Evaluation of background dioxin-like PCB congener profiles in human serum collected during NHANES 2001/2002 using principal components analysis

Scott P[1] Haws L[2], Scott L[3], Harris M[3]
[1]ChemRisk, 20 Stanwix St, Pittsburgh, Pennsylvania USA; [2]Chemrisk, 3420 Executive Center Road, Austin, Texas USA; [3]10375 Richmond Avenue, Houston, Texas USA

Abstract
With the increasing use of biomonitoring to evaluate human exposure, it is important to understand how the profile of the congeners of interest in the potentially exposed population compares to the corresponding congener profile associated with background exposure. In this study, we have performed a principal components analysis (PCA) of the 2001/2002 NHANES dioxin-like PCB data for the general U.S. population to determine if the background dioxin-like PCB congener profiles are affected by age, gender, or race. Overall, the results of the PCA indicated that the dioxin-like PCB congener profile for the NHANES participants changes with age and gender. In general, the contributions from PCBs 157, 167, and 169 decrease with increasing age, while the contribution from PCB 118 increases with increasing age. In addition, males are more likely to have higher contributions of PCB 156 than females of the same age. Finally, there were no apparent differences in congener profile by race. These results indicate that age and gender need to be accounted for when PCA is used to compare the dioxin-like PCB congener profiles from the 2001/2002 NHANES data to those of a potentially exposed population.

Introduction
With the increasing use of serum measurements to evaluate populations potentially exposed to polychlorinated dibenzo-p-dioxins and dibenzofurans (PCDD/Fs) and dioxin-like polychlorinated biphenyls (PCBs) in the environment, the determination of background concentrations of PCDD/Fs and PCBs in the general population is important in order to put those measurements in context. Recently, Ferriby et al.[1] analyzed the weighted 2001/2002 National Health and Nutrition Examination Survey (NHANES) data to assess potential differences in mean total 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) toxic equivalent (TEQ) concentrations between various groups of individuals and to determine serum background TCDD TEQ concentrations for PCDD/Fs and dioxin-like PCBs in the general U.S. population. While it is important to compare the PCDD/F and dioxin-like PCB serum concentrations in a potentially exposed population to background concentrations on a TEQ basis, it is also important to understand how the relative distribution of the 17 2,3,7,8 PCDD/F and 9 dioxin-like PCB concentrations in a potentially exposed group compares to the relative distribution in the general U.S. population. There may be individuals within a potentially exposed population who have above background TEQ concentrations resulting from higher dietary exposures due to regional differences in the type and amount of food consumed unrelated to PCDD/F or PCB exposures of interest.

Because the sources associated with the 17 2,3,7,8-PCDD/F congeners and the 9 dioxin-like PCB congeners may be different, it may be necessary to evaluate these two types of dioxin-like chemicals separately in order to identify any potential PCDD/F exposures versus any dioxin-like PCB exposures. For example, a population expected to be potentially exposed only to PCDD/Fs may have PCDD/F congener profiles similar to NHANES but dioxin-like PCB congeners that are different from NHANES. A combined PCA analysis of the 17 2,3,7,8-PCDD/F and 9 dioxin-like PCBs may indicate differences in the congener profile that are not due to the 2,3,7,8-PCDD/F congeners but to the dioxin-like PCBs.

To compare the congener profile of an individual to the background dioxin-like PCB congener profiles of the general U.S. population, multivariate statistical methods must be used. Principal components analysis (PCA) is a common statistical method used to evaluate multivariate environmental data sets. In this study, we will present the results of a PCA of the 2001/2002 NHANES dioxin-like PCB data and discuss how the congener profiles within the 2001/2002 NHANES data vary based on age, gender, and race. The specific dioxin-like PCBs included in this analysis were those defined by the World Health Organization during their recent re-evaluation of the toxic equivalency factors (TEFs) for dioxin-like compounds and were included in the

2001/2002 NHANES study: PCBs 81, 105, 118, 126, 156, 157, 167, and 169[2].

Materials and Methods

PCA is a multivariate statistical technique that transforms a set of correlated variables into a subset of factors or principal components that are linear functions of the original variables and are uncorrelated.[3] The purpose of PCA is to reduce the dimensions of the data set so that trends in the data can be more easily examined. In terms of dioxin-like PCB congener data, because the concentrations many of the congeners are correlated with each other, PCA is able to transform a data set consisting of the 9 congeners into a subset of factors that is often less than 3. This method has been used in a similar manner at other sites to compare human serum PCDD/F congener profiles to environmental congener profiles.[4,5,6,7,8]

Only data from 2001/2002 NHANES participants with complete dioxin-like PCB congener profiles were selected for this analysis resulting in a sample set of 1,200 participants. This differs from the sample size of Ferriby et al.[1] of 1,081 participants because their participants were required to have complete profiles for both the PCDD/F and dioxin-like PCB congeners, while the current study focused only on the dioxin-like PCBs. Congener concentrations that were reported to be below the limit of detection were set equal to the limit of detection divided by the $\sqrt{2}$. For the PCA, the relative fraction of each congener to the total dioxin-like PCB congeners was estimated for each NHANES participant by dividing the congener concentration by the sum of the dioxin-like PCB congener concentrations.[9] The relative fraction data were then range transformed as a nonparametric method of normalization similar to what has been done in other studies.[10] The PCA was then performed on the covariance matrix of the range-transformed data.

Results and Discussion

The PCA of the 2001/2002 NHANES PCDD/F data resulted in two factors that described 90.4% of the variance in the original data set with the first factor describing 80.4%, and the second factor describing 10.4%.of the variance in the original data set.

Factor 1 is characterized by positive factor loadings for PCBs 157, 167, and 169 (0.276 – 0.286) and a negative loading for PCB 118 (-0.217). For this factor, a positive factor score for a participant indicates that PCBs 157, 167, and 169 contribute more to the total dioxin-like PCB concentration than PCB 118. Conversely, negative factor scores indicate that PCB 118 contributes more to the total. The factor 1 scores tend to decrease with increasing age (Figure 1) indicating that the contributions of PCBs 157, 156, and 169 are higher at younger ages and decrease with age while the contribution of PCB 118 is lower at younger ages and increases with age. There are no apparent differences in factor 1 scores with respect to gender and race.

Factor 2 is characterized by positive loadings for PCBs 105 and 118 (0.0918 – 0.092) and a negative loading for PCB 156 (-0.15). Positive factor 2 scores indicate higher contributions of PCBs 105 and 118 while negative factor 2 scores indicate higher contributions of PCB 156. There is no apparent relationship between this factor and age (Figure 1). However, it appears that males are more likely than females to have negative factor 2 scores. This indicates that males may generally have higher contributions of PCB 156 and lower contributions of PCBs 105 and 118 compared to females (Figure 1). Similar to factor 1, there is no apparent relationship with respect to race.

Figure 2 presents the factor scores plot for factor 1 versus 2. Based on this figure, a shift in the factor 1 and 2 scores occurs based on age. Participants from the youngest age category have factor 1 and 2 scores that lay on a line bounded by factor 1 scores from -0.5 to 1.5 and factor 2 scores from 0 to 1 (Figure 3). As age increases by category, the factor scores shift about 60 degrees so that the factor 1 scores for most participants of the > 60 years age category are less than zero. This indicates that the contributions of PCBs 157, 167, 169, and 105 are predominant for the youngest NHANES participants, and as age increases the contribution of PCB 118 begins to dominate the congener profile of the NHANES participants.

In summary, this analysis shows that there are apparent differences in the dioxin-like PCB congener profiles with respect to age and gender and no differences with respect to race. Because of these differences, any

comparisons of the NHANES participants' congener profiles to a potentially exposed population need to account for the age and gender differences. This similar to what was observed when the PCDD/F data for the 2001/2002 NHANES participants were evaluated[11].

References

1. Ferriby LL, Knutsen JS, Harris M, Unice KM, Scott P, Nony P, Haws LC, Paustenbach D. *J Expo Sci Environ Epidemiol* 2006; online July 5.
2. van den Berg M, Birnbaum L, Denison M, DeVito M, Farland W, Feeley 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 RE. 2006. *Toxicol Sci*. 93(2):223-241
3. Manly, BF. *Multivariate Statistical Methods – a primer, 2nd edition*. Chapman & Hall, 1994, pgs 76-92.
4. Hsu JF, Guo YL, Yang SY, Liao PC. *Chemosphere* 2005, 61:1231-1243.
5. Lee CC, Chen HL, Su HJ, Guo YL, Liao PC. *Chemosphere*, 2005. 59:1465-1474.
6. Lee CC, Guo YL, Kuei CH, Chang HY, Hsu JF, Wang ST, Liao PC. *Chemosphere*, 2006, 65:436-448.
7. Orloff KG, Hewitt D, Metcalf S, Kathman S, Lewin M, Turner W. *J Expo Anal Environ Epidemiol.*, 2001,11:352-358.
8. Hedgemann E, Chang SC, Towey T, Demond A, Adriaens P, Chen Q, Franzblau A, Gillespie BW, Sima C, Garabrant D. *Organohalogen Compounds*, 2006.
9. Shields WJ, Tondeur Y, Benton L, Edwards MR. In: *Environmental Forensics, Contaminant Specific Guide*, Morrison RD, Murphy BL ed., Elsevier, Boston, 2006: 293-312.
10. Wenning R, Paustenbach D, Johnson G, Ehrlich R, Harris M, Bedbury H. *Chemosphere* 1993, 27:55-64.
11. Scott P, Haws L, Scott L, Harris M. *Organohalogen Cmpds.* 2007.

Figure 1. Factor scores with age and gender

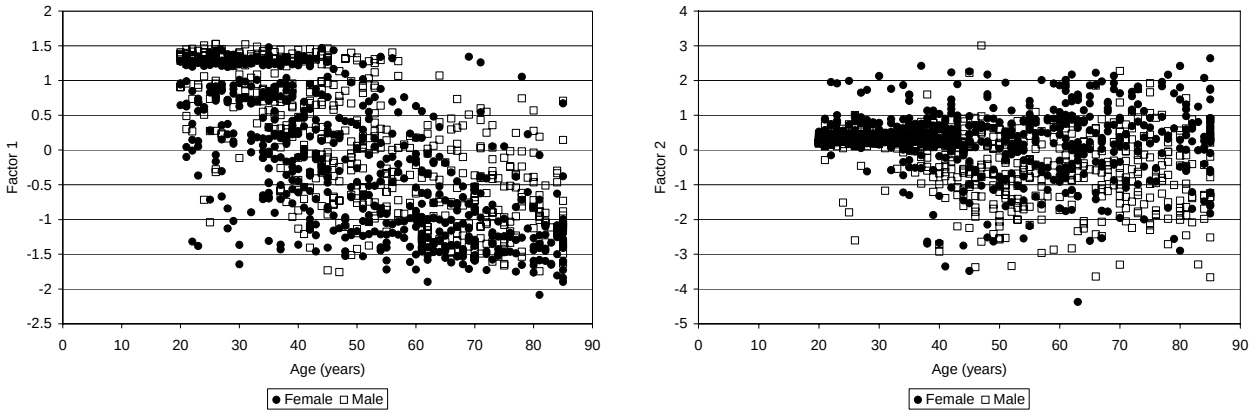

Figure 2. Factor Score Plot of Factors 1 vs 2.

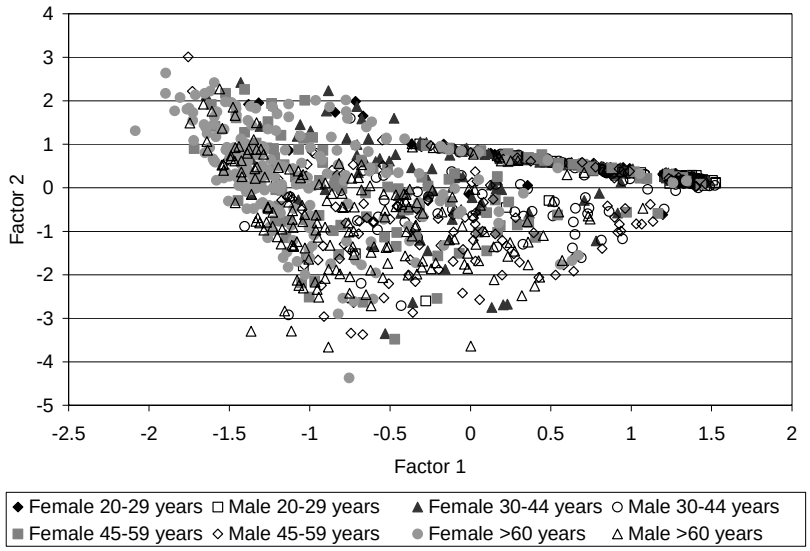

Figure 3. Factor Score Plot of Factors 1 vs 2 by age group.