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LETTER TO THE EDITOR

Exposure Assessment for Decabromodiphenyl Ether (decaBDE) is Likely to Underestimate General U.S. Population Exposure

In a recent article, Hays *et al.* (2003) concluded that current levels of decabromodiphenyl ether (decaBDE) in the United States are not likely to represent an adverse health risk for children. This conclusion is unsupported because their analysis does not take into account the tremendous uncertainty in their estimate of the exposures in the general U.S. population, given that this estimate is based on a single study of 12 people. Hays *et al.* have very likely *underestimated* the highest levels of exposure in the U.S. population. This is especially troubling because of their assertions that the upper estimate results in "significant overestimates of the actual exposure of the population" because of the selection of "extreme" input parameters.

Hays *et al.* evaluated a range of potential exposure scenarios to estimate aggregate exposures of young children to decaBDE. For most of these scenarios, relevant biological measures are not available, so simple exposure models were used to estimate intake rates. However, for the scenario described as "general exposure," which is intended to capture dietary and other uncharacterized exposure sources, they relied on data from a single study of decaBDE levels in serum samples collected in 1988 from 12 U.S. blood donors in Illinois to estimate intakes. For each exposure scenario, intakes were calculated to characterize the mid-range and the upper estimate of exposures. As it turns out, the upper estimate for "general exposure" results in the highest exposure estimate, compared with the other pathways assessed. Thus, the assumptions used for the general exposure pathway, especially the upper estimate of the serum levels in the general U.S. population, determine the outcome of the overall assessment.

It is unlikely that a sample of 12 blood donors in Illinois in 1988 is representative of the population of interest, which is the general population of children in the United States today. Data on time- and age-related trends for other BDEs in Norway from another recent study show that (a) serum levels are increasing over time as use of these chemicals increases and (b) children have higher blood levels than adults (Thomsen *et al.* 2002). Thus, serum levels of decaBDE in children today may be higher than they were in adults in 1988. In addition, the blood donors in the 1988 study were all from the Illinois area and may not be representative of the general U.S. population.

However, even if this sample were representative it is too small to reliably estimate levels of exposure, as can be seen if we calculate an upper confidence limit (UCL) for serum levels. For lognormally distributed data the $UCL_{1-\alpha,p} = \exp(\bar{y} + K_{n,1-\alpha,p}s_y)$ where $\bar{y}$ and s_y are the mean and standard deviation of the natural log-transformed data, $n = 12$, $\alpha = 0.05$, $p = 0.99$, and $K_{n,1-\alpha,p}$ is a value derived from the non-central t distribution (Gibbons and Coleman 2001; Millard and Neerchal 2001).

If we assume that the blood donor data are lognormally distributed, we assume that natural logs of the data are normally distributed. The median is estimated by Hays to be 0.96 ng/g lipid on the original scale, so taking logs and rounding we estimate the mean of the data on the log scale to be approximately 0 ng/g lipid. The maximum of the sample is reported as 33.6 ng/g lipid on the original scale and is reported on the log scale as 3.51 ng/g lipid. We estimate the standard deviation to be approximately equal to 2.0, based on maximizing the probability density function for the maximum.

Thus, the 95% UCL for the 99th percentile = $\exp(0 + 2 \times 3.747) = 1797$ ng/g lipid. This implies that 99% of the distribution of decaBDE will lie below 1797 ng/g lipid with 95% confidence (Gibbons and Coleman 2001). In other words, if we draw many samples, for 95% of them the 99th percentile will be below 1797 ng/g lipid. Thus, in this case, the 95% UCL is 53 times the maximum concentration found in the sample and results in an estimated intake that is, similarly, 53 times higher than the upper estimate of intake in the assessment. While Hays *et al.* concluded that upper estimates of intake were five to ten times below a reference dose, when multiplied by the other parameters specified in the assessment the 95% UCL on the 99th percentile of the serum data gives an estimated intake of 20 mg/kg/day, which is five times higher than the reference dose (4 mg/kg/day) and does not provide assurance that the population is adequately protected.

Another limitation of the Hays *et al.* assessment is the use of this reference dose of 4 mg/kg/day, proposed by a National Academy of Sciences panel in 2000, without discussing recently published findings by Viberg *et al.* (2003) that demonstrate uptake of decaBDE into brain tissue of neonatal mice and subsequent neurological effects at lower dose levels than in previously reported studies.

The issues raised in this letter were discussed by the expert panel for the Voluntary Children's Chemical Evaluation Program (VCCEP) peer consultation review for decaBDE that took place in April 2003. During this review process, the material included in the Hays *et al.* paper was discussed by a panel of experts and further data needs were identified. Measurement of human blood serum was the most significant data needed for decaBDE exposure assessment, with 9 of 13 panelists recommending further work in this area as a priority. The full report of the expert panel can be accessed online at http://www.tera.org/peer/VCCEP/DECA/VCCEP%20DBDPO.pdf (TERA 2003).

Good biomonitoring data are critical to our understanding of chemical exposures and potential risks, and major policy decisions should not be based on such a limited empirical base. In this case, the sample of 12 blood donors indicates that there is

widespread exposure to decaBDE in the U.S. population and that our best exposure models are not adequate to predict the magnitude or distribution of these exposures. Fortunately, the U.S. Centers for Disease Control's national exposure monitoring program (Centers for Disease Control and Prevention 2003) will be adding decaBDE to the list of chemicals to be measured in a population-based sample. These new data will provide a greater level of certainty to risk assessments conducted on these and other chemicals.

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