CONCENTRATIONS OF POLYBROMINATED DIPHENYL ETHERS (PBDES) AND POLYBROMINATED BIPHENYL (PBB) IN THE CIVILIAN, NON-INSTITUTIONALIZED POPULATION OF THE UNITED STATES: 2003-2004

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Abstract

We measured the serum concentrations of ten polybrominated diphenyl ethers (PBDEs) and 2,2',4,4',5,5'-hexabromobiphenyl (BB-153) in a one third subset of the National Health and Nutrition Examination Survey (NHANES) for the survey years 2003 and 2004. The participants were chosen so as to be representative of the civilian, non-institutionalized population of the United States with respect to race/ethnicity, age, and sex. The congener with the highest serum concentration was 2,2',4,4'-tetrabromodiphenyl ether (BDE-47), followed by in descending order 2,2',4,4',5,5'-hexaBDE (BDE-153), 2,2',4,4',5-pentaBDE (BDE-99), 2,2',4,4',6-pentaBDE (BDE-100), BB-153, and 2,4,4'-triBDE (BDE-28).

The National Health and Nutrition Examination Survey (NHANES) provide an ongoing exposure assessment for the civilian, non-institutionalized U.S. population to a wide range of chemicals through biomonitoring. The survey results are reported in CDC's *National Report on Human Exposure to Environmental Chemicals (www.cdc.gov/exposurereport).* In this article we report, for the first time, individual serum data for NHANES participants for polybrominated diphenyl ethers (PBDEs) and 2,2',4,4',5,5'-hexabromobiphenyl (BB-153), based on the NHANES sampling conducted during the years 2003 and 2004.

Introduction

PBDEs and BB-153 are chemicals commonly known as brominated flame retardants (BFRs) of which PBDEs are the most well known class. [1] BB-153 on the other hand, is an older use BFR, but in the U.S. its use was discontinued in the mid-1970s after its accidental contamination into dairy feed in the State of Michigan.[2] This incident led to wide spread exposure of cattle and poultry and ultimately humans who consumed these food items. [2]

PBDEs are produced in three different technical preparations, commonly named according to their average bromine content; i.e., PentaBDE, OctaBDE and DecaBDE. [3] Technical PentaBDE is a mixture of congeners with four to six bromine atoms on the diphenyl ether backbone. This preparation contains approximately 37% by weight of tetraBDEs, 43% of pentaBDEs and 6.8% of hexaBDEs and trace levels triBDEs and heptaBDE. [4] The pentaBDE product has primarily been used to flame retard polyurethane, which is used in furniture applications and in the foam pad used under wall-to-wall carpets. [3,5] This product is present in most modern homes in the United States as has been shown by the analysis of residential dust samples from such homes. [6-9] Interestingly, the residential dust levels of PBDEs originating from this mixture have been reported at much higher concentrations in the United States than in Germany, England, and Australia. [8] In one study, the median level of 2,2',4,4'-tetraBDE (a major constituent of technical PentaBDE) in vacuum cleaner dust was 430 ng/g in the United States while the concentration of this congener was <14, 22, 60 ng/g in residential dust samples collected in Germany, England and Australia, respectively. [8] This large difference in concentration in residential dust from different continents is most likely due to differences in usage patterns of technical PentaBDE as has been reported by the industry. [10] A total of 7,500 metric tones of technical PentaBDE were produced in 2001 of which ~95% were consumed in North America. [10] It is well known that human levels of PBDEs in the United States originating from the technical pentaBDE mixture are the highest in the world.[11,12] The median BDE-47 concentrations have been reported to be in the range of 0.26-2.7 ng/g lipid in Europe [13-16] while in the current study we found a median level of 19 ng/g lipid. Technical PentaBDE has been voluntarily phased out in the United States from the end of 2004. However, due to the wide spread distribution in U.S. homes, as measured in

the indoor environment [6-9], and high environmental levels, as measured and documented in for example herring gull eggs from the Great Lakes [17], it is likely that human body burdens in the United States will remain at an elevated level for the foreseeable future; however, the voluntary withdrawal of the PentaBDE and OctaBDE mixtures from the market at the end of 2004 in the United States is an important first step in limiting and reducing the exposures to the general U.S. population.

The OctaBDE and DecaBDE preparations are used in hard plastics such as those found in the casings of electronic equipments. The 2001 consumption of OctaBDE and DecaBDE in the United States has been estimated to be 1,500 and 24,500 metric tones per year, respectively, which represents 40% and 44% of the total world market, respectively.

Technical OctaBDE is a mixture of congeners with six to eight bromine atoms on the diphenyl ether backbone while the DecaBDE mixture almost exclusively contains the perbrominated diphenyl ether. [18] PBDE congeners containing seven to ten bromine atoms have relatively short biological half-lives in humans; e.g., 2 weeks to 3 months. [19] These congeners are not likely to bio-magnify through the food chain, and thus direct exposures in the indoor environment and occupational exposures are most likely the dominating routes of human exposure. Due to their relatively short half-lives, these congeners have been found at lower levels than congeners present in the PentaBDE mixture, in the general population with no known occupational exposures. [11,20-23] The half-lives for PBDE congeners with fewer than seven bromine substituents have not been determined in humans.

From a toxicological standpoint, PBDEs have been shown in animal dosing studies to cause neurodevelopmental effects in the offspring of the exposed animal, as measured by altered habituation patterns in mice dosed with PBDEs. [24] In these experiments, a single oral dose of BDE-47 (10.5 mg/kg body weight) on post natal day 10, produced a significant effect, and 0.8 mg/kg body weight of BDE-99 produced a similar significant effect. This indicates that BDE-99 is more potent than BDE-47 [24]. Neurodevelopmental damage is believed to be the most sensitive endpoint for PBDE exposure although other potential adverse effects observed in animal experiments include enlarged liver. [25]

In this report, we report the concentrations of ten PBDE congeners (tri- to heptaBDEs) and BB-153 for the NHANES survey years 2003 and 2004. The data are stratified according to age, sex, and race/ethnicity.

Materials and Methods
Survey overview and sampling: The NHANES is administered by the National Center for Health Statistics (NCHS) and the analytical chemistry work was performed by the National Center for Environmental Health (NCEH); both of these National Centers are part of the Centers for Disease Control and Prevention (CDC). The goal of the NHANES is to obtain a representative sample of the civilian, non-institutionalized population residing in the United States, and by assessing the health and nutrition status of this sub-sample of the population, estimate the status of the population as a whole. In order to achieve this goal, a statistically representative sample of the population is collected by dividing the country into geographic areas known as primary sampling units (PSUs). The PSUs are combined to form strata, which are divided into a series of neighborhoods. From these neighborhoods, households are chosen at random, and their residents are interviewed to determine eligibility for participation in the survey. Over sampling of demographic groups, such as Mexican Americans and the socioeconomic underserved, ensures reliable sample size for these demographic groups. This over sampling is adjusted during data analyses by sampling weights. Once a subject has been deemed eligible for the study, an appointment is scheduled at a mobile examination center (MEC) for a complete series of medical and nutritional tests and measures. The MEC consists of four large trailers that contain all medical and diagnostic equipment necessary. Four types of data collection are performed in the MEC: (*i*) physical examination, (*ii*) dental examination, (*iii*) specimen collection and (*iv*) personal interview. Each year approximately 5,000 participants are recruited from 15 locations across the United States.

A 1/3-subset of eligible participants (N=2,305) between the ages of 12 and 85 years of the NHANES 2003/04 survey was chosen for measurement of BFRs; of these, 2,062 serum specimens were available for analysis. The population consisted of 48.4% male subjects and the race/ethnicity distribution of the sub-sample was 71.5% non-Hispanic white (NHW), 12.0% non-Hispanic black (NHB) and 8.2% Mexican Americans (MA). Other race/ethnic groups corresponded to 8.3%. The percentages of the sample below the age of 20 years and above the age of 60 were 12.2 and 17.0%, respectively. After inclusion of sampling weights, this 1/3-subset is

representative of the general population of the United States with regards to race/ethnicity, age, and sex.

Analytical Methods: All sample preparation work was performed in a clean room constructed at the NCEH for the measurement of these chemical classes. This clean room was constructed to reduce the contamination from indoor particles (dust), which are known to contain very high concentrations of the target compounds. [6-9] Inside the clean room, biological safety cabinets were used as a second barrier against particle contamination both for the automated equipment and manual transfers of serum from the original sample container and manual manipulation of sample extracts prior to analysis.

The analytical methodology employed for the measurement of BFRs in serum has been reported previously. [26] Study specimens were analyzed in batches of 24 specimens intermixed with quality control (QC; n=3) and method blank samples (n=3), in accordance with the previously published procedure. [26] The limit of detection (LOD) was calculated using two different methods and the higher of the two was employed for each measurement. Firstly, the LOD was calculated in direct relationship to method blanks, as three times the standard deviation of the method blanks and secondly, in relation to the lowest standard in the calibration curve producing a signal to noise (S/N) ratio greater than three. From each sample result, the average method blank concentration was subtracted. If the resulting amount was found to be less than the highest LOD calculated, the resulting value was substituted by the LOD and the measurement flagged as less than the LOD. Thereafter the calculated results were divided by the sample amount expressed in grams, to derive the final concentration expressed as pg/g serum. The lipid adjusted concentration was calculated and expressed as ng/g serum lipids, by dividing with the total lipid concentration in the serum.

Results and Discussion
At the time this abstract was written sampling weights for the NHANES 2003/04 survey were not available to the general public. Therefore, we cannot discuss the weighted data so our interpretation of the NHANES data is slightly limited. However, at the Dioxin 2007 conference a complete analysis of the survey data will be presented, including population weighted data.

The highest sum of PBDE levels observed for any one subject was 3,680 ng/g lipid. In this subject, the level of BDE-47 was 2,350 ng/g lipid, while the levels of BDE-99, BDE-100 and BDE-153 were 692, 339 and 152 ng/g lipid, respectively. It is important to mention that in this individual, the level of 2,2',4,4',5,5'-hexachlorobiphenyl (CB-153), a marker of traditional POPs, was 13 ng/g lipid. The concentration of the dominating PBDE congener was 180 times higher than that of the dominating marker PCB. Although, no human health effects have as of today been attributed to PBDEs, animal studies have shown neurodevelopmental effects in pups born from mice dosed during a critical window of the developing mice fetus. [24] No such effects have been shown in humans, although epidemiological studies are currently underway. It is also important to point out that the most recent retrospective time trend study conducted in the United States reported increasing levels of PBDEs with time. [27] Further studies will be needed to assess if current levels of PBDEs in the general population in the United States are increasing, have reached a plateau, or have started to decline. It is also important to conduct studies that will target and identify occupational settings or life style factors that result in exposures that produce the very high levels of PBDEs as reported in a subset of this cohort. Efforts are currently underway to address these questions and to help guide a reduction and/or elimination of the sources of exposure to this particular subgroup of the general population of the United States.

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