PROBABILISTIC HUMAN HEALTH RISK ASSESSMENT OF PENTA-, OCTA-, AND DECA- BROMINATED DIPHENYL ETHERS

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Introduction

Brominated flame retardants (BFRs), and specifically polybrominated diphenyl ethers (PBDEs), are believed to be widespread in the environment, and reportedly at levels that monitoring programs have shown are increasing in aquatic biota and in human breast milk and adipose tissues [1,2,3]. The need for restrictions or phase-out of certain PBDEs within the European Union, Sweden, and elsewhere reflect concerns about widespread environmental contamination [4,5]. The European Commission's Existing Substances Programme (ECESP) is the only regulatory organization that has undertaken risk assessments of the PBDEs. Draft human health and ecological risk assessments for penta-, octa-, and deca- brominated diphenyl ethers (PeDBE, OBDE and DBDE, respectively) were recently completed, and likely will influence future regulations in the Europe Union and elsewhere concerning commercial uses of these substances [6,7,8].

At present, our understanding of the information generated from continuous environmental monitoring programs on human health and toxicity to wildlife is limited. Several important considerations posed by growing awareness of increased PBDE levels in the environment include (a) whether levels reported in the diet and human breast milk in Europe, North America, Japan, and elsewhere are sufficient to elicit adverse health effects in children; (b) identification of relevant toxicity endpoints and likely effects-thresholds in humans and wildlife; and, (c) isolation of the predominant environmental sources and pathways of exposure to these compounds. This study represents a first step towards addressing these and other concerns using probabilistic risk assessment. The results are compared to lifetime chronic daily intakes (CDIs) calculated in risk assessments of PeDBE, OBDE and DBDE prepared by ECESP [6,7,8].

Risk Assessment Methods

Exposure Pathways and Assumptions. Exposures to PeDBE, ODBE, and DBDE were calculated for five different age groups (0-2 years, 2-6 years, 6-12 years, 12-18 years, and 18-70 years) and as an aggregate of exposure over a 70-year average human lifetime. Eight exposure pathways were evaluated, including fish ingestion, ingestion of human breast milk (at 0-1 years only), ingestion of drinking water from all household sources, ingestion of dairy products, ingestion of meat products, ingestion of below ground vegetables, ingestion of above ground vegetables and fruits, and inhalation of ambient urban air. Exposure equations were adopted from USEPA [9].

Exposure assumptions and their default point estimates and probability density functions (PDFs) were derived from USEPA [10] and Finley et al. [11]. Body weights and inhalation rates were assumed to be normally distributed in the population. PDFs for ingestion rates were assumed to be lognormally distributed; standard deviations from mean point estimates were used to define the

boundaries of input values randomly selected in Monte Carlo simulations. Oral bioavailability of PeDBE, ODBE, and DBDE was assumed to be 90%, 50%, and 6%, respectively [6,7,8]. Bioavailability through inhalation was assumed to be 75% for all three congener groups [12]. Elimination rates were not incorporated into the assessment because the few available human data contradict results observed in animal studies [12].

Exposure Point Concentrations. Exposure point concentrations in different environmental compartments were adopted from the results of regional scale environmental modeling performed by ECESP [6,7,8]. The average concentration of PeDBE in human breast milk was adopted from Darnerud et al. [13]; quantitative data for ODBE and DBDE were not found in the literature. Mean concentrations in air reflect measurements reported in two ambient urban air samples collected by Sjodin et al. [14]. PDFs for PeDBE, ODBE, and DBDE in different environment compartments were represented as triangular distributions in Monte Carlo simulations. As a first approximation of the wide variability in available published data, concentrations were assumed to vary $\pm$ 50% from point estimates calculated by ECESP [6,7,8]. For human breast milk, minimum and maximum concentrations represented the range reported in nursing Swedish women by Darnerud et al. [13].

Results and Discussion

Point estimates from the deterministic analysis and 50th and 95th percentiles from the probabilistic analysis are presented in Table 1. The results are compared to ECESP [6,7,8] point estimates. Point estimates of CDI over a 70-year lifetime of exposure to DBDE by different exposure pathways were lower than those calculated by ECESP[6]. For ODBE and PeDBE, lifetime CDIs associated with ingestion of drinking water, meat and dairy products, as well as inhalation of air were higher than those calculated by ECESP[7,8]. Total theoretical lifetime exposure was highest for DBDE (2.64×10^{-3}), followed by PeDBE (8.51×10^{-4}) and ODBE (7.80×10^{-5}). The highest theoretical lifetime exposures were associated with consumption of below ground vegetables, meat and dairy products, and fish (PeDBE only), which were one to three orders of magnitude greater than other exposure pathways. Furthermore, theoretical CDIs by children ages 0-2, 2-6, and 6-12 years were higher for all pathways than other age groups, suggesting children are exposed to PeBDEs, ODBE, and DBDE at significantly higher levels than at other ages.

When the results of this risk assessment are compared to animal and human NOAEL and LOAEL values for different toxicity endpoints [13,15], there is some cause for concern, in spite of the uncertainties associated with extrapolating data from animals to humans and estimates derived from occupational exposures. However, much remains unknown or uncertain before more definitive conclusions can be drawn from these comparisons. Nonetheless, the results reported here are consistent with the limited available human data for PeBDEs (specifically BDE-99 and BDE-100 isomers) and DBDE (reported as BDE-209). Assuming average lipid content and absorption and elimination half-lives from Darnerud et al. [13], preliminary calculations suggest theoretical exposures are within the ranges reported in blood serum and human breast milk [13,15].

Summary

Clearly, more research is needed to fully understand the significance of PBDEs in the environment and on human health. There remains a need for balanced scientific reporting of the state-of-knowledge on PBDE toxicology, environmental persistence and degradation, and the significance of current and historical levels in human tissues and the diet. Further risk assessment of exposures

to infants, young children and other sensitive populations where the potential for exposure is high is needed. If dioxin-like potencies and potential adverse effects to the endocrine system are confirmed [16], then considerably more work is needed to evaluate PBDEs as possible endocrine disruptors and to define toxicity benchmarks, possibly at much lower levels, than currently defined from the limited available toxicology information.

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Table 1. Comparison of Theoretical Lifetime Chronic Daily Intakes of PeBDE, OBDE, and DBDE From Different Environmental Compartments Calculated Using Deterministic and Probabilistic Methods in this Study with Results Reported by ECESP [6,7,8] for Regional Scale Environmental Conditions

Environmental Compartment	ECESP Estimated Daily Intake (mg/kg-bw/day)	Deterministic Results Using Default Exposure Point Estimates (mg/kg-bw/day)	Probabilistic Results at the 50th Percentile [a] (mg/kg-bw day)	Probabilistic Results at the 95th Percentile [a] (mg/kg-bw day)
Octabrominated Diphenyl Ether (ODBE)				
Fish	2.50E-09	1.28E-09	1.51E-09	2.32E-09
Below Ground Root Vegetables	2.30E-04	3.88E-05	8.20E-05	1.62E-04
Above Ground Fruits & Vegetables	3.10E-06	8.42E-07	1.77E-06	3.52E-06
Drinking water	8.70E-08	2.37E-07	3.01E-07	4.39E-07
Meat (Beef, Pork & Chicken)	9.70E-06	1.31E-05	1.19E-05	1.65E-05
Dairy Products	5.70E-06	2.49E-05	2.30E-05	3.15E-05
Air	2.40E-08	1.99E-07	1.99E-07	2.75E-07
Breast Milk	NC [b]	--	--	--
Total Local Daily Dose	2.40E-04	7.80E-05	1.19E-04	2.00E-04
Decabrominated Diphenyl Ether (DBDE)				
Fish	5.30E-07	3.27E-08	3.85E-08	5.98E-08
Below Ground Root Vegetables	6.80E-02	1.42E-03	3.00E-03	6.03E-03
Above Ground Fruits & Vegetables	4.40E-05	1.46E-06	3.08E-06	6.16E-06
Drinking water	2.80E-05	8.90E-06	1.14E-05	1.69E-05
Meat (Beef, Pork & Chicken)	2.60E-03	4.09E-04	3.75E-04	5.12E-04
Dairy Products	1.50E-03	8.00E-04	7.32E-04	1.01E-03
Air	8.70E-07	7.22E-08	7.22E-08	1.01E-07
Breast Milk	NC [b]	--	--	--
Total Local Daily Dose	7.30E-02	2.64E-03	4.13E-03	7.18E-03
Pentabrominated Diphenyl Ether (PeDBE)				
Fish (assuming BCF=14,350 l/mg) a	3.60E-05	--	--	--
Fish (assuming BCF=27,400 l/mg) b	6.80E-05	6.29E-05	7.44E-05	1.15E-04
Below Ground Root Vegetables	1.80E-03	5.70E-04	1.20E-03	2.37E-03
Above Ground Fruits & Vegetables	5.00E-06	2.44E-06	5.18E-06	1.03E-05
Drinking water	3.90E-07	1.86E-06	2.35E-06	3.43E-06
Meat (Beef, Pork & Chicken)	2.80E-05	7.06E-05	6.45E-05	8.92E-05
Dairy Products	7.00E-05	1.30E-04	1.19E-04	1.63E-04
Air	5.80E-08	1.35E-07	1.37E-07	1.88E-07
Breast Milk	NC [b]	1.27E-05	1.86E-05	4.52E-05
Total Local Daily Dose a	1.90E-03	--	--	--
Total Local Daily Dose b	2.00E-03	8.51E-04	1.49E-03	2.67E-03

a. Probabilistic analysis was conducted using Monte Carlo methods (Crystal Ball™ v4.0) involving 5,000 iterations of eight different exposure calculations for each of five different age groups using probability density functions for both exposure point concentrations and exposure factors. Results shown represent cumulative chronic daily intakes over an average lifetime (70 years) of theoretical human exposure.
b. Not calculated by ECESP [6,7,8].