornanes and camphenes with more than five chlorines can be present in significant amounts in technical toxaphene (Hainzl et al. 1994). This leads to variability in the PCC content of technical toxaphene as well as variation resulting from weathering and/or metabolic degradation.

The reported estimates of the log octanol–water coefficient (log K_{ow}) differ between studies, ranging from 2.92 (USEPA 1980) to 6.44 (Saleh 1991). As with other organochlorine pesticides (such as DDT), toxaphene tends to accumulate in tissues with the highest lipid content (Rogers and Hall 1987; Muir et al. 1992b). Polychlorocamphenes have been found in wildlife feeding at high trophic levels in the food chain, including fish (Muir 1994; Kidd et al. 1995), birds (Bush et al. 1978), and mammals (Muir et al. 1990).

Contamination of surface waters may continue to occur as a result of the erosion of toxaphene-contaminated soils, yet atmospheric deposition represents the main source of toxaphene entry to the Canadian environment (Seiber et al. 1979). Despite deregistration of pesticides containing PCCs in both Canada and the United States, atmospheric concentrations remain nearly constant, and may be increasing (ATSDR 1994). Probable sources include volatization from historical high-use areas (i.e., southern United States) and ongoing use in other countries. Toxaphene is very resistant to leaching once bound to soil particles (Jaquess et al. 1989), and evaporation of toxaphene functions as a primary route of removal from soil surfaces to the atmosphere. These sources are significant due to "global distillation" (Loganathan and Kannan 1994), resulting in the deposition of PCCs through gas exchange with surface waters and wet and dry fallout in temperate and cold regions. This is demonstrated by contaminated air samples from sites on coastal Newfoundland and in the Northwest Territories, and elevated levels in the tissues of burbot and lake trout from lakes in Yukon—sites far removed from application sites (Palmer 1992; Schindler et al. 1993).

Wildlife in aquatic ecosystems depend on aquatic biota such as fish, shellfish, invertebrates, and plants as their primary source of food. These food resources provide the main exposure route for aquatic-based wildlife species to persistent substances, such as toxaphene, that accumulate in food webs. Table 1 lists the Canadian tissue residue guideline for the protection of wildlife consumers of aquatic biota. Table 2 summarizes toxaphene measurements made in Canadian biota (i.e., post-deregistration in Canada). The data represent both typically low and high levels of toxaphene measured in Canada for each organism.

Table 1. Canadian tissue residue guideline for toxaphene* for the protection of wildlife consumers of aquatic biota (Environment Canada 1997).

Compound	Guideline value ($\mu g \cdot kg^{-1}$ diet ww)
Toxaphene	6.3

*Represents a single maximum concentration of toxaphene in aquatic biota that would not be expected to result in adverse effects on wildlife consumers of aquatic biota.

Table 2. Levels of toxaphene in Canadian biota.

Biota		Tissue	Year	Toxaphene* (µg·kg^{-1} ww)	Reference
Invertebrates	Freshwater	Whole	1993; 1992	0.0022–18.9	Hargave et al. 1994; Schindler et al. 1993
	Marine	Whole	1993	2–3884	Hargave et al.1994
Fish	Freshwater	Muscle	1993/94	3.21–1993	Muir et al. 1994
	Freshwater	Liver	1991; 1990-92	54–2805	Palmer 1992; Kidd et al. 1993
	Marine	Muscle	1984; 1981	14–1000	Muir et al. 1987; Musial and Uthe 1983
	Marine	Liver	1991; 1979	23–1100	Bright et al. 1995; Musial and Uthe 1983
Mammals		Blubber	1988; 1986/87	130–14700	Muir et al. 1992a; 1990
Birds		Egg	1981	<100–1450	Weseloh et al. 1989

*Represents the range of values for toxaphene found in the literature.

Toxicity

Exposure to toxaphene is known to induce adverse effects on cardiovascular, hepatic, renal, endocrine, immunological, and neurological systems, and to decrease longevity in birds and mammals (ATSDR 1994). In addition, genotoxicity and carcinogenicity have been exhibited in laboratory studies (Saleh 1991).

Mammalian Toxicity

Acute oral LD_{50}s of technical grade toxaphene range from as low as 25 mg·kg^{-1} bw in cats to as high as 500 mg·kg^{-1} bw in rabbits (USEPA 1976). Experimental acute toxicity varies with the solvent used for administration; for example, the toxicity of toxaphene is increased by as much as five times by replacing kerosene with corn oil (USEPA 1976). The effect of dietary exposure also varies, with decreased growth rates and lower final body weights observed in guinea pigs fed 2 or 5 mg·kg^{-1} bw per day for 60 d (Chandra and Durairaj 1992) to no significant effect on the growth rate of male rats fed toxaphene at doses up to 45 mg·kg^{-1} bw per day for 26 weeks (Chu et al.1988). These rats, however, did exhibit liver hypertrophy and increase in relative kidney weight.

The mutagenic potential of toxpahene has been observed in the bacterium *Salmonella typhimurium* (ATSDR 1994). Toxaphene is also known to increase chromosomal aberrations in mammalian lymphocyte cultures (Samosh 1974) and to increase the frequency of sister chromatid exchanges in human lymphoid cells (Sobti et al. 1983), suggesting mutagenic capability in mammalian species. The carcinogenicity of toxaphene has been demonstrated in mice fed 4.95 and 9.9 mg·kg^{-1} bw per day for up to 560 d (NCI 1979). Both male and female mice exhibited increased incidence of liver neoplasms and malignant neoplasms at all sites.

Avian Toxicity

Available acute toxicity data suggest birds are at least as sensitive as mammals to the effects of toxaphene. LD_{50}s range from 19.9 mg·kg^{-1} bw for the sharp-tailed grouse *(Tympanuchus phasianellus)* to 581 mg·kg^{-1} for the horned lark *(Eremophilia alpestris).* Long-term exposure to doses of 0.51 mg·kg^{-1} bw per day resulted in impaired growth of bobwhite quail *(Colinus virginianus)* (Hurst et al. 1974). The same effect was observed in ring-necked pheasants *(Phasianus colchius),* black ducks *(Anas rubripes),* and white leghorn chickens *(Gallus domesticus)* at dosage rates as low as 2.2, 2.83, and 5.7 mg·kg^{-1} bw per day, respectively (Genelly and Rudd 1956a; Bush et al. 1977; Mehrle et al. 1979).

Toxaphene has also been observed to impair avian reproduction. Genelly and Rudd (1956b) demonstrated that the dietary exposures of 2.2 mg·kg^{-1} bw per day for 8 weeks resulted in decreased egg production and egg hatchability compared to lower and control doses. Hatchling survival and overall reproductive success were reduced at all treatment concentrations (1.3, 2.2 mg·kg^{-1} bw per day).

Tissue Residue Guideline Derivation

The Canadian tissue residue guideline for the protection of wildlife that consume aquatic biota was developed according to the CCME protocol (CCME 1998).

Mammalian Reference Concentration

For mammals, the most sensitive LOAEL was 1.9 $mg \cdot kg^{-1}$ bw per day (liver hypertrophy in female rats, 182 d) (Chu et al. 1988). The NOAEL was 0.36 $mg \cdot kg^{-1}$ bw per day in the same study. The TDI was the calculated as follows:

$$TDI = (LOAEL \cdot NOAEL)^{0.5} \div UF$$

where UF = the uncertainty factor. The study by Chu et al. (1988) was carried out for 182 d and was, therefore, considered to be subchronic. Although toxicity data exist from other laboratory mammalian species, no information was located on the toxicity of toxaphene to two of the most sensitive aquatic predators, mink and otter. An uncertainty factor of 10 was selected to account for differences in interspecies sensitivities to toxaphene as well as extrapolation from subchronic to chronic effects. Using the data from Chu et al. (1988) and an uncertainty factor of 10, a mammalian TDI of 0.083 $mg \cdot kg^{-1}$ bw per day or 83 $\mu g \cdot kg^{-1}$ bw per day was calculated.

The mammalian TDI was then used in conjunction with the body weights (bw) and daily food intake rates (FI) of the most sensitive wildlife species to calculate the RC of toxaphene, using the following equation:

$$RC = TDI \cdot (bw \div FI)$$

Among wildlife species, those with the highest FI:bw ratios have the greatest potential exposure to toxaphene. These species, therefore, are used to calculate the RCs for toxaphene. The mammalian RC was calculated to be 348 $\mu g \cdot kg^{-1}$ diet ww from a TDI of 83 $\mu g \cdot kg^{-1}$ bw per day, assuming a body weight of 0.60 kg and a food intake rate of 0.143 kg per day ww for female mink *(Mustela vison)* (CCME 1998).

Avian Reference Concentration

For avian species, the most sensitive LOAEL in the toxicological dataset was 0.23 $mg \cdot kg^{-1}$ bw per day (liver weight in broiler chickens) (Bush et al. 1978). The NOAEL in this study was 0.015 $mg \cdot kg^{-1}$ bw per day. The study was carried out for 56 d and, therefore, considered subchronic. An uncertainty factor of 10 was used together with the data from Bush et al. (1978) to calculate an avian TDI of 0.0059 $mg \cdot kg^{-1}$ bw per day or 5.9 $\mu g \cdot kg^{-1}$ bw per day.

The avian RC was calculated to be 6.3 $\mu g \cdot kg^{-1}$ diet ww from a TDI of 5.9 $\mu g \cdot kg^{-1}$ bw per day, assuming a body weight of 0.032 kg, and a food intake rate of 0.03 kg per day ww for Wilson's storm petrel *(Oceanites oceanicus)* (CCME 1998).

Toxaphene Residue Guideline

The lower of the mammalian and avian RCs, 6.3 $\mu g \cdot kg^{-1}$ diet on a wet weight basis, was recommended as the Canadian tissue residue guidelines for toxaphene for the protection of freshwater, marine, and estuarine wildlife that consume aquatic biota.

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