The University of Michigan Dioxin Exposure Study: Methods for an Environmental Exposure Study of Polychlorinated Dioxins, Furans, and Biphenyls

David H. Garabrant  
*University of Michigan School of Public Health, dhg@umich.edu*

Alfred Franzblau  
*University of Michigan School of Public Health, afranz@umich.edu*

James Lepkowski  
*University of Michigan - Ann Arbor*

Brenda W. Gillespie  
*University of Michigan School of Public Health*

Peter Adriaens  
*University of Michigan College of Engineering*

See next page for additional authors

Follow this and additional works at: https://digitalcommons.unl.edu/sociologyfacpub

Part of the Sociology Commons

Garabrant, David H.; Franzblau, Alfred; Lepkowski, James; Gillespie, Brenda W.; Adriaens, Peter; Demond, Avery; Ward, Barbara; LaDronka, Kathy; Hedgeman, Elizabeth; Knutson, Kristine; Zwica, Lynn; Olson, Kristen; Towey, Timothy; Chen, Qixuan; and Hong, Biling, "The University of Michigan Dioxin Exposure Study: Methods for an Environmental Exposure Study of Polychlorinated Dioxins, Furans, and Biphenyls" (2009). Sociology Department, Faculty Publications. 133.  
https://digitalcommons.unl.edu/sociologyfacpub/133

This Article is brought to you for free and open access by the Sociology, Department of at DigitalCommons@University of Nebraska - Lincoln. It has been accepted for inclusion in Sociology Department, Faculty Publications by an authorized administrator of DigitalCommons@University of Nebraska - Lincoln.
Authors
David H. Garabrant, Alfred Franzblau, James Lepkowski, Brenda W. Gillespie, Peter Adriaens, Avery Demond, Barbara Ward, Kathy LaDronka, Elizabeth Hedgeman, Kristine Knutson, Lynn Zwica, Kristen Olson, Timothy Towey, Qixuan Chen, and Biling Hong
The University of Michigan Dioxin Exposure Study: Methods for an Environmental Exposure Study of Polychlorinated Dioxins, Furans, and Biphenyls

David H. Garabrant, 1 Alfred Franzblau, 1 James Lepkowski, 2 Brenda W. Gillespie, 3 Peter Adriaens, 4 Avery Demond, 4 Barbara Ward, 2 Kathy LaDronka, 2 Elizabeth Hedgeman, 1 Kristine Knutson, 1 Lynn Zwica, 1 Kristen Olson, 2,5 Timothy Towey, 4 Qixuan Chen, 3 and Biling Hong 1

1Department of Environmental Health Sciences and Risk Science Center, University of Michigan School of Public Health, Ann Arbor, Michigan, USA; 2Survey Research Center, Institute for Social Research, University of Michigan, Ann Arbor, Michigan, USA; 3Department of Biostatistics, University of Michigan School of Public Health, Ann Arbor, Michigan, USA; 4Department of Civil and Environmental Engineering, University of Michigan College of Engineering, Ann Arbor, Michigan, USA; 5Survey Research and Methodology Program, University of Nebraska–Lincoln, Gallup Research Center, Lincoln, Nebraska, USA

BACKGROUND: The University of Michigan Dioxin Exposure Study (UMDES) was undertaken in response to concerns that the discharge of dioxin-like compounds from the Dow Chemical Company facilities in Midland, Michigan, resulted in contamination of soils in the Tittabawassee River floodplain and areas of the city of Midland, leading to an increase in residents’ body burdens of polychlorinated dibenzodioxins and polychlorinated dibenzofurans.

OBJECTIVES: The UMDES is a hypothesis-driven study designed to answer important questions about human exposure to dioxins in the environment of Midland, where the Dow Chemical Company has operated for >100 years, and in neighboring Saginaw, Michigan. In addition, the UMDES includes a referent population from an area of Michigan in which there are no unusual sources of dioxin exposure and from which inferences regarding the general Michigan population can be derived. A central goal of the study is to determine which factors explain variation in serum dioxin levels and to quantify how much variation each factor explains.

CONCLUSIONS: In this article we describe the study design and methods for a large population-based study of dioxin contamination and its relationship to blood dioxin levels. The study collected questionnaire, blood, dust, and soil samples on 731 people. This study provides a foundation for understanding the exposure pathways by which dioxins in soils, sediments, fish and game, and homegrown produce lead to increased body burdens of these compounds.

KEY WORDS: biomonitoring, diet, dioxins, environmental exposure, epidemiology, population-based, serum, soil, survey. Envir Health Perspect 117:803–810 (2009). doi:10.1289/ehp.11777 available via http://dx.doi.org/ [Online 22 December 2008]

The University of Michigan Dioxin Exposure Study (UMDES) was undertaken in response to concerns that the discharge of dioxin-like compounds from the Dow Chemical Company facilities in Midland, Michigan, resulted in contaminated soils in the Tittabawassee River floodplain and areas of the city of Midland, leading to an increase in residents’ body burdens of polychlorinated dibenzodioxins (PCDDs) and polychlorinated dibenzo furans (PCDFs). The Dow Chemical Company has operated in Midland since 1897 and is believed to have caused two major patterns of environmental contamination: a) an aerosol plume from historic incinerators that deposited PCDDs on surficial soils downwind of the plant, principally to the north and northeast in the city of Midland; and b) contamination of the Tittabawassee River downstream of the Dow plant to the southeast with materials from chloralkali operations dating back to the World War I era. In addition, this facility was a major producer of 2,4-dichlorophenoxyacetic acid and 2,4,5-trichlorophenoxyacetic acid during the Vietnam conflict era and has produced a number of products derived from chlorophenols. The contaminant distribution of the Tittabawassee River is currently undergoing extensive mapping, and heavily contaminated areas are being remediated.

The goals of the study focus on assessing the human body burdens of dioxins [the 29 PCDD, PCDF, and polychlorinated biphenyl (PCB) congeners with dioxin-like activity (Van den Berg et al. 1998, 2006)] and the factors that predict those body burdens. Other instances of environmental exposure to dioxins have resulted in increased body burdens of these compounds: residents of Seveso, Italy, who were exposed by a release from a trichlorophenol reactor in 1976 (Bertazzi et al. 2001; Landi et al. 1998); the Ranch Hand cohort (Akhtar et al. 2004) and Vietnamese civilians (Baughman and Meselson 1973; Dwernychuk et al. 2002; Schecter et al. 1986, 2003) exposed to Agent Orange during the Vietnam era; and victims of the Yusho (Masuda 2003; Rappe et al. 1978) and Yucheng (Guo and Yu 2003) rice oil poisoning incidents in 1968 and 1979, respectively. These studies have documented the occurrence of chloracne among heavily exposed subjects and have suggested excess cancer incidence, diabetes, and other endocrine-related health effects. Thus, it is important to document exposure pathways and their relationship to the body burden of dioxins as a prerequisite to the determination of any potential health effects.

In this article, we describe the hypotheses to be tested: the design of the multistage population sampling; the survey instruments used; methods for collection of soil and household dust samples; the analytical methods for measuring dioxins in serum, household dust, and soil; the survey methods used to calculate sample weights; and the methods used for imputing item missing values.

The hypothesis to be tested is whether contamination of the environment by dioxins from the Dow Chemical Company’s operations in Midland, Michigan, is associated with increased body burdens of dioxins among some residents of the surrounding area of Midland, Saginaw, and southwestern Bay counties. For the purposes of this study, we use the term “contamination” to mean the presence of dioxins above background levels in environmental media, where “background” is defined as the concentration that would occur in an area without known point sources of that substance [U.S. Environmental Protection Agency (EPA) 2003]. The study includes populations who live both in and out of the Tittabawassee River floodplain and the plume area downwind of Dow, and who live in a region of Michigan (Jackson and Calhoun counties) that has no known industrial sources of dioxins. By studying
these populations, it is possible to understand whether the serum dioxin levels among people who live in the Tittabawassee River floodplain are different than those among similar people who live in the same region of Michigan out of the floodplain and whether they are different than those among people who live in other parts of Michigan. An additional central goal of the study is to communicate the results and the implications of the results in an effective manner to the study participants and to the population in the Saginaw and Midland region.

A number of studies of PCDDs, PCDFs, and PCBs in human serum lipids (Ferrilby et al. 2007; Lorber 2002; National Center for Environmental Health 2005; Patterson et al. 2004, 2008, 2009; Pinsky and Lorber 1998; U.S. EPA 2003; Wong et al. 2008) show that serum levels have a complex relationship with age, sex, race/ethnicity, birth cohort (and historic period of exposure), and congener half-life. There is a need for additional studies to examine the relationship between environmental media and human blood samples.

**Materials and Methods**

**Schedule.** We began developing the study protocol in the winter of 2004 and completed it in the summer of 2004. Field interviews, blood collection, soil sampling, and household dust collection were conducted in the summer and fall of 2004 and the spring and summer of 2005. All fieldwork ceased during the winter of 2005, when soil samples could not be collected because of frozen ground. Laboratory analyses of blood, soil, and household dust began as samples were collected and were completed in the spring of 2006. Statistical analyses of the data began in fall 2005.

**Sample design and subject selection.** The sample design was a stratified, multistage area probability sample of households and persons. We defined the population as persons residing in Midland and Saginaw counties, Williams Township in Bay County, and Jackson and Calhoun counties, all of whom were >18 years of age, had lived in their current residence continuously for at least 5 years, and currently lived in a residence outside the floodplains of the Shiawassee and Saginaw Rivers in Saginaw County. The sample used a two-stage area probability selection of housing units in the study area, and a third stage of selection of an eligible person within each sample housing unit. The first stage of selection employed stratified cluster sampling methods in which a sample was drawn from a list of all U.S. Census blocks in the study counties.

We divided the list into four groups (Figure 1): a) blocks in Midland and Saginaw and parts of Bay counties that contained any land area in the Federal Emergency Management Administration–defined 100-year floodplain of the Tittabawassee River below the Dow Chemical Company facility in Midland, and above the point where the Tittabawassee and Shiawassee Rivers join and have a mixed floodplain; b) blocks in the area of deposition of emissions stacks at the Dow Chemical Company in Midland, as defined by environmental modeling of the plume of the historical emission data; c) blocks outside of the Tittabawassee floodplain (item a above) or the plume (item b above) and outside the floodplain of the Shiawassee and Saginaw rivers; and d) blocks in Jackson and Calhoun counties (control area for the study).

We defined the aerosol plume by a geostatistical simulation-based method that combined the process-based modeling of atmospheric deposition from an incinerator with the probabilistic modeling of residual variability of field samples. We used the approach to delineate areas with high levels of dioxin around the Dow plant, accounting for 53 field data points and the output of the U.S. EPA Industrial Source Complex (ISC3) dispersion model. We simulated 100 realizations of soil toxic equivalent (TEQ) values on a grid with a 50-m spacing. We used these realizations to identify census blocks (Figure 1) that were predicted to have elevated soil TEQ values (Goovaerts et al. 2008a, 2008b).

We recruited and hired interviewers from Midland and Saginaw counties. They were trained in general interviewing techniques, the specific study protocol and questionnaire, and refusal aversion techniques. Study staff monitored daily data collection progress, which achieved high response rates. Sample households were visited by interviewers multiple times, if necessary, to obtain cooperation. Interviewers also offered a financial incentive totaling $100 if the person participated in the interview and the blood, soil, and household dust sampling.

Each household was screened to determine whether eligible persons lived in the household. If one or more eligible persons lived in the household, we chose one at random to interview. Each respondent eligible for the blood draw was asked to provide a blood sample collected through an in-home visit from a phlebotomist from a local health care facility. If the respondent owned the housing unit, she/he was asked to permit household dust to be collected by vacuuming. We asked respondents who owned the property to permit soil samples to be gathered from around the housing unit (excluding apartments and condominiums).

In fall 2004, the first replicate in Midland and Saginaw counties was available for study. “Replicate” refers to random samples chosen from a target population, in which a first sample is taken and then a replicate sample is taken from the same target population. Replicate sampling is valuable in estimating the variances of parameter estimates. In spring 2005, the second replicate in Midland and Saginaw counties and the entire sample in Jackson and Calhoun (the control) counties were available for study.

Between the fall 2004 and spring 2005 data collection, we converted the survey interview from paper-and-pencil format to
we computed blood value in parts per trillion for the estimates that would be sound estimates for weights in all analyses to compute weighted because the weighted value could be overly each person. Unequal probability of selection weight for adjustment factors and multiplied times the predicted probabilities of cooperation. These models produced pre interested or did not have the time to provide a because not be contacted despite repeated attempts or further adjust nonresponse weights for all samples. We used the inverse of predicted probabilities from each of these models as a nonresponse adjustment weight. We trimmed extremely small predicted probabilities from each of these models to minimize the influence of any single case on the overall estimate, while maintaining as much of the original predictions as possible.

Interviews. Survey questionnaires were developed through a process of writing or adopting questions from other surveys, review by project stakeholders and the scientific advisory board (SAB), and pretesting in a small sample of residents in Midland and Saginaw counties. All eligible adults gave written informed consent and completed a 1-hr standardized interview administered by the Survey Research Center at the University of Michigan. An important component of the questionnaire was an event history calendar (EHC), which collects significant time-varying information using cues from the respondent’s lifetime to assist in recall. The interviewer recorded major life events, such as marriage or childbirth, on the EHC, along with major national and local current events to help respondents anchor when events occurred. The questionnaire consisted of 10 sections, each of which contained lifetime recall questions. The respondent was asked to recall possible dioxin exposure pathways over their entire lifetime in 1-year intervals. Much of the interview was devoted to questions about consumption of fish, game, poultry, dairy, and produce and whether it came from contaminated areas; activities such as hiking, camping, picnicking, and water sports in the contaminated areas; occupational history, particularly work at Dow and in other settings where PCDD, PCDF, or PCB exposure would have occurred.

Nonresponse follow-up study. For a subset of households that were not contacted or for which eligibility was not determined, or for which the selected respondent did not complete the questionnaire, we asked them again to participate in the UMDES. A shortened questionnaire, which collected information on key study variables, was administered to subjects who agreed to participate in this nonresponse follow-up study. We did not collect blood, soil, and household dust samples. These data permitted comparisons of nonrespondents and respondents on key study variables from the questionnaire to assess the degree of nonresponse bias. Nonresponse follow-up activities took place during January and February 2005 and October and November 2005, immediately after the end of main data collection. We constructed nonresponse adjustment weights using response propensity models, which use a logistic regression predicting the likelihood of being a respondent, conditional on being eligible for response. Models were run for each of the following stages of nonresponse: a) contact, given status as an occupied housing unit; b) screening, given initial contact; c) interview, given successful screening and eligibility for the interview; d) giving blood or not, conditional on being eligible to give blood; e) giving dust, conditional on being eligible to give dust; f) giving soil, conditional on being eligible to give soil; and g) giving blood, dust, and soil, conditional on being eligible to give all samples.

We used the same “global” weight for all analyses.

We further adjusted the data to account for missing values for items or missing values for a single variable for an individual who otherwise provided data. Many analysts “ignore” the missing values in a variable by using “case-wise deletion” of missing data features in statistical software. Ignoring the missing values effectively imputes or assigns the mean of the cases without missing values to the value for each case for which the value is missing. In the careful population inference methods being used for the UMDES, we imputed the item missing values in the survey questionnaire, the household dust, and the soil samples. We used a sequential regression imputation procedure (Raghunathan et al. 2001) to replace values for missing items in the UMDES questionnaire data, and used imputed values in estimating various statistics from the survey.

Nonresponse follow-up study. For a subset of households that were not contacted or for which eligibility was not determined, or for which the selected respondent did not complete the questionnaire, we asked them again to participate in the UMDES. A shortened questionnaire, which collected information on key study variables, was administered to subjects who agreed to participate in this nonresponse follow-up study. We did not collect blood, soil, and household dust samples. These data permitted comparisons of nonrespondents and respondents on key study variables from the questionnaire to assess the degree of nonresponse bias. Nonresponse follow-up activities took place during January and February 2005 and October and November 2005, immediately after the end of main data collection. We constructed nonresponse adjustment weights using response propensity models, which use a logistic regression predicting the likelihood of being a respondent, conditional on being eligible for response. Models were run for each of the following stages of nonresponse: a) contact, given status as an occupied housing unit; b) screening, given initial contact; c) interview, given successful screening and eligibility for the interview; d) giving blood or not, conditional on being eligible to give blood; e) giving dust, conditional on being eligible to give dust; f) giving soil, conditional on being eligible to give soil; and g) giving blood, dust, and soil, conditional on being eligible to give all samples.

We used the inverse of predicted probabilities from each of these models as a nonresponse adjustment weight. We trimmed extremely small predicted probabilities from each of these models to minimize the influence of any single case on the overall estimation, while maintaining as much of the original predictions as possible.

Interviews. Survey questionnaires were developed through a process of writing or adopting questions from other surveys, review by project stakeholders and the scientific advisory board (SAB), and pretesting in a small sample of residents in Midland and Saginaw counties. All eligible adults gave written informed consent and completed a 1-hr standardized interview administered by the Survey Research Center at the University of Michigan. An important component of the questionnaire was an event history calendar (EHC), which collects significant time-varying information using cues from the respondent’s lifetime to assist in recall. The interviewer recorded major life events, such as marriage or childbirth, on the EHC, along with major national and local current events to help respondents anchor when events occurred. The questionnaire consisted of 10 sections, each of which contained lifetime recall questions. The respondent was asked to recall possible dioxin exposure pathways over their entire lifetime in 1-year intervals. Much of the interview was devoted to questions about consumption of fish, game, poultry, dairy, and produce and whether it came from contaminated areas; activities such as hiking, camping, picnicking, and water sports in the contaminated areas; occupational history, particularly work at Dow and in other settings where PCDD, PCDF, or PCB exposure would have been likely; and residential history. All questions included the historic periods when the activities occurred. The complete interview questionnaire is available on the UMDES website (University of Michigan 2008).

Confidentiality procedures and protection of human subjects in research. The study was unusual in that it addressed the potential economic risks to subjects from participation. The Michigan Department of Environmental Quality considers any property with soil levels

Table 1. Cooperation rates for interview, blood, household dust, and soil sampling and final interview response rate, by study area.

| Study area          | Cooperation rate (%) | Interview response rate (%) |
|---------------------|----------------------|-----------------------------|
|                     | Interview | Blood | Dust | Soil |                     |
| Floodplain/near floodplain | 83.7     | 83.9  | 91.0 | 91.3 |                     |
| Other Midland/Saginaw and plume | 82.4     | 73.7  | 90.9 | 93.2 |                     |
| Jackson/Calhoun     | 82.2     | 78.4  | 93.8 | 91.9 |                     |
| Total               | 82.9     | 79.6  | 91.7 | 92.0 | 74.3               |
Table 2. WHO TEFs (1998 and 2005) for humans and UMDES median LODs for blood, dust, and soil samples.

| Congener | TEF | LOD | Serum, lipid adjusted (pg/g-lipid) | Soil (pg/g) | Dust (pg/g) |
|----------|-----|-----|----------------------------------|-------------|-------------|
|          | 1998 | 2005 |                                 |             |             |
| PCDDs    |      |      |                                 |             |             |
| 2,3,7,8-Tetrachlorodibenzo-p-dioxin (PCDD) | 1.0 | 1.0 | 0.5 | 0.2 | 0.5 |
| 1,2,3,7,8-Penta Coryllo (PCDD) | 0.5 | 0.2 | 1.0 | 0.4 | 0.5 |
| 1,2,3,6,7,8-Hexachlorodibenzo-p-dioxin (PCDD) | 0.3 | 0.1 | 2.0 | 0.8 | 2.0 |
| 1,2,3,4,7,8-Hexachlorodibenzo-p-dioxin (PCDD) | 0.3 | 0.1 | 3.0 | 0.9 | 2.0 |
| 1,2,3,6,8,9-Hexachlorodibenzo-p-dioxin (PCDD) | 0.3 | 0.1 | 2.0 | 0.7 | 1.0 |
| 1,2,3,4,6,7,8-Heptachlorodibenzo-p-dioxin (PCDD) | 0.001 | 0.0003 | 2.0 | 0.4 | 2.0 |
| OCDD |      |      |                                 |             |             |
| 1,2,3,7,8-Tetrachlorodibenzofuran (OCDF) | 0.1 | 0.1 | 0.4 | 0.2 | 0.8 |
| 1,2,3,7,8-Penta Coryllo (OCDF) | 0.05 | 0.03 | 0.4 | 0.2 | 1.0 |
| 1,2,3,7,8-Penta Coryllo (OCDF) | 0.5 | 0.3 | 1.0 | 0.5 | 1.2 |
| 1,2,3,6,7,8-Hexachlorodibenzofuran (OCDF) | 0.5 | 0.3 | 1.0 | 0.5 | 1.2 |
| 1,2,3,6,7,8-Hexachlorodibenzofuran (OCDF) | 0.5 | 0.3 | 1.0 | 0.5 | 1.2 |
| 1,2,3,6,8,9-Hexachlorodibenzofuran (OCDF) | 0.5 | 0.3 | 1.0 | 0.5 | 1.2 |
| 1,2,3,4,6,7,8-Heptachlorodibenzofuran (OCDF) | 0.01 | 0.01 | 0.4 | 0.2 | 1.0 |
| OCDF |      |      |                                 |             |             |
| 1,2,3,7,8-Tetrachlorodibenzofuran (OCDF) | 0.001 | 0.0003 | 2.0 | 0.4 | 2.0 |
| 1,2,3,7,8-Penta Coryllo (OCDF) | 0.001 | 0.0003 | 2.0 | 0.4 | 2.0 |
| 1,2,3,7,8-Penta Coryllo (OCDF) | 0.001 | 0.0003 | 2.0 | 0.4 | 2.0 |
| 1,2,3,4,6,7,8-Heptachlorodibenzofuran (OCDF) | 0.001 | 0.0003 | 2.0 | 0.4 | 2.0 |
| 1,2,3,4,5,6,7,8-Octachlorodibenzofuran (OCDF) | 0.001 | 0.0003 | 2.0 | 0.4 | 2.0 |

Table 3 lists dioxin congeners and median limits of detection (LOD) for whole-weight and lipid-adjusted–weight congeners. A total of 946 persons had analyzable blood samples (Table 3).

Household dust sampling and analysis. Dust sampling was conducted in the home of each respondent who had completed the interview and blood draw, after consent of the respondent, if the respondent was an owner of the residence. Participants who did not own the residence (e.g., renters, adult children of owners) did not have legal authority to give...
permission for sampling without the property owner’s consent. In consequence, their dust was not sampled, even though they otherwise participated in the study. All household dust samples were collected using high-volume small-surface samplers (HVSS; CS-3, Inc., Sandpoint, ID). Vacuums were equipped with a cyclone and a fine-particle filter capable of capturing 99.99% of particles > 0.3 μm in mean aerodynamic diameter. One composite sample was collected in each household from sampling locations that presented the highest potential for human contact with dust. Locations were generally a frequently occupied living space (living room or family room) and a high-traffic pathway (front hall, kitchen entryway, or other high traffic hallway). Samples were taken from both hard and soft surfaces, with carpets and area rugs being preferred sampling surfaces. Samples were not taken from undisturbed dust in generally inaccessible areas because there was no way to tell when such samples became contaminated or whether there had been any exposure by the participants. The sampling protocol was based, with minor modifications, on the American Society for Testing and Materials (ASTM) D 5438-00 method (ASTM 2000). The sampling technicians attempted to collect a minimum of 10 g total dust.

The sampling technician recorded the total surface area of the sampling area (typically 1–2 m²) on a preprinted field data sheet, as well as the surface types where the sample was taken. Technicians transported samples on ice in a dedicated 4°C cooler until delivery to Vista Analytical Laboratory for analysis of the World Health Organization (WHO) 29 PCDD, PCDF, and PCB congeners using internal modifications of U.S. EPA method 8290 (U.S. EPA 1994) and method 1668 (U.S. EPA 1999), and using the laboratory methods described above for serum samples. LODs were between 1 and 8 pg/g for all PCDD, PCDF, and PCB congeners except octachlorinated dibenzo-furan (OctaCDF), PCB-114, PCB-123, and PCB-167, for which the LODs were between 20 and 40 pg/g (Table 2). For household dust, dioxin concentrations < LOD, we assigned a value equal to the LOD divided by the square root of 2 (LOD/√2). We sampled a total of 764 residences for household dust (Table 3).

**Soil sampling and analysis.** Soil sampling was conducted at the residence of each respondent who had completed the interview and blood draw after giving consent, if the respondent was an owner of the residence. Participants who did not own the property (e.g., renters, condominium owners, and adult children of owners) did not have legal authority to give permission for sampling without the property owner’s consent. In consequence, their soil was not sampled, even though they otherwise participated in the study. Each property was sampled in multiple locations by a sampling technician using a push core sampler to collect a core of soil from the surface to a depth of 6 in. (15 cm). Surface vegetation at the site of the core was also collected except in situations where garden plants might be damaged. For selection of locations for sampling, technicians followed a protocol that identified the house perimeter, property areas where skin contact was likely (e.g., gardens), and areas in or near the floodplain of the Tittabawassee River. The sampling protocol is portrayed schematically in Figure 2.

Up to four sampling stations were located around the perimeter of the house (areas covered by pavement, cement, or gravel were not sampled). We determined locations where activities occurred that were likely to result in skin contact with soil from the interview responses. If the respondent worked in a flower garden, it was sampled. If there was a vegetable garden, it was sampled regardless of whether the participant worked in it, based on the assumption that the homegrown vegetables were consumed by all members of the household. Up to two gardens (soil contact areas) were sampled. For residences located in the floodplain, one additional station at the lowest, safely accessible location on the respondent’s property in the floodplain was sampled, referred to as the near-river sample. Thus, each residence had a maximum of seven sampling stations (four house perimeter samples, two soil contact samples, and one near-river sample).

Each sampling station was defined by laying out a 3-foot-diameter sampling ring, and three equally spaced cores were collected within the ring. All sample location coordinates were established using global positioning system procedures, for mapping purposes, and to relocate sample sites, if necessary. Technicians stored all sealed sample cores on ice (4°C) before transport to the University of Michigan Environmental and Water Resources Engineering laboratories, where they were extruded, separated into strata by depth, and composited across cores. Samples were stratified so that the top 0–1 in. (0–2.5 cm) could be examined separately from the 1–6 in. (2.5–15 cm) sample because surficial deposition of aerosols would be expected to affect only the top 1–2 cm of soil, whereas contamination from other pathways (e.g., fluvial deposition in the river floodplain) would be expected to affect deeper soil. Ultimately, each residence yielded the following analytical samples: house perimeter set 0–1 in. (0–2.5 cm) depth composite; house perimeter set 1–6 in. (2.5–15 cm) depth composite; and house perimeter set surface vegetation composite.

If there was a soil contact set, the residence yielded two additional samples: a) soil contact set 0–6 in. (0–15 cm) composite (we did not sample the top 1 in. (2.5 cm) separately because garden soil is routinely turned over, soil additives and mulch are routinely

### Table 3. Number of participants, by region.

| Sample type        | Floodplain | Near floodplain | Midland plume | Other Midland/Saginaw | Jackson/Calhoun | Total across all areas |
|--------------------|------------|-----------------|---------------|------------------------|-----------------|------------------------|
| Interviews         | 326        | 264             | 71            | 304                    | 359             | 1,224                  |
| Blood              | 251        | 197             | 48            | 199                    | 251             | 946                    |
| Household dust     | 207        | 159             | 37            | 163                    | 198             | 764                    |
| Soil               | 203        | 164             | 37            | 168                    | 194             | 766                    |
| Interviews, blood, dust, and soil | 195 | 156 | 35 | 162 | 183 | 731 |

### Figure 2. Schematic location of soil samples from each participants’ property and stratification of soil samples indicating three soil samples taken within each ring.

- **House perimeter**
- **Soil contact**
  - Vegetable garden
  - Flower garden
- **Near river** (if the property was in the Tittabawassee River floodplain)

**Dioxin exposure study methods**

Environmental Health Perspectives • VOLUME 117 | NUMBER 5 | May 2009

807
incorporated into the soil, and spring planting and pulling of plants in the fall routinely disturb the soil strata. Moreover, root vegetables such as carrots do not grow just in the top 1 in.; and b) soil contact set surface vegetation composite (if available). In addition, residences in the Tittabawassee River floodplain yielded the following samples: near-river set 0–1 in. (0–2.5 cm) depth composite; near-river set 1–6 in. (2.5–15 cm) depth composite; and near-river set surface vegetation composite.

A total of 766 residences were sampled in the five counties in Michigan from October through December 2004 and from March through September 2005. A total of 2,081 samples were analyzed for the 29 dioxin, furan, and PCB congeners (Table 2) by Varta Analytical Laboratory using internal modifications of U.S. EPA methods 8290 (U.S. EPA 1994) and 1668 (U.S. EPA 1999) as described above for serum samples. LODs were substantially < 1 pg/g for all PCDD, PCDF, and PCB congeners except PCB-167 (LOD = 3 pg/g; Table 2). We assigned soil dioxin concentrations that were less than the LOD a value of LOD/√2.

All of the 0–1 in. (0–2.5 cm) house perimeter composite samples were analyzed. If any part of the property was in the floodplain, then we also analyzed all remaining composites (1–6 in. and vegetation house perimeter; 0–1 in., 1–6 in., and vegetation floodplain; and 0–6 in. and vegetation soil contact). If the respondent did not live in the floodplain but had a vegetable garden or worked in a flower garden, we analyzed the 0–6 in. and vegetation composites for the soil contact set. If the TEQ of the 0–1 in. house perimeter composite for any property outside the floodplain was > 8 pg/g, then we analyzed the 1–6 in. and vegetation house perimeter composites. The trigger value of 8 pg/g TEQ represents the 75th percentile of the background distribution for the lower peninsula of Michigan (i.e., we expected 25% of soil samples to be > 8 pg/g).

Stakeholder involvement. Stakeholders, which we defined as entities that had a direct interest and that were actively involved in the dioxin issue in Midland/Saginaw [including the Michigan Department of Community Health; Michigan Department of Environmental Quality; Midland, Saginaw, and Bay county health departments; environmental groups (Lone Tree Council and Ecology Center); the Dow Chemical Company; and the Agency for Toxic Substances and Disease Registry (ATSDR)] played a key role in the development of the study protocol. We held numerous face-to-face and telephone meetings with stakeholders to review the study goals, objectives, and draft protocol. Stakeholders submitted multiple sets of written comments, and the study team provided written responses that were posted on the UMDES website (University of Michigan 2008). The process of stakeholder involvement resulted in major modifications to the study protocol, including: a) important changes to the questionnaire; b) addition of the Midland plume area as a separate study group; and c) addition of Jackson and Calhoun counties as control areas. Stakeholders did not participate in the selection of the study participants, sample collection, or laboratory or statistical analyses. Stakeholders were invited to all SAB meetings, and they had opportunities to discuss the study design, conduct, and analysis with the investigators and privately with the SAB. We treated the Dow Chemical Company in the same manner as all other stakeholders.

The SAB. We reported to an independent SAB made up of four scientists who were nominated by the stakeholders and appointed by the University of Michigan, with membership based on independence, qualifications in research relevant to dioxin issues, and scientific stature. Neither Dow nor any other stakeholder played any role in the selection of the SAB members. The members of the SAB are listed in the acknowledgments; their affiliations are posted on the UMDES website (University of Michigan 2008). The SAB oversaw all aspects of the study conduct, including a) reviewing and commenting on the draft study design; b) convening in person in Michigan twice yearly for 1–2 days each time to meet with the investigators, representatives of the Michigan Department of Community Health and other health officials, representatives of the community advisory panel (CAP), and stakeholders; c) monitoring the conduct of the UMDES; d) providing feedback to the investigators regarding the conduct of the UMDES; and e) reviewing and commenting on draft reports and manuscripts before they were released to the public and scientific community.

Role of the Dow Chemical Company. Funding for this research was available through an unrestricted grant from the Dow Chemical Company to the University of Michigan. We gave Dow periodic accounting reports to assure Dow that funds were properly spent on study activities. We reported research progress and results to Dow only in public settings at the SAB–stakeholder meetings, open scientific conferences, and meetings with county, state, and federal agencies and in public meetings in the Midland/Saginaw area. Dow played no role in the study design, data collection, data analysis, or data interpretation beyond providing written comments that the investigators posted to the UMDES website (University of Michigan 2008).

Communications plan and CAPs. Because potential exposures to environmental toxicants such as dioxins are a public health concern, residents and public health professionals in the Tittabawassee River area had a great interest in the design and execution of this study. The research team was committed to proactive community engagement in the design and implementation of the study. The research team’s community outreach efforts had three key areas:

• We conducted research and focus groups to clarify the concerns of the community. We identified key community leaders, including elected officials, school superintendents, clergy, members of the news media, and heads of nonprofit organizations, whom we selected for interviews. These investigations allowed identification of areas that could be addressed by the study team and helped to guide interactions with the community.

• We formed two CAPs (one for Midland/Saginaw/Bay counties and one for Jackson/Calhoun counties) with membership based on independence, representation of community groups, and stature and respect in the community. We solicited nominees during focus groups and key-person interviews. The CAPs provided feedback to us regarding the concerns of the community, and they helped to inform the community about the conduct and progress of the study. The memberships of the CAPs are posted on the UMDES website (University of Michigan 2008).

• We developed a broad outreach/educational campaign to describe the efforts of the research team and to provide critical information to the public. The campaign involved media resources at the University of Michigan and in the communities, website development, area physicians, elected officials, public health officials, key community leaders, and regular, open meetings with the public. The outreach/educational campaign included descriptions of the research study, periodic updates on study progress, findings from the study as they became available for release, and interpretations of the findings [examples are available on the UMDES website (University of Michigan 2008)]. We conducted research to determine how best to communicate results that are relevant to the community’s needs and concerns. Individual participants were sent the results of their tests (measurements of serum, household dust, and soil) by mail, if they wished to receive them. We disseminated a 41-page booklet with a lay summary of results to the study participants and to the general public. Aggregate data are being presented in scientific reports that are posted to the UMDES website (University of Michigan 2008) after peer-review by the SAB.

Results and Discussion

This study has a number of unique features. First, informed consent for taking soil and household dust samples included discussion of
the potential economic risks to subjects from participation in the research. Recent publica-
tions have highlighted the importance of this issue (Brody et al. 2007). This is a complex
issue that other researchers need to consider and that we discussed at length with our insti-
tutional review board and with legal counsel for the University of Michigan. An adult may
give consent to be interviewed and provide a blood sample without consideration of other
parties’ rights. However, taking household dust and soil samples must include consideration of
who actually owns the sample. If a subject lives in a condominium, for example, the subject
owns the structure but does not own the land on which the building is located and therefore
does not have an unbridged right to give a soil sample. The consent of the property owner
should also be obtained, particularly where the value of the property may be adversely affected
by finding contaminants in the soil. Obtaining consent of the property owner would have
revealed that the subject was a participant in the study, which would necessarily have vio-
lated the confidentiality of the participant; for this reason we did not perform soil sampling
unless the participant owned the land.

We considered household dust to be the property of the participant, provided that the participant
owned the structure (e.g., a house or condominium), whether or not the participant
owned the land. In these instances, we asked the participant to consent to household dust
sampling. In instances where the participant was the adult child (or other relative) of and
lived with the property owner, we did not take soil or dust samples. Again, this would
have violated the confidentiality of the participant.

Almost all of the participants (> 98%) asked to receive the results of their blood
dioxin analyses. In contrast, only 64% asked to receive their soil results. We believe this lower
number reflected the potential economic risks to participants from knowing the contami-
nation levels on their properties. Protection of the study participants included protection
from economic risk consequent to their know-
ing the dust and soil results from their prop-
cer. By not receiving their results, they could participate in the study yet be no different in
terms of risk than nonparticipants.

Our participation rates were high, even in the control areas (Jackson/Calhoun coun-
ties); in fact, these rates were higher than we anticipated when we planned the study. We
believe this was due to the intense concern in the contaminated area regarding the risks of
dioxin pollution and the widespread desire of the general public to participate in charac-
terizing these risks and in taking appropriate actions to reduce risks. Communications with
the affected population were a central part of this study and have been ongoing since the
study planning began. Including the affected population in the study design, keeping them
updated on study progress, and reporting the results in public meetings in a timely manner
have led to widespread acceptance of the findings as providing a factual basis for addressing
the dioxin pollution.

We based our laboratory analyses on large samples of serum (~ 25 mL), household dust
(10 g), and soil (10 g), which allowed us to achieve low LODs for all PCDDs, PCDFs, and
PCB congeners. For the PCDD and PCDF congeners of greatest concern, we achieved low
LODs, and few samples had unmea-
ured levels. This allowed us to make impor-
tant inferences about the dioxin levels in the
blood in the referent population, as well as to
characterize the full range of the distribution
for each congener in blood, household dust,
and soil. Comparisons of mean and median
values across populations, and inferences about differences in these measures between
population groups, are greatly improved when they are based on measurements rather
than assumptions about values < LOD. Our
LODs for serum were substantially less than
those reported for the National Health and
Nutrition Examination Survey (NHANES)
2001–2002 data (Patterson et al. 2008)
primarily because we had larger serum samples
for analysis that comparable to those reported
for the NHANES 2003–2004 data for most
congeners (Patterson et al. 2009).

In this study we collected complete ques-
tionnaire, blood, dust, and soil samples on
731 people (Table 3) of the 1,324 who com-
pleted the questionnaire and the 946 who gave
good blood samples. We are not aware of any popu-
lation-based studies that have included this
large a sample of participants with concurrent
blood, household dust, and soil measurements of
dioxins and interview data about past expo-
sure and activities in the contaminated area.
Although we did not include measurements of the dioxin content of fish, game, or pro-
duce from the contaminated areas, we are
conducting other research that will character-
ize these samples. Moreover, questionnaire
information about past consumption of these
foods is essential in determining whether they
are associated with increased serum levels.
The insights to be gained from this study will
provide a strong foundation for understand-
ing the exposure pathways by which diox-
ins in soils, sediments, fish and game, and
homegrown produce lead to increased body
burdens of these compounds, especially in
settings where there has been extensive and
prolonged environmental contamination.

An important concern is often raised in the
investigation of industrial contamination sites,
as illustrated by this study. On the one hand,
high-quality, expensive research is needed to
identify the extent of the contamination and
the impact on the human population, which
should be paid for by the entities that cre-
ated the pollution. On the other hand, there
is often concern in the affected communities
that research paid for by the industry will not fairly
address the issues. In the present instance,
there are also concerns in the affected com-
munities that neither the government agen-
cies nor the environmental groups will fairly
address the issues. We set up our study to
provide a credible method by which community
concerns could be addressed, and to that end
we sought extensive community input and
participation, rigorously protected the confi-
dentiality of our participants, set up an inde-
pendent advisory board to which we reported,
and had no reporting relationship to Dow, kept
our methods and results transparent, and built
an extensive communications program. These
methods have resolved a myriad of practical
problems and are applicable across a broad
range of settings.

REFERENCES

Ahtkar FZ, Garabrant DH, Ketchum NS, Michalek JE. 2004.
Cancer in US Air Force Veterans of the Vietnam War.
J Occup Environ Med 46:123–136.

American Association for Public Opinion Research. 2006.
Standard Definitions: Final Dispositions of Case Codes and
Outcome Rates for Surveys. 4th ed. Lenexa, KS:American
Association for Public Opinion Research.

Altman DG. 2000. Standard Practice for Collection of Floor Dust
for Chemical Analysis. ASTM D5438-00. West Conshohocken,
PA:American Society for Testing and Materials.

Baughman RW, Meselson M. 1973. An analytical method for
detecting TCDD (dioxin) levels of TCDD in samples from
Vietnam. Environ Health Perspect 5:27–35.

Bertazzi PA, Consonni D, Bachietti S, Rubagotti M, Baccarrelli A,
Zoccheti C, et al. 2001. Health effects of dioxin exposure:
a 26-year mortality study. Am J Epidemiol 153:1031–1044.

Brody JG, Morella-Frosch R, Brown P, Rudel RA, Altman RG,
Frye M, et al. 2007. Improving disclosure and consent: “is it
safe?”: new ethics for reporting personal exposures to
environmental chemicals. Am J Public Health 97:1547–1554.

Dwernychuk LW, Cau HB, Hatfield CT, Bovo TG, Hung TM,
Dung PT, et al. 2002. Dioxin reservoirs in southern Vietnam—
a legacy of Agent Orange. Chemosphere 47:117–137.

Ferryl LL, Knutsen JS, Harris M, Unice KM, Scott P, Nony P,
et al. 2007. Evaluation of PCB serum concentration data from
the 2001–2002 National Health and Nutrition Examination
Survey of the United States population. J Expo Sci Environ
Epidemiol 17:356–371.

Govaerts P, Trinh HT, Dandam AH, Tewey T, Chang S-C,
Gwinn D, et al. 2008a. Geostatistical modeling of the spatial
distribution of soil dioxin in the vicinity of an incinerator. 1. Theor-
y and application to Midland, Michigan. Environ Sci Technol
42(10):3648–3654.

Govaerts P, Trinh HT, Dandam AH, Tewey T, Chang S-C,
Gwinn D, et al. 2008b. Geostatistical modeling of the spa-
tial distribution of soil dioxin in the vicinity of an incin-
erator. 2. Verification and calibration study. Environ Sci
Technol 42(10):3655–3661.

Guo YL, Yu M-L. 2003. The Yucheng rice oil poisoning incident.
In: Dioxins and Health (Schecter A, Gasiewicz TA, eds).
Hoboken, NJ:Wiley Interscience, 893–919.

Kish L. 1965. Survey Sampling. New York: John Wiley & Sons.

Landi MT, Consonni D, Patterson DD, Needham LL, Lucier G,
Kish L. 1965. Survey Sampling. New York:Wiley Interscience,
893–919.

Kish L. 1965. Survey Sampling. New York: John Wiley & Sons.

Lambi MT, Consonni D, Patterson DD, Needham LL, Lucier G,
Kish L. 1965. Survey Sampling. New York:Wiley Interscience,
893–919.

Landi MT, Consonni D, Patterson DD, Needham LL, Lucier G,
Kish L. 1965. Survey Sampling. New York:Wiley Interscience,
893–919.

Lambi MT, Consonni D, Patterson DD, Needham LL, Lucier G,
Kish L. 1965. Survey Sampling. New York:Wiley Interscience,
893–919.

Lambi MT, Consonni D, Patterson DD, Needham LL, Lucier G,
Kish L. 1965. Survey Sampling. New York:Wiley Interscience,
893–919.
