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Prenatal PBDEs and Neurodevelopment: Animal Studies and Human Health Assessment

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Herbstman et al. (2010) reported an association between polybrominated diphenyl ether (PBDE) levels in cord blood and neurodevelopmental effects in the children at specific ages. As a basis for their work, the authors cited several animal studies that reported causal relationships between prenatal exposure to PBDEs and developmental neurotoxicity. We are concerned that Herbstman et al.'s research suffers from investigator bias based on the reasons that follow.

First, the U.S. Environmental Protection Agency (EPA) cosponsored an expert panel that refuted the experimental design employed in most of the studies cited by Herbstman et al. (2010) as a basis for their work. The U.S. EPA expert panel concluded that the experimental design failed to control for litter effects (Holson et al. 2008).

Next, the potential for specific brominated flame retardants to cause developmental neurotoxicity has been evaluated under Good Laboratory Practice (GLP) standards and according to validated test guidelines. In each case, the claims of developmental neurotoxicity from non-GLP, non-guideline studies were not reproducible (reviewed by Williams and DeSesso 2010). This is significant because in Europe, data generated from studies performed under GLP and according to validated test guidelines are considered the highest quality and most reliable (European Chemicals Agency 2008). Further, regulatory agencies in Europe and the United States seem to have shifted their stance on the non-GLP, non-guideline studies that have reported brominated flame retardant-induced developmental neurotoxicity. For example, when the European Union issued their Risk Assessment Report on hexabromocyclododecane (HBCD), a brominated flame retardant (European Chemicals Bureau 2008), they stated that

... Eriksson et al. (2006) [i.e., the study reporting HBCD-induced developmental neurotoxicity] is not performed according to current guideline and GLP However, similar results on developmental neurotoxicity have been published for decabromodiphenylether by the same authors using the same method [e.g., Viberg et al. (2003), which was cited by Herbstman et al. (2010)]. For decabromodiphenylether it has been agreed to perform a new toxicokinetics/developmental neurotoxicity study according to a modified OECD guideline

and GLP. The results from this new decabromodiphenylether study will serve as guidance on how to interpret the data from the Eriksson study, and may also serve as a basis on how to proceed with further testing of neurotoxicity.

For two of the studies cited by Herbstman et al. (2010), which were used by the U.S. EPA for deriving reference doses for PBDEs 153 and 209 (U.S. EPA 2008a, 2008b), the U.S. EPA was unable to obtain the raw data. However, when the raw data were obtained for the PBDE 209 study (i.e., Viberg et al. 2003) by a third party, who subsequently provided the data to the U.S. EPA, the agency acknowledged that the data were not suitable for use with human health assessment (U.S. EPA 2010).

We mention the above information because Herbstman et al. (2010) cited only animal studies that reported PBDE-induced developmental neurotoxicity as support for their work. Although the authors discussed one epidemiological study that reported findings inconsistent with their own, Herbstman et al. (2010) reverted back to the positive animal studies as support for their work. They did not discuss or cite any animal studies that reported contradictory findings. This is significant because it may have introduced a formidable source of bias when Herbstman et al. (2010) were interpreting their results. The exclusion may also mislead the readership of *EHP*.

M.B. has received a total of US\$2,000 from the brominated flame retardant industry for his contribution to three publications in 2008–2009, but he received no form of remuneration for his work on this letter.

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REFERENCES

- Eriksson P, Fischer C, Wallin M, Jakobsson E, Fredriksson A. 2006. Impaired behaviour, learning and memory, in adult mice neonatally exposed to hexabromocyclododecane (HBCDD). *Environ Toxicol Pharmacol* 21(3):317–322.
- European Chemicals Agency. 2008. Guidance on Information Requirements and Chemical Safety Assessment - Chapter R.4: Evaluation of available information. Available: http://guidance.echa.europa.eu/docs/guidance_document/information_requirements_r4_en.pdf?vers=20_08_08 [accessed 8 October 2010].
- European Chemicals Bureau. 2008. Risk Assessment: Hexabromocyclododecane, CAS-No.: 25637-99-4, EINECS-No.: 247-148-4. Available: http://ecb.jrc.ec.europa.eu/documents/Existing-Chemicals/RISK_ASSESSMENT/REPORT/hbcdreport044.pdf [accessed 8 October 2010].
- Herbstman JB, Sjödin A, Kurzon M, Lederman SA, Jones RS, Rauh V, et al. 2010. Prenatal exposure to PBDEs

and neurodevelopment. *Environ Health Perspect* 118:712–719.

- Holson RR, Freshwater L, Maurissen JPY, Moser VC, Phang W. 2008. Statistical issues and techniques appropriate for developmental neurotoxicity testing: a report from the ILSI Research Foundation/Risk Science Institute expert working group on neurodevelopmental endpoints. *Neurotoxicol Teratol* 30(4):326–348.
- U.S. EPA (U.S. Environmental Protection Agency). 2008a. Toxicological Review of 2,2',4,4',5,5'-Hexabromodiphenyl Ether (BDE-153) (CAS No. 68631-49-2). EPA/635/R-07/007F. Available: <http://www.epa.gov/ncea/iris/toxreviews/1009tr.pdf> [accessed 8 October 2010].
- U.S. EPA (U.S. Environmental Protection Agency). 2008b. Toxicological Review of Decabromodiphenyl Ether (BDE-209) (CAS No. 1163-19-5). EPA/635/R-07/008F. Available: <http://www.epa.gov/ncea/iris/toxreviews/0035tr.pdf> [accessed 8 October 2010].
- U.S. EPA (U.S. Environmental Protection Agency). 2010. Freedom of Information Act Request: HQ-FOIA-00149-10. EPA response dated 22 March 2010. Washington, DC:U.S. EPA [available on request].
- Viberg H, Fredriksson A, Jakobsson E, Örn U, Eriksson P. 2003. Neurobehavioral derangements in adult mice receiving decabrominated diphenyl ether (PBDE 209) during a defined period of neonatal brain development. *Toxicol Sci* 76(1):112–120.
- Williams AL, DeSesso JM. 2010. The potential of selected brominated flame retardants to affect neurological development. *J Toxicol Environ Health B Crit Rev* 13(5):411–448.

Prenatal PBDEs and Neurodevelopment: Accuracy of Assessment

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Herbstman et al. (2010) measured eight polybrominated diphenyl ethers (PBDEs) in cord blood and reported that children of mothers with higher cord blood concentrations of PBDEs 47, 99, and 100 scored lower on mental and physical development tests at 12, 24, 36, and 72 months of age. Here, we raise several issues that limit the conclusions that may be drawn from their study.

In the study by Herbstman et al. (2010), only 210 cord blood specimens from 329 mothers were available, and assessments were conducted for only 96–118 children at each age. Several congeners were measured in the study; overall, the percentage of individual congeners below the limit of detection (LOD) ranged from 18.6% to 96.1%. For congeners on which major assessments were conducted, the range of values < LOD was 18.6–50.2%. Herbstman et al. (2010) did not state how many samples were < LOD for each assessment, so it is possible that the percentage was even higher and may have led to a large impact on the results, particularly given the small sample size for each assessment.

Herbstman et al. (2010) measured PBDEs in cord blood and maternal blood only once, but individual levels most likely changed over the course of the pregnancy and over the period when developmental assessments were conducted. The median values were relatively low, and there was no reliable indication of inter-individual variability, so even small changes