

A FOLLOW-UP INVESTIGATION OF HIGH SERUM OUTLIERS FROM THE UNIVERSITY OF MICHIGAN DIOXIN EXPOSURE STUDY

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Keywords: Humans, Environmental samples, Dietary intake, Blood, North America, PCBs, PCDD/PCDF, TEQs

Introduction and Study Goals

The University of Michigan Dioxin Exposure Study (UMDES) has collected information based on questionnaires and samples of blood, soil and/or house dust from over 1,300 randomly selected subjects in Midland, Saginaw, Bay, Jackson and Calhoun counties. A full description of the study, all protocols, and results can be found at the study web site: www.umdioxin.org. A primary goal of the study is to determine whether dioxins, furans and polychlorinated biphenyls (hereinafter collectively referred to as 'dioxins') in soil and/or house dust are related to or explain serum levels of these contaminants, with adjustment for other known risk factors (i.e., diet, occupation, age, body mass index, etc.). More generally, the study seeks to understand sources of variation in the observed serum and environmental measurements. Not surprisingly, the distributions of results (serum, house dust, and soil) are skewed, with a small number of high toxic equivalency (TEQ) values. While some of these high values are not unexpected (e.g., a high TEQ in soil sampled from the flood plain of the Tittabawassee River), others appear to be outliers, with no clear or obvious explanation based on a review of other lab tests or information obtained from the structured interview/questionnaire. This study seeks to better understand serum outlier values, and is intended as an exploratory investigation to generate hypotheses as to why some UMDES subjects have unusually high levels of dioxins in their serum. Separate studies are underway to investigate outlier results for soil and house dust, and those results will be reported separately.

Methods

To be eligible for this follow-up study, a person must have been a participant in the UMDES. They must have completed an initial interview and provided a blood sample for analysis, and the serum results must have been an outlier, as defined below. We only sought to re-interview subjects for this follow-up study who requested and received their previous laboratory test results (i.e., if a subject had a serum result that met the criterion to be an outlier, but he chose to not receive his serum results, then we did not seek to re-interview this person for the follow-up study). Subjects from all geographic areas included in the UMDES were eligible for this outlier study (i.e., all five counties – Midland, Saginaw, Bay, Jackson and Calhoun counties). Nine hundred and forty-six subjects completed initial interviews and also provided blood samples.

It is well known that serum dioxin levels are, in part, a function of age and body mass index (BMI).¹ For this investigation an outlier is defined as a subject with a total serum TEQ that is more than 2.5 studentized residuals above the mean of the log-transformed total serum TEQ results after adjustment for age and BMI. Adjusting the serum TEQ for age and BMI provides a better mechanism for identifying true outliers. This study only focuses on statistically defined outliers at the high end of the distribution, and not those at the low end. The distribution of serum TEQ results is highly skewed (approximately log-normal) and an 'outlier' from the low end of the distribution would only differ from an 'average' value by a small absolute amount (in the original, untransformed scale). Given

the small absolute differences involved, it was considered unlikely that much could be learned from pursuing such cases. The current definition of 'outlier' is based solely on total TEQ in serum and does not consider congener-specific results, or other factors. Other possible definitions for outliers may be considered in a later study.

Subjects eligible to be re-interviewed were contacted by telephone and asked to participate in the outlier study. If they agreed, then a face-to-face interview was scheduled. The follow-up interview was semi-structured, and included topics that were covered in the original questionnaire (e.g., questions about residential history, occupational history, recreational activities (e.g., fishing and hunting, gardening and spraying pesticides), pregnancy history (for women only), basic demographic information, and diet – the full original questionnaire is posted on the study web site: www.umdioxin.org). Follow-up interviews also included open-ended questions that sought more information about these topics, and also other topics that may potentially impact the levels of dioxins in serum, but were not covered in the original questionnaire. For example, we asked about hobbies or other activities performed in the home or on the property by the subject and also by other occupants of the house, details about the construction of the home or other structures on the property, whether the house had been damaged by fire, fireplaces or other burning activities (e.g., trash burning), and whether fill dirt or other materials may have been deposited on the property. Subjects were also asked for their opinions as to why their serum dioxin levels might be high. Given the long half lives of most dioxin-like compounds in humans², the low limits of detection achieved for serum measurements in this study, and the extensive QA/QC that documented excellent reliability of results of serum analyses³, no repeat serum measurements were sought for this follow-up investigation. Participants were paid \$50 as an incentive for participating in the follow-up interview. All aspects of this follow-up study were reviewed and approved by the University of Michigan Institutional Review Board.

Results/Discussion/Conclusions

[Results, discussion and conclusions will be forthcoming at the time of the Dioxin 2006 conference.]

Acknowledgements

The authors acknowledge the Dow Chemical Company for funding the study and Ms. Sharyn Vantine for her continued assistance.

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