A Monte Carlo Analysis of the Variability of Human Body Burdens of Polybrominated Diphenyl Ether Flame Retardants in North America and Associated Risk

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Introduction

There have been a number of recent reports on the exponentially rising levels of polybrominated diphenyl ethers (PBDEs) in human tissues, including mother's milk, in North America.[1,2,3,4] These average or median observed levels for the United States are the highest in the world and those for Canada are lower but still the second highest. Moreover, when the distribution of body burdens is considered, some significant portion of the population has very high concentrations, which are, as noted, rising exponentially

Although the sample population average or median levels - viewed exclusive of the rising trend, and of any additive or interaction effects due to the known body burdens of other BFRs, or other structurally and toxicologically similar compounds, such as PCBs, PBBs, PCDDs, and PCDFs - are arguably seen as providing a margin of safety for adults, there is no similar complacency available for the human fetus and neonate. As well, for the highest exposed members of the population, this caveat gains much greater currency for both adult and offspring.

The aim in this paper is to examine - using Monte Carlo methods applied to the reported human milk (lipid weight) concentrations - the probability distributions, and the population percentiles of the times required to reach a critical value of 1250 ng/g found by the Jacobsons, [5] for PCBs, to be associated with learning impairments, intellectual deficits, and IQ loss in the offspring. In addition, as a test approximation for the additional body burdens of PCBs and other related compounds, the times required to reach 1000 ng/g, a concentration at which some deficits were also observed, are also simulated.

Methods and Materials

The data on milk concentrations, trends, and doubling times from these and other related studies was reviewed and extracted, and subject to Monte Carlo analysis using Crystal Ball (Decisioneering Inc.). The analysis combines the probability distributions of several estimated doubling times and reported concentration data as initial conditions, and, assuming a first-order kinetic process, estimates the length of time to reach the critical value of 1250 ng/g (1000 ng/g), and the population percentiles in each time estimate.

Results and Discussion

The first data set analysed is by Ryan, et al,[1] with arithmetic mean of 43 ng/g and standard deviation of 62 ng/g, (range; 0.9 – 281.9) combined with doubling time estimates from data reported in references 6 and 7 (in years: 1.73; 2.00; 2.22; 3.0; 5.0) with mean 2.8 years and standard deviation of 1.3 years. Note that the Ryan, et al, reported data trend itself had doubling times of 2 years for the mean levels and 3 years for the median.

TABLE 1: Forecast: RYAN TIME TO 1250 ng/g at T2 ~ 2.8

Percentile	Value	Percentile	Value
0%	4.3	50%	13.8
10%	8.3	60%	15.3
20%	9.8	70%	17.1
30%	11.1	80%	19.6
40%	12.4	90%	23.8
		100%	78.4

The main issue of focus in this Table 1 shows that 10% of the population, reflecting the higher exposed subgroups, could reach the critical value of 1250 ng/g in about 8 years, and 20% in about 10 years.

The second data set was from Schecter, et al [2] with mean of 73.9 ng/g and standard deviation of 103.3 ng/g (range; 6.2 – 418.8). The same doubling time distribution was used. Note that Schecter et al, does not report on any trends.

TABLE 2: Forecast: SCHECTER TIME TO 1250 ng/g at T2 ~ 2.8

Percentile	Value	Percentile	Value
0%	3.0	60%	12.6
10%	6.5	70%	14.2
20%	7.8	80%	16.3
30%	8.9	90%	19.7
40%	10.0	100%	46.7
50%	11.2		

In Table 2 the results indicate a significant lowering of the time for those in the highest exposed groups to reach 1250 ng/g – 6.5 years for the 10% and almost 8 years for the 20%.

The third data set is from the Environmental Working Group, [3] with a mean of 158.75 ng/g and a standard deviation of 272.75 ng/g (range; 9.0 – 1,078). Again, the same doubling time was used. Note also that no trends were reported.

The results in Table 3 reflect the higher concentrations reported by the EWG report. Here we see that the highest exposed 10% of the population could reach the critical concentration in just over 3 years and 20% in just over 4 years.

TABLE 3: Forecast: EWG TIME TO 1250 ng/g at T2 ~ 2.8

Percentile	Value	Percentile	Value
0%	0.5	60%	8.2

10%	3.3	70%	9.6
20%	4.3	80%	11.6
30%	5.2	90%	14.8
40%	6.1	100%	42.6
50%	7.1		

In order to capture some further uncertainty in the doubling times, as for example reported by Hites [4], and in concentrations, such as 1000 ng/g, that may induce subtle effects in offspring, other simulations were done. Hites reported a global meta-analysis of concentrations and estimated a global doubling time in humans of 4.9 years with a standard deviation of 0.6 years.

However, he also reported that the North America data were always above the regression line – in recent years by a factor greater than 10. Therefore, other regression data from his report on Great Lakes herring gull egg concentrations that visually seemed for present purposes a reasonable fit to the North American trend data he reported was used. This data had a doubling time of 3.4 years and a standard deviation of 0.3 years.

As shown in Table 4, increasing the doubling time increases the time for the 20% most exposed of the EWG population to reach 1250 ng/g in 7 years. 10% of this group could reach this concentration in 5.5 years.

TABLE 4: Forecast: EWG TIME TO 1250 ng/g at T2 ~ 4.9

Percentile	Value	Percentile	Value
0%	1.0	60%	12.5
10%	5.5	70%	14.4
20%	7.0	80%	17.2
30%	8.4	90%	21.5
40%	9.6	100%	46.6
50%	11.0		

While the full results are not shown here, simulating the same 4.9 year doubling time to reach 1000 ng/g yields times of 4.1 years for the 10% most exposed in the EWG population, and 5.6 years for the 20%.

Similarly, simulating the 3.4 year doubling time to 1250 ng/g yields 3.9 years for the 10% most exposed, and 5 years for the 20%. To reach 1000 ng/g at the 3.4 year doubling time requires 2.8 years for the 10% most exposed of the EWG population and 3.9 years for the 20%.

This last example may be a best estimate for North America and should be a focus for monitoring as a most sensitive population. Supporting this is the still unaccounted for cumulative body burdens of other compounds that are structurally similar, have known similar effects as PBDEs on the thyroid economy, neurotransmitter effects, hearing, and learning and memory, and may be additive or interactive in their actions.[6, 7]

There are two final results to report. Using the Schecter mean data, with the 3.4 year doubling and 1250 ng/g critical value, yields times of 8.3 years for the highest 10% exposed in that population, and 9.3 years for the 20%. As well, using the Schecter median (34 ng/g) as the initial concentration, and the 2.8 year doubling time, results in 10% of this population reaching 1250 ng/g in 7.1 years, and 20% in 8.5 years.

Conclusions

There is a need in risk assessment to move beyond the focus on the average or median body burden, tissue or human milk concentrations, to account for the population distribution of the concentrations, and the percentiles in the tails of the distribution, particularly the high exposure portion.

The analysis presented here indicates that at present trends a significant proportion of the North American population could already be exposed to toxicologically relevant concentrations of PBDEs, or in as little as 3 years.

Worsening this situation is the unfilled need to account for the cumulative past and current exposures and body burdens of other compounds with similar toxicological pathways and effects. Unfortunately, this is never done in regulatory risk assessment and is therefore a logical next step. The widespread and growing prevalence of hypothyroidism and childhood neurodevelopment disorders in North America underlines this need.[7]

While for health effects the high concentration group needs special attention, the lowest exposure group might provide clues to sources and source strengths by comparison to the high group. This is especially needed because we know little about source strengths.

References

1. Ryan, J. J., Patry, B., Mills, P., and Beaudoin, N.G.. 2002. Organohalogen Compounds, Vol. 58, pp 173-176.
2. Schecter, A., Pavuk, M., Papke, O., Ryan, J., Birnbaum, L., Rosen, R. 2003. Environ. Health Perspec. Vol. 111 No. 14, 1723-1729.
3. Lunder, S., and Sharp, R. 2003. Environmental Working Group, California, USA. Internet search January 2004 at www.ewg.org/reports/mothersmilk
4. Hites, R.A. 2004. Environ. Sci. Technol. 38, 945-956.
5. Jacobson, J.J., and Jacobson, S.W.. 1996. The New England Journal of Medicine, Volume 335, Number 11, September 12, 1996. Pp. 783-789.
6. Muir, T., and Alaee, M. 2002. Organohalogen Compounds, Vol. 58, pp. 237-240. Also, Poster presentation at Dioxin 2002, Barcelona, Spain. Available on request.
7. Muir, T. 2003. Organohalogen Compounds, Vol. 60, pp. 195-198 Also, Poster presentation at Dioxin 2003, Boston, USA. Available on request.