# CONCENTRATIONS OF DIOXIN-LIKE COMPOUNDS IN THE U.S. POPULATION: AN EVALUATION OF DATA TRENDS AND THE EFFECTS OF DEMOGRAPHIC CHARACTERISTICS ON REFERENT TOTAL TEQ LEVELS

Nguyen LM, Chen CL, Scott LLF

ChemRisk, San Francisco, CA, USA

**Abstract**
Biomonitoring can be a critical tool in assessing exposure to potentially harmful chemicals. Yet interpretation of biomonitoring data can be complex and requires understanding of temporal trends in chemical body burden and proper interpretation of reference concentrations measured in the general population. In this study, we evaluated data trends for the 2001-2002 and 2003-2004 NHANES PCDD/F and dioxin-like PCB serum concentration data in order to estimate reference levels of total TEQ concentrations for a variety of subpopulations. We also assessed the influence of various demographic characteristics, including geographic region, on concentrations of total TEQ. Lower limits of detection (LODs) for the 2003-2004 survey have allowed for more accurate estimations of background levels of PCDD/Fs and dioxin-like PCBs in the general population. Due either to a result of these lower LODs and/or decreasing exposure of the general population, total TEQ body burden appears to be steadily declining; however, the congeners that contribute the greatest to total TEQ has remained relatively static. As expected, age had the greatest overall effect on total TEQ concentrations, both independently and adjusted for other characteristics such as race/ethnicity and gender, with a clear increasing trend in total TEQ concentrations with increasing age.

**Introduction**
Biomonitoring has proven to be a fundamental tool in studying potentially harmful environmental chemicals.[1-3] In humans, biological specimens such as blood, urine, breast milk and exhaled breath are commonly measured for exogenous substances or their metabolites. One source of biomonitoring data is the National Health and Nutrition Examination Survey (NHANES), a series of cross-sectional surveys designed to assess the health and nutritional status of civilian, non-institutionalized adults and children in the United States (U.S.). The survey is conducted every two years by the National Center for Health Statistics (NCHS) and the Centers for Disease Control and Prevention (CDC). Information from both interviews and physical examinations conducted at a mobile examination center (MEC) is combined to create a comprehensive set of nationally representative analytical data.

We previously described data from the 2001-2002 NHANES survey and presented serum reference levels of polychlorinated dibenzo-p-dioxins and dibenzofurans (PCDD/Fs) and dioxin-like polychlorinated biphenyls (PCBs) for the general U.S. population.[4,5] More recently, serum concentration data for these chemicals has been released for the 2003-2004 survey period,[6] allowing for the analysis of temporal trends in levels of these compounds. Furthermore, development of reference levels of these substances by various subpopulations will facilitate more accurate assessments of levels in potentially exposed individuals and/or groups and present a more accurate portrayal of potential fluctuations in exposure to chemicals in the environment. Here, we present total TEQ reference concentrations by geographic region, age, race/ethnicity, tobacco smoke exposure, gender and poverty level for the general U.S. population using the 2003-2004 NHANES data.

**Materials and Methods**
PCDD/F and PCB analytes were measured at the CDC laboratory using high-resolution gas chromatography and/or isotope-dilution high-resolution mass spectrometry (HRGS/ID-HRMS) as described in the *Third National Report on Human Exposure to Environmental Chemicals*.[7] Publicly available data – such as the PCDD/F and PCB serum concentration data, age, gender, etc. – were merged with geographic data obtained from NCHS's Research Data Center (RDC) using each individual's unique participant identifier. .

All 2,3,7,8-substituted PCDD/Fs and nine of the twelve dioxin-like PCB congeners were included in these analyses. However, total TEQ concentrations were estimated only for participants with complete congener profiles (i.e. were not missing any congener data). Total TEQ concentration was calculated by summing the product of the lipid weight concentration for each congener and the associated 2005 WHO TEF.[8] Samples with concentrations below the limit of detection (LOD) were assumed to have a concentration equal to the LOD divided by the square root of two ($C_{ND} = LOD / \sqrt{2}$).

Participants with serum cotinine levels less than 1 ng/mL were categorized as nonsmokers or as having no exposure to environmental tobacco smoke (ETS); participants with levels between 1 and 10 ng/mL were categorized as having some exposure to ETS; and participants with levels higher than 10 ng/mL were classified as active smokers. Poverty index was assessed using poverty-to-income ratio (PIR) as follows: poor, PIR <1.25; low income, 1.25≤ PIR <2.00; middle income, 2.00≤ PIR <4.00; and high income, PIR ≥4.00. Race/ethnicity was categorized as non-Hispanic black, non-Hispanic white, Mexican-American and "Other." Participants with a reported race/ethnicity of "Other Hispanic" and "Other" were combined into one group to provide more reliable TEQ estimates. Geographic region was categorized using the Census Bureau definitions of "Northeast," "Midwest," "South," and "West."

Weighted summary statistics and ninety-five percent (95%) confidence intervals for the geometric mean TEQ were calculated for the various subgroups of interest. The average percent contribution of each congener to total TEQ was calculated by averaging the percent contribution of that congener to the total TEQ across all subjects. Because LODs are not reported in the NHANES data file, they were calculated only for those participants noted to have a concentration below the LOD using the equation $LOD = C_{ND} * \sqrt{2}$.

The association between each demographic characteristic (i.e., region, age, gender, race/ethnicity, tobacco smoke exposure and poverty index) and total TEQ concentration was evaluated both independently as well as adjusted for all other variables. All analyses were conducted using SAS and SUDAAN software, and utilized an alpha level of 0.05. For multiple comparisons within each subgroup, the Bonferroni Correction was used.

**Results and Discussion**

As presented in Table 1, the limits of detection for the PCDD/F and non-ortho PCB congeners were very low across survey periods. Nonetheless, for most congeners, average LODs for the 2003-2004 data were half of that for the 2001-2002 data. More notably, the average LODs for the mono-ortho PCBs decreased considerably (i.e. by a factor of ~45) from 2001-2002 to 2003-2004.

**Table 1: Limits of Detection (pg/g wet weight) by Congener and Survey Period**

| | *2001-2002* | | *2003-2004* | |
|---|---|---|---|---|
| **Congener** | **Average** | **Range** | **Average** | **Range** |
| TCDD | 0.02 | 0.01-0.04 | 0.01 | 0.00-0.02 |
| 1,2,3,7,8-PeCDD | 0.02 | 0.01-0.05 | 0.01 | 0.00-0.02 |
| 1,2,3,4,7,8-HxCDD | 0.03 | 0.01-0.07 | 0.02 | 0.01-0.07 |
| 1,2,3,6,7,8-HxCDD | 0.03 | 0.02-0.08 | 0.03 | 0.01-0.07 |
| 1,2,3,7,8,9-HxCDD | 0.03 | 0.01-0.08 | 0.02 | 0.01-0.07 |
| 1,2,3,4,6,7,8-HpCDD | 0.03 | 0.02-0.05 | 0.03 | 0.01-0.06 |
| OCDD | 1.26 | 0.40-2.75 | 0.56 | 0.23-1.20 |
| TCDF | 0.02 | 0.01-0.04 | 0.01 | 0.01-0.03 |
| 1,2,3,7,8-PeCDF | 0.02 | 0.01-0.05 | 0.01 | 0.01-0.04 |
| 2,3,4,7,8-PeCDF | 0.02 | 0.01-0.05 | 0.01 | 0.01-0.04 |
| 1,2,3,4,7,8-HxCDF | 0.02 | 0.01-0.04 | 0.02 | 0.01-0.04 |

| | | | | |
|---|---|---|---|---|
| 1,2,3,6,7,8-HxCDF | 0.02 | 0.01-0.05 | 0.02 | 0.01-0.05 |
| 1,2,3,7,8,9-HxCDF | 0.02 | 0.01-0.05 | 0.02 | 0.01-0.05 |
| 2,3,4,6,7,8-HxCDF | 0.02 | 0.01-0.05 | 0.02 | 0.01-0.05 |
| 1,2,3,4,6,7,8-HpCDF | 0.02 | 0.01-0.05 | 0.02 | 0.01-0.06 |
| 1,2,3,4,7,8,9-HpCDF | 0.02 | 0.01-0.06 | 0.02 | 0.01-0.06 |
| OCDF | 0.07 | 0.02-0.18 | 0.02 | 0.01-0.07 |
| PCB105 | 29.97 | 28.28-57.98 | 0.71 | 0.57-1.13 |
| PCB118 | 30.13 | 28.28-57.98 | NA | NA |
| PCB156 | 30.10 | 28.28-57.98 | 0.67 | 0.57-1.13 |
| PCB157 | 29.95 | 28.28-57.98 | 0.66 | 0.57-1.13 |
| PCB167 | 29.94 | 28.28-57.98 | 0.68 | 0.57-1.13 |
| PCB189 | 29.93 | 26.87-57.98 | 0.67 | 0.57-1.13 |
| PCB 126 | 0.03 | 0.01-0.06 | 0.04 | 0.02-0.07 |
| PCB 81 | 0.08 | 0.03-0.23 | 0.03 | 0.02-0.08 |
| PCB 169 | 0.03 | 0.02-0.06 | 0.03 | 0.02-0.07 |

Figure 1 illustrates the fraction of samples below the limit of detection (LOD) for each congener by survey period. The greater percentage of detects for the 2003-2004 data, particularly for the mono-ortho PCBs, is likely a function of decreased LODs for this survey period rather than an increase in concentrations from 2001-2002. Indeed, as shown in Figure 2, geometric mean concentrations declined considerably for all age groups.

**Figure 1: Percent of Samples Below the Limit of Detection (LOD) by Survey Period**

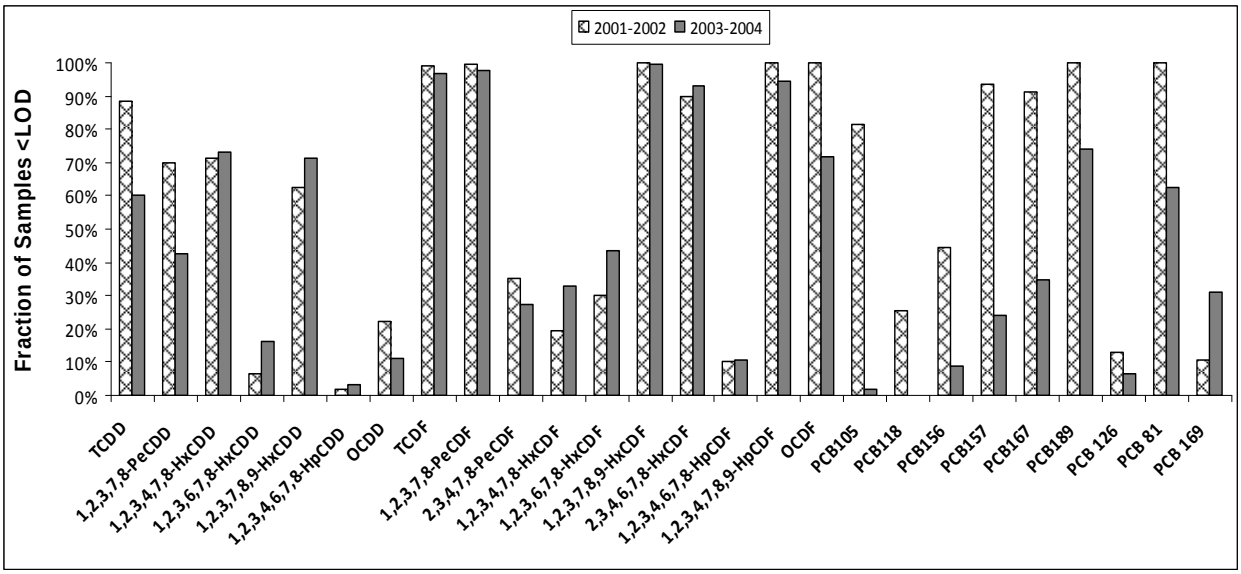


**Figure 2: Geometric Mean Total TEQ Concentrations by Age Group and Survey Period**

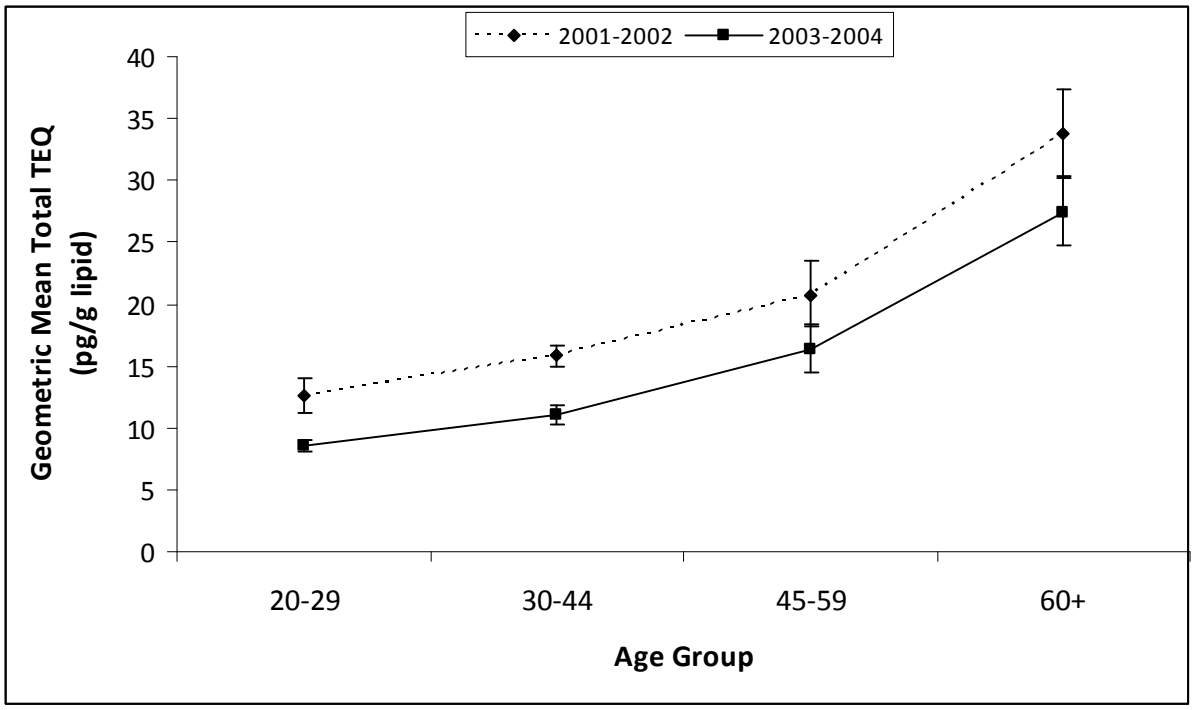
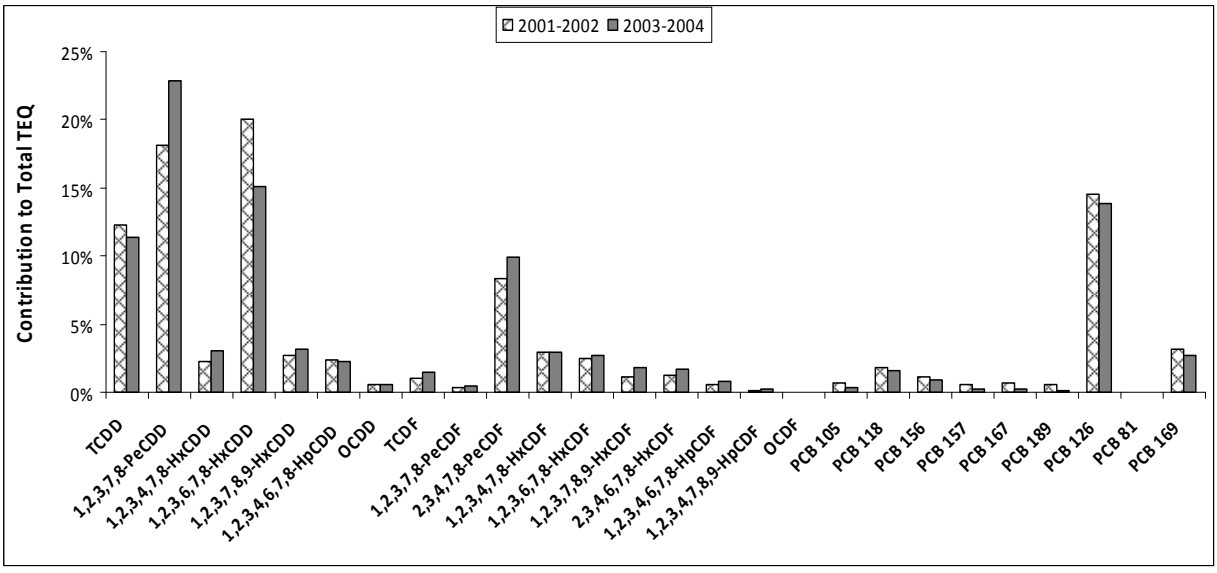



Figure 3 compares the percent contribution to total TEQ by survey period. The largest differences in the percent contribution of individual congeners between the two surveys were observed for 1,2,3,7,8-PeCDD (an increase of 5%) and 1,2,3,6,7,8-HxCDD (a decrease of 5%). Regardless, the same five congeners (TCDD, 1,2,3,7,8-PeCDD, 1,2,3,6,7,8-HxCDD, 2,3,4,7,8-PeCDF, and PCB 126) contributed approximately 73% to total TEQ concentrations for both periods.

**Figure 3: Percent Contribution of Individual Congeners to Total TEQ by Survey Period**



Reference levels of total TEQ by subpopulation are summarized in Table 2. A total of 1,660 participants had complete congener profiles, with total TEQ concentrations ranging from 2.7 to 189.5 pg/g lipid (ppt). Analysis of the independent effects of gender and region demonstrated that total TEQ levels did not vary significantly among the four regions or between males and females. For tobacco smoke exposure, race/ethnicity, and poverty index, the overall effects were significant ($p=0.002$, $p=0.002$, and $p=0.026$, respectively); however, concentrations did not necessarily vary significantly among all the different levels of each subpopulation. For example, total TEQ concentrations were significantly higher for non-smokers compared to smokers ($p<0.001$) but no difference was observed between non-smokers or smokers and individuals exposed to only environmental tobacco smoke. A similar trend was observed for poverty index. Specifically, total TEQ concentrations did not vary among participants classified as having low, middle and high incomes yet these three groups all had significantly higher concentrations of total TEQ than poor participants ($p=0.010$, $p=0.006$, and $p=0.005$, respectively). As expected, we observed a highly significant trend in increasing total TEQ concentration with increasing age ($p<0.001$). Consistent with the results of previous analyses of the 2001-2002 data by Scott et al. (2008),[5] levels in oldest age group were just over three times that of the youngest age groups (i.e. 12-19 and 20-29 years).

Interestingly, in the adjusted model only age and tobacco smoke exposure had overall significant effects ($p<0.001$ and $p=0.026$, respectively). Even after adjusting for all other variables, significant differences in total TEQ levels among all age groups were observed ($p<0.001$ for all comparisons), suggesting a very strong age-effect. In contrast, total TEQ concentrations only varied significantly between smokers and individuals exposed to environmental tobacco smoke ($p=0.005$) with respect to tobacco smoke exposure. While the overall effect of geographic region was not significant in the adjusted model, total TEQ levels were consistently higher in the Northeast and Midwest, particularly at the higher percentiles. This suggests that if upper-bound values from the referent group are to be used in a comparative analysis (e.g., to an exposed group), the influence of region may need to be considered.

**Table 2: Weighted TEQ ($WHO_{2005}$) Summary Statistics Estimated Using the 2003-2004 NHANES PCDD/F and Dioxin-like PCB Serum Concentration Data**

| | N | Geometric Mean | 95% CI | Min | 50th | 75th | 90th | 95th | Max |
|---|---|---|---|---|---|---|---|---|---|
| ***Total*** | 1660 | 13.1 | 12.4-13.9 | 2.7 | 12.3 | 20.3 | 30.9 | 37.4 | 189.5 |
| ***Geographic Region*** | | | | | | | | | |
| West | 415 | 12.3 | 10.8-14.2 | 3.3 | 11.7 | 19.3 | 27.5 | 33.7 | 48.6 |
| South | 497 | 12.8 | 11.8-13.7 | 2.7 | 12.6 | 20.0 | 27.9 | 34.0 | 93.7 |
| Northeast | 294 | 13.6 | 12.4-14.9 | 3.3 | 12.3 | 21.6 | 33.6 | 40.5 | 119.2 |
| Midwest | 454 | 13.9 | 11.8-16.1 | 3.1 | 12.7 | 21.1 | 34.8 | 44.7 | 189.5 |
| ***Race/Ethnicity*** | | | | | | | | | |
| Non-Hispanic White | 755 | 13.7 | 12.9-14.4 | 2.7 | 13.2 | 21.1 | 31.8 | 37.7 | 119.2 |
| Non-Hispanic Black | 398 | 13.1 | 11.6-14.6 | 3.5 | 11.4 | 20.0 | 31.9 | 53.4 | 189.5 |
| Mexican American | 381 | 9.9 | 8.5-11.4 | 3.1 | 9.0 | 13.6 | 19.7 | 25.0 | 93.7 |
| Other | 126 | 12.6 | 11.5-13.7 | 4.1 | 11.1 | 20.4 | 25.0 | 33.6 | 78.7 |
| ***Age*** | | | | | | | | | |
| 12-19 | 527 | 7.6 | 7.2-7.9 | 3.3 | 7.2 | 9.4 | 12.1 | 14.2 | 36.8 |
| 20-29 | 218 | 8.6 | 8.1-9.1 | 2.7 | 8.3 | 10.6 | 13.1 | 16.6 | 24.1 |
| 30-44 | 297 | 11.1 | 10.3-11.9 | 3.6 | 11.3 | 15.0 | 20.0 | 23.5 | 36.4 |
| 45-59 | 230 | 16.3 | 14.4-18.4 | 5.2 | 16.7 | 22.4 | 28.5 | 33.8 | 58.6 |
| 60+ | 388 | 27.4 | 24.8-30.3 | 4.8 | 27.5 | 35.9 | 48.6 | 59.5 | 189.5 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| ***Tobacco Smoke Exposure*** | | | | | | | | | |
| None/Non-Smoker | 1164 | 13.7 | 13.1-14.4 | 2.7 | 12.6 | 22.0 | 33.7 | 39.7 | 122.1 |
| Environmental Exposure | 126 | 11.8 | 9.8-14.2 | 3.9 | 10.6 | 16.2 | 26.9 | 35.4 | 189.5 |
| Smoker | 369 | 11.8 | 11.1-12.7 | 3.6 | 12.0 | 17.4 | 23.8 | 27.7 | 84.1 |
| ***Gender*** | | | | | | | | | |
| Male | 811 | 12.7 | 11.9-13.6 | 3.1 | 11.8 | 19.4 | 28.9 | 34.6 | 106.3 |
| Female | 849 | 13.5 | 12.8-14.3 | 2.7 | 12.7 | 21.1 | 33.5 | 38.7 | 189.5 |
| ***Poverty Index*** | | | | | | | | | |
| Poor | 503 | 11.4 | 10.5-12.3 | 3.3 | 10.0 | 17,0 | 27.0 | 35.3 | 109.5 |
| Low | 302 | 13.6 | 12.2-15.0 | 4.2 | 12.2 | 21.1 | 35.8 | 46.2 | 189.5 |
| Middle | 406 | 13.3 | 12.4-14.4 | 3.3 | 12.3 | 21.0 | 29.5 | 36.0 | 119.2 |
| High | 372 | 13.7 | 12.6-15.0 | 3.1 | 13.8 | 20.5 | 30.6 | 36.6 | 91.4 |

Increases in biomonitoring by various governmental agencies and industrial and manufacturing businesses to evaluate potential exposure of populations and/or individuals has increased the need for understanding temporal trends in chemical body burden for the general population as well as a demand for relevant, useful reference statistics for interpreting biomonitoring results. Similar to Scott et al. (2008),[5] the results of the analyses presented here provide the scientific and regulatory communities with descriptive reference levels for various subpopulations and general trends in body burden for PCDD/Fs and dioxin-like PCBs that will be useful in exposure and risk assessment. Nonetheless, caution should be taken when using these data for risk management purposes. Such use will require consideration of the most relevant information. Since human exposure is not static, reference levels should reflect the changing nature of background exposures in the general population. The updated reference concentrations presented will be useful in evaluating levels of exposure for potentially sensitive communities. .

**Acknowledgements**
The authors of this study would like to thank the staff at the NCHS Research Data Center in Hyattsville, MD for their help and support.

**References**

1. NRC (National Research Council). Human Biomonitoring for Environmental Chemicals. National Research Council, Committee on Human Biomonitoring for Environmental Toxicants. National Academies Press, Washington, DC, 2006.
2. Paustenbach D. and Galbraith D. *Environ Health Perspect* 2006;114:1143.
3. Paustenbach D. and Galbraith D. *Reg Toxicol Pharmacol* 2006;44:249.
4. Ferriby L.L., Knutsen J.S., Harris M., Unice K.M., Scott P., Nony P., Haws L.C. and Paustenbach D. *J Expo Sci Environ Epidemiol* 2007;17:358.
5. Scott L.L.F., Unice K.M., Scott P., Nguyen L.M., Haws L.C., Harris M. and Paustenbach D. *J Expo Sci Environ Epidemiol* 2008;18:524.
6. NCHS (National Center for Health Statistics). *National Health and Nutrition Examination Survey Data*. US Department of Health and Human Services, Centers for Disease Control and Prevention: Hyattsville, MD, 2005.
7. CDC (Centers for Disease Control and Prevention). *Third National Report on Human Exposure to Environmental Chemicals.* US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Environmental Health: Atlanta, GA, 2005 NCEH Pub. No. 05-0579.
8. Van den Berg M., Birnbaum L.S., Denison M., DeVito M., Farland W., Freely M., Fiedler H., Hakansson H., Hanberg A., Haws L., Rose M., Safe S., Schrenk D., Tohyama C., Tritscher A., Tuomisto J., Tysklind M., Walker N. and Peterson R.E. *Toxicol Sci* 2006;93:223.