Development of Blood Guidance Values for Chlordane and Toxaphene with Application to the Canadian Arctic

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Abstract

Background: Currently, no threshold blood guidance values exist to evaluate risks of exposures to chlordane and toxaphene. **Objective:** To develop guidance values for chlordane and toxaphene and evaluate risks in the general Canadian population and Inuit of the Canadian Arctic. **Methods:** Oral reference doses were converted to blood concentrations using biomonitoring equivalents (BEs). The percentage exceeding BEs was determined using biomonitoring data from the Canadian Health Measures Survey (CHMS) Cycle 1 2007-2009 and the Inuit Health Survey (IHS). **Results:** The chlordane lipid-adjusted BEs (mg/kg) were cis-chlordane: 0.09-0.72; trans-chlordane: 0.21-0.72; cis-nonachlor: 0.36-0.82; and trans-nonachlor: 0.53-1.44. The toxaphene lipid-adjusted BEs were 4.39-38.38 (No. 26), 6.40-19.19 (No. 50), and 6.40-15.35 (No. 62). None of the general Canadian population exceeded BEs. **Conclusions:** General Canadian population exposures are well below thresholds for toxicity. Consultations with risk assessors and Inuit partners will occur to further refine BEs and discuss application to Inuit biomonitoring data.

Introduction

Chlordane and toxaphene are persistent organochlorine pesticides that bioaccumulate in biota and humans. Concentrations in blood are often used as biomonitors to measure population exposures and health risks. However, currently there are no threshold blood guidance values to evaluate the potential risks of such exposures.

Methods

Oral reference doses were converted to internal blood concentrations , a value known as a BE. Reference doses were obtained from various national and international regulatory agencies and sources, such as Health Canada, the Environmental Protection Agency, and European Union. Pharmacokinetic parameters for individual isomers of chlordane and toxaphene were obtained from published literature of dosing experiments using animal models. Parameters were inputted into a one-compartment pharmacokinetic model to obtain a lipid-adjusted steady-state blood concentration corresponding to the external doses resulting in no-observed adverse effect levels (NOAELs). The steady-state concentration was then allometrically scaled to a human BE.

Results

Table 1: Chlordane Oral Reference Doses

Reference Dose (mg/kg/d)	Toxicity Endpoint	NOAEL (mg/kg/d)	LOAEL (mg/kg/d)
ATSDR 1994 (MRL): 0.0006	Hepatocellular hypertrophy (rats, 30 month study)	0.055	0.273
JMPR 1994 (pTDI): 0.0005	Hepatic toxicity* (rats, 32 month study)	0.05	N/A
EPA 2009 (RfD): 0.0005	Hepatic necrosis (mice, 26 month study)	0.15	0.75

Table 2: Chlordane BEs

Human BE based on NOAEL (mg/kg lipid)			
Cis-Chlordane	**Trans-Chlordane**	**Cis-Nonachlor**	**Trans-Nonachlor**
0.10-0.27	0.23-0.52	0.39-0.62	0.59-0.94
0.09-0.24	0.21-0.47	0.36-0.57	0.53-0.85
0.14-0.72	0.45-0.72	0.51-0.82	0.90-1.44

Table 3: Toxaphene Oral Reference Doses

Reference Dose (mg/kg/d)	Toxicity Endpoint	NOAEL (mg/kg/d)	LOAEL (mg/kg/d)
MATT 2012 (pTDI): 0.018 (weathered toxaphene)	Altered hepatic foci expressing placental glutathione-S-transferase in rats (indication of tumour promotion)	1.8	Not observed

Table 4: Toxaphene BEs

Human BE based on NOAEL (mg/kg lipid)		
Parlar No. 26	**Parlar No. 50**	**Parlar No. 62**
4.39-38.38	6.40-19.19	6.40-15.35

Table 5: Trans-Nonachlor CHMS Cycle 1

Population	$N_{Weighted}$	Geometric Mean (µg/kg lipid) (95% CI)
Whole	23 279 744	6 (5-7)
Males	11 661 741	6 (5-7)
Females	11 618 003	6 (5-7)
Women Child-Bearing Age	3 139 048	3 (2-4)
Young (18-25)	2 752 504	2.1 (1.7, 2.5)
Middle (40-55)	8 234 753	7 (6-8)
Elderly (≥60)	4 886 233	14 (12-16)

* >40% of observations for cis-chlordane, trans-chlordane, cis-nonachlor, toxaphene Parlar No. 26 and 50 were below the limit of detection.

Conclusions

The set of BE values derived for chlordane and toxaphene isomers can be used to evaluate risks of exposures in human populations. The levels of chlordane and toxaphene in the general Canadian population are below the threshold levels. These BEs and interpretation of Inuit data will be discussed with Northern partners and risk assessors from Health Canada. In addition, more complex modeling strategies will be attempted for selected isomers.

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