

DEVELOPMENT OF PCDD/F TEQ SERUM REFERENCE VALUES FOR THE US POPULATION FOR USE IN EVALUATING BIOMONITORING RESULTS

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Introduction

The CDC's National Center for Health Statistics (NCHS) conducts a survey every two years to collect health and nutritional information on the U.S. population. The National Health and Nutrition Examination Survey (NHANES) conducted during 1999-2000 supplied data on 116 chemicals measured in the blood of selected survey participants and was the first NHANES survey to include polychlorinated dibenzo-p-dioxin (PCDD) and polychlorinated dibenzofuran (PCDF) serum analyses¹. Although this survey provided the first opportunity to assess referent levels of certain environmental chemicals in the U.S. population, the PCDD/F data was found to have high detection limits and lacked analytical results for two of the 2,3,7,8-substituted PCDD/Fs. Recently, the CDC released the 2001-2002 NHANES data for PCDD/Fs. Sample collection methodologies for this survey were adjusted, possibly in an effort to address concerns regarding detection limits and analyses were conducted for all seventeen 2,3,7,8-substituted PCDD and PCDF congeners. This dataset also contained results for 9 dioxin-like polychlorinated biphenyls (PCBs). However, for the purposes of this analysis, only PCDDs and PCDFs were considered.

As the need to characterize populations potentially exposed to PCDD/Fs due to accidental industrial releases or contact with historically-contaminated environmental media continues to increase, so to does the need for valid referent concentrations of these chemicals in the human population. Hence, the objective of this project was to provide scientists, regulatory agencies, the regulated community, and the general public with descriptive reference statistics for PCDD/F levels in the U.S population using the 2001-2002 NHANES data. An additional objective of this project was to demonstrate the utility of these reference values by evaluating recent PCDD/F biomonitoring results for a group of individuals from Southern Mississippi that reportedly combusted wood treated with either creosote or pentachlorophenol in their homes.

Materials and Methods

The CDC measured PCDD/Fs in blood serum collected from a subset of NHANES participants that were surveyed between 2001 and 2002². Complete details regarding the procedures, survey components, IRB review, confidentiality, questionnaires, and examination are available at the CDC National Center for Health Statistics website: <http://www.cdc.gov/nchs/nhanes.htm>. Information specific to the current (1999-2004) NHANES survey including operations manuals and consent documentation is available at: <http://www.cdc.gov/nchs/about/major/nhanes/nhanes99-02.htm>.

All 2,3,7,8-substituted PCDD/Fs were quantified in this study. PCDD/F content of the samples was measured using high-resolution gas chromatography and/or isotope-dilution high-resolution mass spectrometry (HRGS/ID-HRMS) as described in the NHANES Third Report³. Non-detect concentrations (ND) of PCDD/Fs in human serum were addressed using the approach of the Detection Limit (DL) / $\sqrt{2}$.

Statistical analyses of NHANES 2001-2002

Lipid-adjusted PCDD/F serum concentration data (PCDD/F in pg/g) was released in May 2005 as part of the NHANES 2001-2002 survey. Results were obtained from the CDC website. The data files were converted from a SAS format to Microsoft Excel format using the SYSTAT 11.0 statistical software package. Serum concentration data were linked to gender, race, smoking status, and age demographics using the unique survey participant identifier assigned to each subject. Only data from participants with complete PCDD/F and dioxin-like PCB profiles were selected for analysis. PCDD/F TEQs for individual subjects were calculated by summing the product of each congener's concentration and the associated 1998 World Health Organization (WHO) toxic equivalency factors (TEF)⁴.

The mean, geometric mean, and 25th, 50th, 75th and 95th percentile TEQ concentrations were characterized by gender, race, smoking status and age for the unweighted data set using Microsoft Excel (data not shown). To eliminate any bias inherent in the NHANES 2001-2002 study design, weighted summary statistics were also calculated using the dioxin subset specific two year weights included in the NHANES dioxin data file (NCHS 2005a). The CDC recommends the

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use of the two year weights when developing population level reference values. These weighted statistics were calculated using SYSTAT and then summarized using Microsoft Excel. Ninety-five percent (95%) confidence intervals for the weighted mean TEQ levels were calculated using Sudaan Version 9⁵. This program estimated the upper and lower 95% confidence limits using the Taylor series method as outlined in the NHANES 1999-2004 analytic guidelines^{6,7}.

PCDD/F Biomonitoring Results – Southern Mississippi

Fifty ml of serum from 10 individuals who reportedly combusted creosote or pentachlorophenol treated wood in their homes was collected by LabCorp of Laurel, Mississippi and sent to ERGO Laboratory, Gelerstrasse 1, D-22305, Hamburg, Germany for PCDD/F analysis⁸. The laboratory quantified the seventeen 2,3,7,8-substituted PCDD/Fs using high resolution gas chromatography and high resolution mass spectrometry (HRGC/HRMS). Lipid analysis was performed using a gravimetric method. Non-detect concentrations (ND) of PCDD/Fs in human serum were managed using the approach of the Detection Limit (DL) / $\sqrt{2}$ and the TEQ was calculated using the WHO TEFs⁴.

Results and Discussion

Results from the analysis of the NHANES 2001-2002 data are summarized below in Table 1. There were 1,081 individuals with complete congener profiles and the PCDD/F TEQ ranged from 3.6 to 139.2 pg/g lipid. Both age and race appear to impact the TEQ. For example, males 20-29 have a mean TEQ of 11.7 pg/g lipid (CI 10.5 – 12.9), whereas males 60+ have mean TEQ of 28.5 pg/g lipid (CI 25.2 – 31.8). Additionally, the mean TEQ for Mexican-Americans appears to be substantially lower than Non-Hispanic Whites and Non-Hispanic Blacks.

Table 1: Descriptive Statistics for the Weighted PCDD/F TEQ for Various Subgroups from NHANES 2001-2002^a

Group	N	Mean	95% CI	Min	25th	50th	75th	95th	Max
All samples	1081	18.7	16.5 - 21.0	3.6	10.6	14.4	21.4	45.2	139.2
Male	473	18.1	15.8 - 20.4	5.1	11.0	13.8	20.2	43.5	122.7
Female	608	19.3	16.9 - 21.7	3.6	10.0	14.9	22.6	49.0	139.2
Smoker	245	15.2	13.4 - 17.0	3.9	9.8	12.9	18.0	34.7	80.8
Non-smoker	836	20.0	17.5 - 22.6	3.6	11.0	15.0	23.8	49.0	139.2
All 20 - 29 years	197	11.2	9.9 - 12.6	3.6	8.3	10.7	12.9	21.3	36.0
All 30 - 44 years	305	14.1	13.0 - 15.2	4.2	9.8	12.3	16.5	28.3	89.7
All 45 - 59 years	228	19.2	15.7 - 22.8	3.9	11.9	15.9	21.5	38.9	94.9
All 60+ years	351	31.7	27.6 - 35.9	4.6	18.0	26.5	41.1	68.5	139.2
Non-Hispanic White	568	19.7	17.2 - 22.1	3.9	11.0	15.1	22.9	46.8	119.4
Non-Hispanic Black	194	20.9	18.1 - 23.7	4.6	10.7	15.0	23.4	57.9	139.2
Mexican-American	238	13.0	11.6 - 14.4	3.6	8.4	10.9	13.8	26.3	122.7
Other Hispanic	45	14.2	11.9 - 16.5	5.5	9.7	12.7	16.2	35.2	36.9
Other Race	36	13.9	11.2 - 16.7	4.4	9.7	12.1	16.1	28.3	48.0
Male 20-29	72	11.7	10.5 - 12.9	5.1	9.6	11.3	13.7	16.8	21.3
Male 30-44	124	14.4	12.8 - 16.0	5.9	10.5	13.0	16.9	28.3	89.7
Male 45-59	121	19.0	15.5 - 22.6	6.0	11.8	15.0	20.6	43.1	94.9
Male 60+	156	28.5	25.2 - 31.8	5.9	15.8	24.0	37.5	53.6	122.7
Female 20-29	125	10.9	8.8 - 12.9	3.6	7.5	9.9	12.0	23.0	36.0
Female 30-44	181	13.9	12.2 - 15.5	4.2	9.0	11.7	16.4	26.3	54.3
Female 45-59	107	19.4	15.6 - 23.2	3.9	13.3	18.0	22.6	37.8	87.2
Female 60+	195	34.0	28.1 - 39.8	4.6	19.1	27.5	42.8	70.7	139.2

^aPCDD/F TEQ reported as pg/g lipid

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Because of the robust sampling design of the NHANES project, these data are suitable reference values for the U.S. population.

Table 2 summarizes the TEQ, age and gender of 10 individuals from Southern Mississippi that reportedly combusted creosote or pentachlorophenol treated wood in their homes. TEQs ranged from 11.7 to 35.7 pg/g lipid among the 3 males and 7 females in this group. The results reported in Table 1 demonstrated that age clearly impacts the TEQ of a person with older individuals generally have higher TEQs than younger individuals. Because of this, it is important to consider age when evaluating PCDD/F biomonitoring results.

Parameter	Biomonitoring Subjects									
	1	2	3	4	5	6	7	8	9	10
TEQ (pg/g lipid)	17.1	25.2	16.3	35.8	20.0	25.5	32.8	11.8	29.4	32.2
Age (years)*	61	50	64	61	47	63	53	47	49	63
Gender	Female	Female	Male	Female	Female	Male	Female	Female	Male	Female

*age at time of blood collection and analysis

Comparison of the TEQ of the 10 individuals from Southern Mississippi to the NHANES reference values is illustrated in Figure 1 below. TEQs for the 10 individuals from Southern Mississippi all fall below the 95th percentile of their respective age and gender reference values developed from the NHANES 2001-2002 PCDD/F results. Interestingly, the TEQ for 5 individuals falls below the mean for their age/gender categories and 5 individual TEQs are above the mean for their age/gender categories. Within any normally distributed dataset, one would expect half of the results to be above the mean and half to be below the mean. Comparison of the biomonitoring results for these individuals to the NHANES 2001-2002 TEQ reference values does not indicate elevated PCDD/F serum values. Rather, the TEQ for each of these individuals fall within the range expected for the general U.S. population suggesting that these individuals have not had unusual or elevated exposure to PCDD/Fs.

Our use of the NHANES 2001-2002 results for the development of PCDD/F TEQ reference values is an improvement over previous efforts for several reasons including (1) the large number of samples utilized for the development of reference values, (2) only samples with complete congener profiles were utilized, (3) sample selection was designed to be representative of the United States and (4) the underlying data are publicly available. Additionally, the recent NHANES Third Report³ does not provide summary statistics in a manner that is useful for evaluating PCDD/F biomonitoring results.

References

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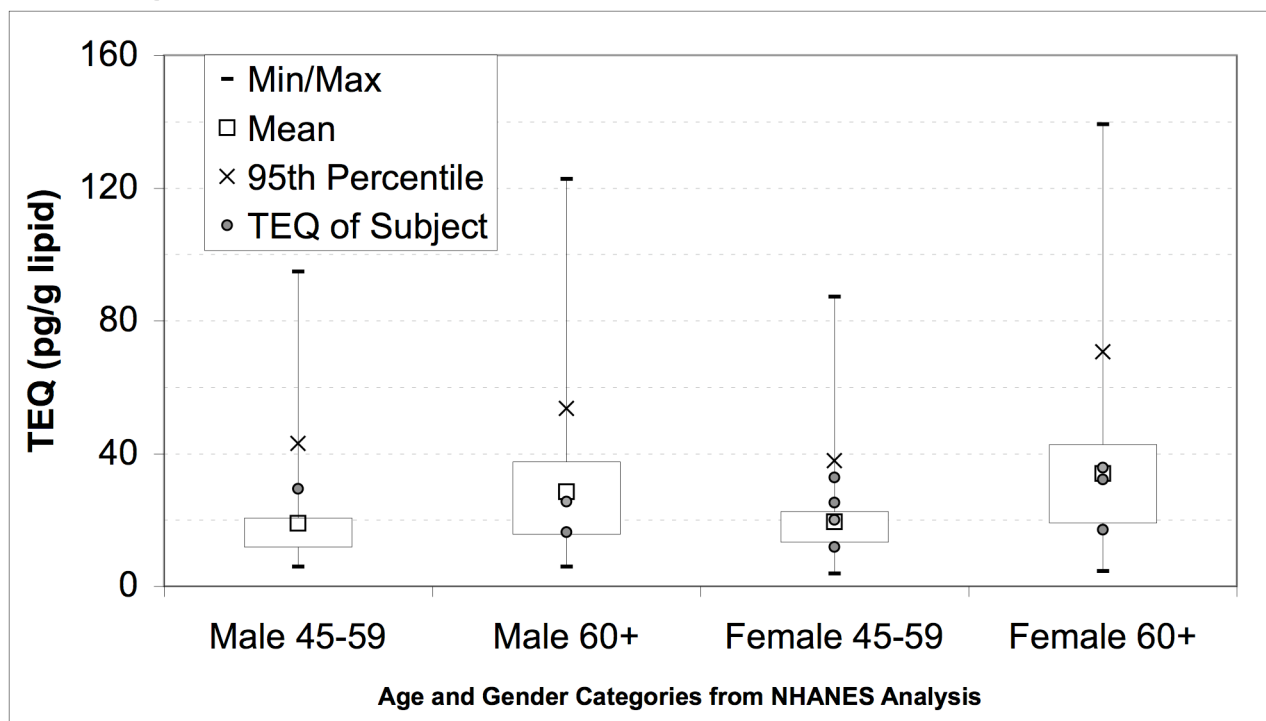
⁶Centers for Disease Control (CDC). NHANES 1999-2000 Addendum to the NHANES III Analytic Guidelines. Updated August 30, 2002.

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⁷Centers for Disease Control (CDC). NHANES Analytic Guidelines. June 2004 version.

⁸Affidavit of Dr. Vera Byers, dated November 15, 2004. Provides description of serum collection and PCDD/F analysis.

Figure 1: Comparison of PCDD/F TEQ of 10 Individuals from Southern Mississippi to NHANES 2001-2002 PCDD/F TEQ Reference Values



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