making it difficult to decide which congeners should be measured. There is currently no consensus on which to be measured; this topic will be reviewed and recommendations made. Temporal trends in human PBDE levels will be presented and compared with temporal trend for dioxins, dibenzofurans and PCBs. New toxicological findings with respect to pharmacokinetics, neurological, reproductive and developmental, endocrine, and cancer endpoints will be presented. Finally, human risk assessment will be considered.

310 PBDES IN US HUMANS, FOOD AND ENVIRONMENTAL SAMPLES.

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Polybrominated diphenyl ether (PBDE) flame retardants were measured in US human milk and blood, food and environmental samples. All 59 milk samples were positive for multiple congeners measured. Milk was collected beginning in 2001 from various locations in the US. PBDEs varied from 6.2 to 419 ppb lipid. In blood, we found levels from 4 to 366 in our first 39 individual analyses. In this series men had lower levels than women, although not statistically significant. Two samples of pooled blood from 100 people each had levels of 78 and 80 ppb lipid in 2003, similar to that observed in pooled serum from 100 people the same year, 62 ppb lipid. These levels are a magnitude higher than previously observed in some earlier European studies. In contrast, the concentration in a pooled archived serum sample from 100 people in 1973 was only 0.8 ppb lipid. This increasing trend is opposite to that observed for dioxins and PCBs. 44 foods of animal origin from Texas supermarkets all tested positive for multiple congeners, including the fully brominated BDE 209 congener, with highest levels in fish (especially salmon), followed by meat and then dairy. US levels are higher than published European and Japanese studies. Daily intake of PBDEs was estimated to be 163, 200 pg/kg body weight daily in US nursing infants during the first year of life and 11, 000 pg/kg daily in Germany, approximately 3, 826 pg/kg body weight for ages 2-5, and approximately 1, 300 pg/kg BW daily for ages > 19 years. Unlike dioxins and PCBs where almost all intake is from the route of consumption of animal food, it has been speculated that respiratory and dermal intake may contribute a greater portion of intake for PBDEs. Therefore, we also measured PBDEs in swipes from computer and computer monitor casings and in carpet vacuum sweepings. All samples were positive. Comparing our findings with other recent studies, we conclude that the highest levels of PBDEs in human milk, blood and in food worldwide exist in the USA. (This abstract does not reflect USEPA policy.)

311 TOXICOKINETICS OF BDE 47 IN MICE.

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Polybrominated diphenylether (PBDE) congener patterns found in environmental samples and human tissue are not consistent with congener patterns found in the commercial PBDE mixtures; it is therefore essential to understand the toxicokinetic properties associated with the individual PBDE congeners. Currently, knowledge of the absorption, distribution, metabolism, and excretion is restricted to a small number of congeners which have been examined in limited *in vivo* and *in vitro* models. In general, the toxicokinetic parameters of PBDEs are dependent on the degree of bromination. With the exception of the fully-brominated congener, the PBDEs appear to be well absorbed, slowly metabolized, and distribute to lipophilic tissues. For 2, 2', 4, 4'-tetrabromodiphenyl ether (BDE 47), the major congener found in human and wildlife samples, differences in excretion rates and routes have been reported between rats and mice. In this study, the distribution and excretion of a single, oral dose (1 mg/kg) of BDE 47 was examined in adult, female C57BL/6 mice for 21 days following administration. BDE 47 was found in all tissues at all time points and distribution was dictated by lipophilicity. Elimination of BDE 47 appears to be biphasic. Highly perfused tissues have α and $\beta t\ ½$ values of approximately 1 and 10 days, respectively. Elimination from lipophilic tissues was roughly five times slower. Although the terminal half life is long, the majority of the dose (>80%) is eliminated during the α-phase. The rapid excretion of unmetabolized BDE 47 and other congeners in urine and feces suggests the presence of an active transport mechanism which may play a major role in understanding the species differences in elimination; initial results from renal transport studies support this hypothesis. Characterization of these toxicokinetic parameters will provide data needed for the development of a PBPK model which can be used in human health risk assessment. (This abstract does not reflect EPA policy. This work was partially funded by EPA NHEERL-DESE CT826513).

312 DEVELOPMENTAL NEUROTOXICITY OF PBDES IN MICE AND RATS.

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Our environment contains a vast number of contaminant including the brominated flame retardants, polybrominated diphenyl ethers (PBDEs). The PBDEs are widely found in the environment and is increasing in human milk. This means that an individual can be exposed to PBDEs during its whole lifetime, including the lactation period. We have examined the neurotoxic effects of exposure to PBDEs during a defined critical period of rapid brain development in neonatal mice and rats. The neonatal period is characterized in many mammalian species by rapid development of the immature brain. It has been shown that numerous toxicants can induce permanent disorders in brain function when administered to the neonatal mouse during the brain growth spurt (BGS). In mice and rats this period is postnatal, spanning the first 3-4 weeks of life and in the human, the BGS begins during the third trimester of pregnancy and continues throughout the first two years of life. Our studies have identified a defined critical period during the BGS in mice when the brain is vulnerable to insults of low doses of PBDEs. It has also been shown that it is the presence of PBDEs or their metabolites in the brain during this defined critical period that is crucial to evoke neurotoxic effects. Exposure to PBDEs during the short critical period of brain development leads to permanent altered spontaneous behaviour, deficits in learning and memory and disturbances in the cholinergic system, in the adult. These effects are dose-response related and tend to get worse with age. The potency of PBDEs to induce neurotoxic effects does not appear to be gender, strain or species specific, because the neurotoxic effects are induced in both male and female mice of different strains and in rats. In conclusion, the observed developmental neurotoxic effects of PBDEs are similar to the effects seen after neonatal exposure to certain PCBs and the presence of both these compounds in the environment and in human milk suggests that further attention should be focused on the neurotoxicology of PBDEs.

313 PBDE LEVELS AMONG US WOMEN, DAILY INTAKE AND RISK OF HARM TO THE DEVELOPING BRAIN AND REPRODUCTIVE ORGANS.

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The polybrominated diphenylethers (PBDEs) are a class of flame retardants widely used in electronics, furniture and textiles. PBDEs slowly migrate from these products and are now ubiquitous, measured in indoor and outdoor air, home and office dust, streams and lakes, and terrestrial and marine biota. Like PCBs and dioxins, many PBDEs are persistent and bioaccumulative, and are long lived in the body. The more bioaccumulative commercial mixtures of PBDEs have been recently banned in California, Maine and Hawaii and the European Union. Tissue levels among residents of North America are approximately 10 to 40 times higher than those of individuals in Europe or Japan, and recent data suggest that PBDE body burdens continue to rise over time in North American wildlife and humans. Five PBDEs namely, PBDE-47, 99, 100, 153, and 154, comprise more than 90 % of the PBDEs measured in US residents. The primary health concerns of PBDEs appear to be developmental effects, including harm to the developing brain and reproductive organs. PBDE levels in serum, adipose tissue, or breastmilk have been reported for individuals in six groups of women in the US The distribution of lipid-normalized PBDE concentrations among women residing in the US was determined to be lognormal with a mean value of 87.6 ng/g and a 95th percentile estimate of 304 ng/g. Using the US body burden data and congener-specific estimates of half-lives in humans, daily intake of the sum of the five most prevalent PBDEs in people (PBDE-47, 99, 100, 153, 154) was estimated to be 4.8 ng/kg-d (median), 11 ng/kg-d (mean), and 38 ng/kg-d (95th percentile). Finally, the potential health risks posed by the PBDEs are addressed by comparing tissue concentrations in humans to estimated and measured tissue concentrations in rodents associated with developmental neurotoxicity and reproductive effects. Assuming effects in rodents are predictive of human health, the comparison suggests that the current margin of exposure is small for a significant portion of the population.

314 DEVELOPMENTAL TOXICOLOGY EVALUATIONS: ISSUES WITH INCLUDING NEUROTOXICOLOGY AND IMMUNOTOXICOLOGY ASSESSMENTS.

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Evaluation of offspring following maternal exposures during gestation and lactation (i.e. reproductive/developmental toxicology [RDT]) has historically been a routine part of the safety assessment process. Recently, increased attention has focused on the effects of agricultural and industrial chemicals, as well as pharmaceuticals, on