Health Consultation

FOLLOW-UP EXPOSURE INVESTIGATION

CALCASIEU ESTUARY

(a/k/a MOSSVILLE)

LAKE CHARLES, CALCASIEU PARISH, LOUISIANA

EPA FACILITY ID: LA0002368173

MARCH 13, 2006

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Agency for Toxic Substances and Disease Registry
Division of Health Assessment and Consultation
Atlanta, Georgia 30333

Health Consultation: A Note of Explanation

An ATSDR health consultation is a verbal or written response from ATSDR to a specific request for information about health risks related to a specific site, a chemical release, or the presence of hazardous material. In order to prevent or mitigate exposures, a consultation may lead to specific actions, such as restricting use of or replacing water supplies; intensifying environmental sampling; restricting site access; or removing the contaminated material.

In addition, consultations may recommend additional public health actions, such as conducting health surveillance activities to evaluate exposure or trends in adverse health outcomes; conducting biological indicators of exposure studies to assess exposure; and providing health education for health care providers and community members. This concludes the health consultation process for this site, unless additional information is obtained by ATSDR which, in the Agency's opinion, indicates a need to revise or append the conclusions previously issued.

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Executive Summary

The Agency for Toxic Substances and Disease Registry (ATSDR) conducted a follow-up exposure investigation in Calcasieu Parish, Louisiana to evaluate blood dioxin concentration changes in residents. Participants in this follow-up investigation were involved in previous blood dioxin sampling projects. The purpose of this investigation was to 1) determine whether participants had ongoing, elevated dioxin exposures since their initial testing, and 2) evaluate potential current environmental sources of dioxin exposure.

Two groups from Calcasieu Parish previously participated in dioxin blood sampling projects. The first set of participants comprised 11 community members whose testing was conducted in 1997 and funded by a Lake Charles law firm. The second group of participants was involved in ATSDR's 1998 exposure investigation. For this follow-up investigation, ATSDR was able to contact 22 community members who previously participated in one of the blood dioxin sampling projects and offered to resample their blood for dioxin to determine concentration changes since their initial testing. Of the 22 participants in the follow-up exposure investigation, 5 were originally part of the 1997 sampling project while the other 17 were previously sampled during ATSDR's 1998 exposure investigation.

Blood dioxin results from the 22 participants were compared to multiple population-based reference groups. The purpose of this comparison was to evaluate participants' results against background blood dioxin concentrations in the U.S. general population. Using these comparisons, most of the older participants in the follow-up exposure investigation had higher-than-expected blood dioxin concentrations. Still, the few participants who were younger than 45 years of age at the time of blood sampling had dioxin concentrations consistent with general population levels.

Analyses of the changes in blood dioxin levels between the initial and follow-up sampling events provided mixed results. The average total blood dioxin concentration for the group had a statistically significant decrease and the average dioxin toxicity had a small, insignificant decrease. While most participants had decreased total dioxin concentrations and dioxin toxicity levels in their blood in the follow-up sampling, based on both of these measures some participants did increase. Excluding, however, two elderly individuals, participants with increased dioxin concentrations or dioxin toxicity levels had very small proportional changes.

This follow-up exposure investigation also included environmental sampling at participants' residences to better determine whether elevated sources of dioxin were present in and around their homes. Potential exposure to environmental dioxin sources was evaluated using limited sampling of soil in participants' yards, indoor house dust, private well water, homegrown fruits and vegetables, and locally caught fish. Environmental sampling results were normal for all environmental media except for locally caught fish. Many of the fish samples exceeded the Food and Drug Administration's action level. That said, however, most of the fish exceeding the action level were caught from water bodies with fishing advisories currently in place.

ATSDR conducted extensive statistical analyses of biological and environmental sampling results and reviewed questionnaire data obtained from participants. The analyses tested for correlations between dioxin concentrations in blood, environmental samples, and demographic or exposure characteristics reported by participants. The analyses detected very few consistent correlations. Because environmental sampling in and around participants' homes did not

document any significant sources of dioxin exposure—excluding fish samples—and all participants with elevated levels were 45 years of age or older, ATSDR hypothesizes that the elevated blood dioxin levels in older participants are primarily associated with historical dioxin exposures.

Objective

This Exposure Investigation was conducted for two purposes:

1. to determine whether exposure to dioxin* is ongoing for participants from the 1998 exposure investigation and for community members who had serum dioxin testing conducted in 1997, and
2. to evaluate potential current environmental sources of dioxin exposure.

To assess possible ongoing sources of community exposure to dioxin, various environmental samples were collected and analyzed for dioxin. These samples included fish caught by participants, private well water, surface soil, indoor floor and attic dust, and homegrown fruits, vegetables, and nuts. Interested residents whose blood had been sampled previously were re-sampled to determine how their dioxin levels changed over time.

Background

In 1997, the Region VI U.S. Environmental Protection Agency (EPA) and a community group from Calcasieu Parish, Louisiana requested that the Agency for Toxic Substances and Disease Registry (ATSDR) evaluate dioxin levels reported in 11 human blood samples. Dioxin results from area sediment samples and a composite clam sample were also provided. ATSDR issued a health consultation concluding that blood serum dioxin levels were elevated in many of the blood samples and recommended identification of the dioxin exposure source(s) (ATSDR 1998).

In response to this recommendation, ATSDR conducted an exposure investigation (EI) in the Mossville, LA, community in December 1998. The purpose of this EI was to "determine if there was evidence for increased exposure to dioxins in residents of Mossville" (ATSDR 1999). Sampling conducted in this investigation consisted of blood samples from 28 residents, surface soil samples from three residences, and eggs from chickens raised at the home of one of the participants. All samples were analyzed for dioxin. Most participants had blood serum dioxin levels above the comparison population. Still, the soil and egg samples did not contain dioxin at levels of health concern. Two recommendations documented in the 1998 EI were to 1) evaluate potential pathways for human exposure to dioxin from environmental and dietary sources, and 2) evaluate strategies to assess past exposures to dioxin (ATSDR 1999).

Following the completion of the 1998 EI, community members expressed concern that the source(s) of their dioxin exposures had not yet been identified. In 2001, ATSDR reviewed information from the previous investigations along with environmental sampling data generated by EPA. Using this review, ATSDR developed a follow-up EI to 1) conduct more comprehensive environmental sampling at participants' residences to better determine if sources of dioxin are present in their current home environments, and 2) re-sample participants' blood to evaluate how their dioxin levels are changing over time. The working hypothesis is that, in the absence of elevated dioxin exposures above normal (i.e., background) levels experienced by the general population in industrialized countries, typical human metabolic processes would be expected to decrease dioxin blood levels over time.

The determination of current environmental sources of dioxin is a straightforward procedure and involves the sampling and direct laboratory measurement of this contaminant in various environmental media. Nevertheless, the evaluation of changes in participants' blood levels over time is a more difficult task due to a variety of possible factors. Dioxin is a ubiquitous

contaminant in industrialized parts of the world. Residents of these areas are exposed to low levels of dioxin through diet and contact with environmental contamination in soil, air, and water.

Before conducting this EI, our hypothesis that blood serum dioxin levels should be decreasing included the assumption that participants were not being exposed to dioxin levels above background. But we could not directly calculate the degree to which participants' blood serum dioxin levels were anticipated to decrease due to normal metabolic processes in the absence of those unusual or elevated exposures (i.e., above background levels). Many variables that affect changes in blood serum dioxin levels have been documented in the published literature. These include the initial dioxin concentration, age, individual metabolic variability, the percentage of body fat, and changes in the percentage of body fat, between samplings (Lorber 2002; Michalek et al. 2002; Pinsky and Lorber 1998; Tepper et al. 1997). Therefore, our evaluation of participants' blood serum dioxin levels can determine whether these levels are increasing or decreasing; but due to these many unquantifiable variables, it cannot accurately predict the anticipated degree of change.

"Dioxin," as used in this report, refers to a collection of toxicologically similar compounds, including polychlorinated dibenzo-*p*-dioxins, polychlorinated dibenzofurans, and coplanar polychlorinated biphenyls. The structurally unique forms of these chlorinated aromatic compounds are referred to individually as congeners. Due to the complex naming conventions used to describe congeners, an abbreviated nomenclature was adopted for this report. A key for determining the full name for each congener is found in Table 1.

Methods

Target Population

In September 2001, ATSDR sent letters explaining the follow-up investigation to the 28 participants from the 1998 EI. These letters discussed their previous blood dioxin results and expressed ATSDR's interest in collecting environmental samples around their homes and resampling their blood for dioxin. After disseminating the letters, ATSDR representatives contacted the 1998 EI participants to determine their interest in the follow-up investigation. Seventeen individuals from this group agreed to participate. In this report these individuals are collectively referred to as the "1998 cohort."

ATSDR also attempted to recruit the 11 individuals who had their blood tested for dioxin in 1997. This recruitment process was difficult, given that the identities of all eleven individuals were never revealed to ATSDR. A community member who previously served as a point of contact between these participants and ATSDR agreed to contact these individuals and inform them of ATSDR's follow-up investigation. The community member requested the individuals contact ATSDR if they were interested in participating in the follow-up EI. Five of the 11 original participants contacted ATSDR and agreed to be retested. Of the remaining six original participants, two were deceased and four others declined to participate or had moved to other areas of the country. In this report, these five community members are referred to as the "1997 cohort." These five, together with the 17 individuals from the 1998 cohort, participated in this investigation. ATSDR arranged to meet participants at their homes and conduct the biological and environmental sampling. Initially, these appointments were scheduled for the week of September 17th, 2001. The terrorist attacks of September 11th, 2001, resulted in the rescheduling of sampling to the week of November 26th, 2001.

On November 27th, 2001, ATSDR held a public availability meeting to explain the purpose of the EI and answer any questions or concerns expressed by community members. From November 27th–29th, ATSDR representatives met with participants and collected environmental and biological samples. A licensed phlebotomist accompanied ATSDR to each residence and performed the blood sampling. During these visits ATSDR representatives conducted environmental sampling.

Consent Forms

Before collecting any biological or environmental samples, ATSDR explained the purpose of the EI and answered questions. Each participant in the investigation was required to sign an informed consent form to participate. The consent forms can be found in the EI protocol (Appendix A).

Sampling and Laboratory Analysis

Biological

Biological sampling was restricted to the 1997 and 1998 participants for whom ATSDR had prior congener-specific, blood dioxin data. Because no children were involved in the initial samplings, children were not included in the 2001 follow-up EI. Participants were excluded if they were pregnant or if they had medical conditions such as anemia or bleeding disorders that precluded them from safely donating an 80-milliliter blood sample. The consent of a personal physician was obtained for cases where the medical eligibility of participants was in question.

A licensed phlebotomist collected an 80-milliliter blood sample by venipuncture from most of the participants (95%, 21/22). A 10-millilter blood sample was obtained from one participant due to phlebotomy difficulties. Blood samples were collected in 10-ml glass Vacutainer® tubes. Following collection, blood samples were held at room temperature for 1–2 hours and allowed to clot. The samples were then stored on ice and shipped over night for analysis to the Centers for Disease Control and Prevention's National Center for Environmental Health (NCEH) Laboratory in Atlanta, Georgia.

Serum samples were analyzed for dioxin using gas chromatography/isotope dilution-high resolution mass spectroscopy. These samples were also analyzed for total lipid content so results could be expressed as blood lipid concentrations.

Environmental

Seventeen household environments were tested in this EI. In three cases, more than one EI participant lived in the home. Samples were collected from surface soil in the yard (n=20), indoor dust (n=18), attic dust (n=14), private well water (n=3), garden vegetables (n=3), fruits (n=3), and nuts (n=3). Some participants provided locally caught fish (n=8). Samples were collected as outlined in the EI protocol (Appendix A) and stored on ice. At the end of each sampling day, samples were shipped overnight to the U.S. EPA Environmental Chemistry Laboratory at Stennis Space Center in Bay St. Louis, MS. Water, soil, indoor dust and attic dust samples were analyzed for dioxin using EPA Methods 8082 and 8290. Fish and edible plant material were analyzed using EPA Method 1613 as amended.

Because of the limited volumes of indoor floor surface dust and attic dust collected, samples were not sieved through a 150-μm screen as indicated in the EPA method discussed in the EI protocol (Appendix A). In addition, because the entire dust sample was not weighed prior to

extraction procedures, surface loading of dioxin could not be calculated. Five of the environmental samples—one attic dust sample and four indoor dust samples—failed the laboratory's quality assurance/quality control criteria. In April 2003 ATSDR representatives resampled two of these locations after obtaining permission from the individual participants. The remaining participants chose not to have resampling of these residential environmental media.

Laboratory analytical variability

CDC's National Center for Environmental Health laboratory provided coefficients of variation for individual serum dioxin congeners that ranged from 10.6–21.1 percent. These coefficients of variation were based on analyses of 130 samples. These analyses used several different automated cleanup systems along with samples spiked with a primary internal standard solution. Mean serum congener concentrations for the 130 samples fell within 0.1–0.3 ng/L for most of the dioxin and furan congeners, 0.5–0.6 ng/L for the coplanar PCB congeners, and 5.1 ng/L for the OCDD congener. Standard deviations for dioxin congeners fell between 0.02 and 0.07 ng/L except for OCDD, which had a standard deviation of 0.6 ng/L. Furan congener standard deviations fell between 0.02 and 0.04 ng/L. Coplaner PCB congener standard deviations fell between 0.05 and 0.09 ng/L.

Statistical Analysis

Treatment of Nondetects

Environmental and biological congener-specific sampling data were reported as either quantitative, semi-quantitative, or zero concentration results. For quantitative results, congeners were detected by the analytical equipment, and a specific concentration was reported. Semi-quantitative results were numerical estimates generated for congeners found at levels slightly below the method detection limit but above the instrument's detection limit. In this report, the semi-quantitative (or estimated) results provided by the lab are treated the same as quantitative results. For congeners not detected by the labs (often reported as nondetect), a value of zero was assigned for the concentration. For

- statistical analysis of the data, and
- for comparisons between
  - the 2001 EI biological results,
  - two of the reference populations,
  - the Lafayette Parish regional reference, and
  - the three states' meta-analysis,

national reference-nondetect values were assigned a concentration equal to one-half of the instrument detection limit. The two reference populations relied on similar assignments for nondetect values. Thus using the same assumptions for nondetect values in the 2001 EI biological sampling enabled direct comparisons between the 2001 EI subjects and the two reference populations. In addition, as indicated in the data tables, one-half of the instrument detection limit was used for statistical analyses of the serum results.

Biological

Because dioxin compounds often exist as mixtures, the health risk from exposure is difficult to evaluate. The concept of toxicity equivalent factors (TEFs) was developed to facilitate

comparison of potential human health impacts from dioxin mixtures. A TEF is an estimate of an individual congener's relative toxicity to that of 2378D [Van den Berg et al. 1998]. TEFs are multiplied by each congener's concentration to derive the specific toxicity equivalent quotient (TEQ) for that congener. In a mixture, the total toxicity equivalents quotient (total TEQ) is the sum of individual TEQs and indicates the overall toxicity.

In 1998, the World Health Organization evaluated new scientific data and recommended revised TEFs for some dioxin-like compounds (Van den Berg et al. 1998). Dioxin blood serum samples for the 1997 cohort were originally reported using the older TEF values. For this EI, 1997 blood dioxin TEQ values were recalculated using the new TEFs. This recalculation insured that the 1997 results were directly comparable to the 2001 sampling results.

Serum dioxin results from this investigation were log-normally distributed. Therefore, mean, median, geometric mean, and ranges were calculated. In evaluating the serum dioxin concentration change over time, we used both nonparametric (Wilcoxon signed rank test) analyses on untransformed results, and we used parametric (paired 2-sided t-test) analyses on log-transformed results. These analyses were applied to total concentration and total TEQ as well as to individual congener concentrations and to TEQ data.

Environmental

Dioxin concentrations in surface soil, indoor floor dust, attic dust, and fish were log-normally distributed. Descriptive statistics including TEQ mean, median, geometric mean, and ranges were calculated for these environmental samples. Parametric tests using log-transformed results and nonparametric tests using non-transformed results were used in evaluating congener-specific associations between environmental media and between environmental media and serum. The distribution of dioxin concentrations for homegrown fruit, vegetables, and nuts were approximately normal. Statistically based comparisons between a) environmental and serum data, and b) environmental and food data, could not be conducted because of the small number of fish, vegetable, fruit, and nut samples. Because no dioxin was found in private well water samples, no statistical analyses are available for these results.

Associations between biological and environmental data

Total TEQ and congener specific environmental results were compared to blood serum results to determine any significant associations. If associations were present, this could indicate a source of exposure. Three types of statistical analyses were conducted. Spearman rank correlation and linear regression analyses determined if current blood concentrations were significantly associated with potential environmental sources. These two analyses used 2001 serum dioxin and environmental concentrations. A general linear model (GLM) for repeated measures analysis determined if the log transformed change in serum dioxin was significantly associated with current log transformed environmental results. This analysis used data from both biological samplings as well as environmental data from the 2001 sampling.

Associations between biological and demographic data

GLM for repeated measures, Spearman rank correlation, and linear regression analyses were used to evaluate associations between biological and demographic data. These statistical tests determined if changes in serum dioxin concentrations were significantly associated with participants' age, self-reported weight change, body mass index (BMI), sex, duration of

residence, and fish/crawfish consumption. These tests also determined whether 2001 serum dioxin concentrations were significantly associated with demographic variables.

Associations between environmental and demographic data

Congener-specific concentrations in environmental media were compared to determine if significant associations existed between soil, indoor dust, and attic dust by residence. Because the data were log-normally distributed, Spearman rank correlation and linear regression tests were used in this analysis. The same tests determined if significant associations existed between congener-specific environmental data and selected demographic results, including age of house and duration of residence.

Comparisons to reference groups

No accurate, population-based reference data are available for current blood serum dioxin concentrations in the U.S. population. Nevertheless, that dioxin body burdens in the U.S. population have been decreasing steadily since their peak in the 1960s and 1970s is universally accepted (Aylward and Hays 2002; Lorber 2002). This decrease is correlated with the documented decline in U.S. environmental levels over the same time period (Cleverly et al. 1996; Smith et al. 1992).

Because of the lack of appropriate reference data for the U.S. population, four different serum dioxin data sets were used as comparisons for the follow-up EI: 1) a 1999 meta-analysis of selected groups in three states in the United States; 2) the 2002 ATSDR Division of Health Studies (DHS) Lafayette, Louisiana, comparison population; 3) the 1999-2000 sampling described in the Second National Report on Human Exposure to Environmental Chemicals published by the CDC's NCEH; and 4) the Third National Report on Human Exposure to Environmental Chemicals published by NCEH**.**

In 1999, ATSDR and NCEH developed unpublished comparison values for blood dioxin levels in the U.S. population based on studies conducted between 1995 and 1997 in three states (Orloff 2001; EPA 2000). These comparison values were developed because U.S. blood dioxin levels are decreasing and reference ranges from studies conducted in the 1980s are inappropriate for current evaluations (Aylward and Hays 2002; Lorber 2002). ATSDR used these comparison values in the first Mossville EI report (ATSDR 1999).

In 2002, ATSDR's DHS conducted a statistically based dioxin exposure study in Calcasieu and Lafayette Parish, Louisiana. In this analysis Lafayette Parish was the unexposed or comparison population. The Lafayette comparison group data obtained through the expanded exposure study represents the most current index of regional blood dioxin levels.

In January 2003, NCEH published the Second National Report on Human Exposure to Environmental Chemicals (CDC 2003). This report documented concentrations for over 100 chemicals in participants' blood and was gathered from a statistically based sample of the U.S. population. As part of this project, serum dioxin levels were obtained for approximately 1200 participants during the time period 1999–2000. Due, however, to the limited individual serum volumes, a large number of these were nondetects. Consequently, total TEQ values for the U.S. population were not reported. Also, few congeners were consistently detected in this analysis. Only six congeners were detected in enough individuals to generate 95th percentile values. Therefore, the 2001 EI results were only compared to these six congeners.

In July 2005, NCEH published the Third National Report on Human Exposure to Environmental Chemicals (CDC 2005). Like the Second Report described above, this project documented blood concentrations for many environmental contaminants in a representative sample of the U.S. population. Serum dioxin concentrations were reported for approximately 1200 participants during the time period 2001–2002. A total of 10 congeners were detected in enough individuals to generate 95th percentile values. The 2001 EI results are compared to these 10 congeners.

Congener half-life comparisons

This analysis involved a comparison of paired blood dioxin measurements from the 22 exposure investigation participants. The purpose of this analysis was to determine how a person's dioxin concentrations changed over time. Individual dioxin congeners are eliminated from the body at varying rates. Therefore, three congeners were evaluated individually to determine how their concentrations in the participants changed since the initial sampling. This comparison assumed that participants' current blood serum dioxin concentrations were a result of historic exposures, and no significant exposures contributed to their blood dioxin level since the initial sampling in either 1997 or 1998. All blood serum dioxin results in this analysis were directly comparable, given that they were measured using similar laboratory methodologies and reported on a lipid-adjusted basis.

Residents in this investigation fell into two categories based on the timing of their initial blood sampling. It is important to establish the timing of the initial blood sampling for the two groups—the 1997 and 1998 cohorts—the elapsed time between samplings is required for half-life calculations. In this comparison, expected congener-specific blood dioxin concentrations were estimated for each participant using congener half-life data combined with the elapsed time between sample collections. The expected blood dioxin concentration was then compared to the actual concentration obtained through the biological sampling in the 2001 follow-up EI. Five of the 22 participants—the 1997 cohort—had their initial blood dioxin sampled through an independent community organization on June 17th, 1997. The other 17 participants—the 1998 cohort—were in ATSDR's first EI and had initial blood dioxin samples taken during December 14th–15th, 1998 (ATSDR 1999). All 22 participants provided a second blood dioxin sample during November 27th–29th, 2001. Therefore, the elapsed time between sampling for the 1997 cohort was 4.46 years and for the 1998 cohort was 2.96 years.

Three congeners were selected for this analysis. These congeners were chosen based on three criteria: 1) the length of the reported half-life in the body, 2) the most reliable half-life estimates as documented in the published literature, and 3) the predominant contributor to the mean total TEQ. Specifically, 1234678D was chosen because it had the shortest reported half-life. Congener 2378D was selected because it was the most studied dioxin congener and therefore had the most reliable half-life estimates. Congener 12378D was selected because it contributed the most towards the mean serum total TEQ in the EI population.

In analyzing each participant's congener concentration, a range of reported half-lives was used to generate expected blood dioxin levels. Many factors influence congener specific half-lives, so it was not appropriate to assume that a single reported half-life was applicable to all individuals. Accordingly, to generate high and low estimates for participants' expected congener concentration, the shortest and longest reported half-lives were used for each congener.

Results

Participant Demographics

The 22 participants ranged from 23 to 78 years of age, with a mean of 57.4 years and a median of 60 years. Thirteen males and 9 females participated in the EI, of whom 17 were African-American and 5 were Caucasian. All 5 Caucasian participants were males and were members of the 1997 cohort.

Table 2 provides descriptive characteristics of participants in this exposure investigation. Most participants (77.3%, 17/22) were 45 years of age or older. The majority of participants (86.4%, 19/22) had a body mass index (BMI) at or above 25 kg/m^2, which is considered overweight. All participants lived in Calcasieu Parish for at least 10 years, and most (86.4%, 19/22) lived in Calcasieu Parish for more than 30 years. Many participants reported consuming locally caught fish (59.1%, 13/22) and locally caught crawfish (68.2%, 15/22).

Biological

Tables 3–5 display mean concentrations and mean TEQs for total dioxin and congener-specific 2001 serum sampling results by sex and cohort. Changes in mean concentrations and mean TEQs for total dioxin and congener-specific serum levels between initial and follow-up samplings are presented in table 6. Parametric and nonparametric statistical analyses for significant increases and decreases in congener-specific concentrations and total TEQs between biological sampling events are provided in tables 7–10. Because the sampling data did not follow a normal distribution, the significance of concentration changes was evaluated using both parametric and nonparametric tests. The paired 2-sided t-test was the parametric method used in analyzing log transformed serum results. The nonparametric Wilcoxon sign rank test was used on unadjusted sampling results. Mean congener-specific contributions to total TEQ by sex and cohort are displayed in tables 11–13. The changes in mean congener-specific contributions to total TEQ between initial and follow-up samplings are displayed in table 14.

Concentration

Total concentration

In the 2001 biological sampling, lipid-adjusted serum dioxin concentrations ranged between 258.6–3630.3 parts per trillion (ppt). The mean, median, and geometric mean for dioxin concentrations were 1128.3, 773.3, and 904.3 ppt, respectively. Tables 3–5 contain mean concentrations and concentration ranges by sex. There were differences in total concentration by sex. Serum dioxin concentrations for females ranged from 504.9–2619.6 ppt. The mean, median, and geometric mean dioxin concentrations for females were 1457.1, 1558.7, and 1262.7 ppt, respectively. Dioxin concentrations in males ranged from 258.6–3630.3 ppt. For males, the mean, median, and geometric mean dioxin concentrations were 900.7, 692.8, and 717.7 ppt, respectively. Two dioxin congeners-OCDF and 3344P-were not detected in any biological samples and therefore not reported in the tables or discussed in the report. There were also differences in 2001 serum concentrations by cohort. In 2001, the 1997 cohort had serum dioxin concentrations ranging from 258.6–990.7 ppt with mean, median, and geometric mean serum dioxin concentrations of 697.6, 815.6 and 638.0 ppt. In 2001, the 1998 cohort had dioxin concentrations ranging from 306.2–3630.3 ppt. Mean, median, and geometric mean concentrations for the 1998 cohort were 1255.0, 790.8 and 1002.0 ppt, respectively.

Total concentration changes

In most participants total dioxin concentrations decreased between sampling events (63.6%, 14/22). Considered as a group, total dioxin concentrations had a mean decrease of 252.6 ppt, from a mean of 1380.9 ppt in the initial serum testing to a mean of 1128.3 ppt in the 2001 follow-up sampling. Differences occurred in total concentration change by sex and by cohort. Most males (69.2%, 9/13) had a decrease in total dioxin concentration, with a mean decrease of 437.0 ppt. Many females (55.6%, 5/9) had decreases in total concentration, but overall they had a mean increase of 14.5 ppt. A majority of participants (60%, 3/5) from the 1997 cohort had increases in total dioxin concentration. The mean concentration for this group, however, decreased by 124.5 ppt. The 1998 cohort also had a majority (70.6%, 12/17) of participants with decreasing total dioxin concentrations. The mean decrease in total dioxin concentration for the 1998 cohort was 289.9 ppt.

Results from parametric and nonparametric statistical tests for changes in total concentration are detailed in tables 7–10. Using both parametric and nonparametric statistical tests, the decrease in mean total dioxin concentration for all EI participants was significant. When analyzed by cohort, the 1997 group did not have a significant mean decrease, while the 1998 cohort's decrease was significant based on both statistical tests. For the 1998 cohort, there was a significant mean decrease in males based on both statistical tests, but this decrease was not statistically significant in females.

Congener-specific concentrations

Tables 3–5 provide congener-specific concentrations by sex and cohort. OCDD was the most prevalent congener in all serum samples with a mean concentration of 730.7 ppt, ranging from 206.0–2580.0 ppt. The next most prevalent congener was 1234/678D with a mean concentration of 126.4 ppt, ranging from 13.8–524.0 ppt. Other prominent congener concentrations included 1234678D, 33445P, and 334455P.

Congener-specific concentration changes

Mean congener-specific concentration changes between the initial and follow-up serum sampling are detailed in Table 6. The majority of congeners (72.2%, 13/18) had mean decreases in concentration. Of these, OCDD had the largest mean decrease followed by 1234678D, 1234678F, and 33445P.

Results from parametric and nonparametric statistical analyses of changes in mean congener-specific concentrations are provided in tables 7–10. In general, results from the parametric and nonparametric tests were similar. In other words, most changes in mean congener-specific concentrations were either significant or not significant based on results from both statistical tests. But some exceptions to this trend appeared. Congeners 2378D, 1234/678D, 12378F, 1234/678F, and 334455P had conflicting trend results based on the two statistical tests. That is, one statistical test indicated a decrease in the mean congener concentration, while the other test indicated an increase in mean concentration. These discrepancies are partly related to the use of log transformed and untransformed mean concentration data as well as to the small sample size. Nevertheless, according to both tests, all statistically significant mean congener-specific concentration changes had the same trend.

Congener-specific concentration changes by cohort

Statistical analyses of congener-specific concentration changes by cohort are presented in tables 7 and 8. Three congeners (2378F, 123789F, and 1234678F) had significantly decreased mean concentrations in both the 1997 and 1998 cohorts when analyzed using parametric and nonparametric statistical tests. Some congeners (123789D, 1234678D, OCDD, and 1234789F) decreased significantly in the 1998 cohort based on both statistical tests, but they did not decrease significantly in the 1997 group based on both tests. Conversely, one congener (234678F) decreased significantly in the 1997 cohort based on both statistical tests, but it did not decrease significantly in the 1998 group based on these tests. Most importantly, according to both statistical tests no congeners with significantly increased mean concentrations appeared in both cohorts .

In the 1997 cohort, four congeners had significantly decreased mean concentrations according to both statistical tests. Only one congener (23478F) had a significant increase in mean concentration based on either of the statistical tests. Still, this significant increase for 23478F was based on the nonparametric test and was not significant according to the parametric test.

For the 1998 cohort, half of the congeners had significantly decreased mean concentrations according to both statistical tests. Only one congener (3445P) had a significant increase in mean concentration based on either of the statistical tests. This congener had conflicting results, given that the nonparametric test indicated a significant increase while the parametric test indicated a significant decrease.

Congener-specific concentration changes for males by cohort

Statistical analyses of congener-specific concentration changes for males in the two cohorts are presented in Tables 9 and 10. Three congeners (2378F, 123789F, and 1234678F) had significantly decreased mean concentrations in males from both the 1997 and 1998 cohorts when analyzed using parametric and nonparametric statistical tests. Many congeners (12378D, 123789D, 1234678D, OCDD, and 1234789D) decreased significantly in males from the 1998 cohort based on both statistical tests but did not decrease significantly in males from the 1997 cohort based on these tests. Conversely, one congener (234678F) decreased significantly in males from the 1997 cohort based on both statistical tests but did not decrease significantly in males from the 1998 group based on these tests. Most importantly, there were no congeners with significantly increased mean concentrations in males from both cohorts based on both statistical tests.

For males in the 1997 cohort, four congeners had significantly decreased mean concentrations according to both statistical tests. Only one congener (23478F) had a significant increase in mean concentration based on either of the statistical tests. This significant increase for 23478F was, however, based on the nonparametric test and, according to the parametric test, was not significant.

In males from the 1998 cohort, a majority of congeners had significant decreased mean concentration based on both statistical tests. Only one congener (2378D) had an increased mean concentration based on both tests. But according to both tests this increased mean concentration was not statistically significant.

Congener-specific concentration changes for the 1998 cohort by sex

Statistical analyses of congener-specific concentration changes by sex in the 1998 cohort are presented in tables 9 and 10. Males and females in the 1998 cohort exhibited some differences in their changes in mean congener concentrations. Males and females had significant decreases in mean concentrations of two congeners (1234679D and 123789F) based on both statistical tests. However, males also exhibited significant decreases in mean concentration for many other congeners (12378D, 123789D, 1234678D, OCDD, 2378F, 1234678F, 1234789F, and 3445P) based on both statistical tests. A review of both statistical tests disclosed that females from the 1998 cohort did not show significant decreases in mean concentration for these congeners.

Males did not have significant increases in mean concentration for any of the congeners analyzed. Still, one congener (2378D) had a nonsignificant increase in mean concentration based on both statistical tests, and another (1234/678D) had a nonsignificant increase in mean concentration based solely on the parametric test. In general, almost every mean congener concentration decreased in males, and the majority of these decreases were statistically significant.

Females in the 1998 cohort did not have as clear trends in mean congener concentration changes as did their male counterparts. Two congeners (1234/678F and 334455P) had significant increased mean concentrations based on both statistical tests. Five other congeners also had increased mean concentrations based on the statistical tests, though most of these were nonsignificant changes. Conversely, two congeners (1234679D and 123789F) had significant decreased mean concentrations based on both statistical tests. Six other congeners also had decreased mean concentrations based on the statistical tests, though most were nonsignificant changes. Females in the 1998 cohort showed no consistent trends in mean congener concentration changes.

TEQ

Total TEQ

Tables 3–5 contain descriptive statistics for mean total TEQs and standard deviations by cohort and sex in the 2001 investigation. Lipid adjusted serum dioxin total TEQs in the 22 samples ranged from 4.1– 245.2 ppt. The mean, median, and geometric mean for total TEQs were 61.0, 39.9, and 40.8 ppt, respectively. Total TEQs in females ranged from 10.2– 245.2 ppt. The mean, median, and geometric mean serum dioxin total TEQs in females were 89.9, 73.9, and 58.2 ppt, respectively. For males, dioxin total TEQs ranged from 4.1–126.5 ppt. The mean, median, and geometric mean total TEQs in males were 41.1, 33.5, and 31.9 ppt, respectively. There were also differences in total TEQs by cohort membership. The 1997 cohort had total TEQs ranging from 4.1– 60.8 ppt. The 1997 cohort had mean, median, and geometric mean total TEQs of 35.7, 39.7 and 26.5 ppt. The 1998 cohort had total TEQs ranging from 10.2– 245.2 ppt. The mean, median and geometric mean total TEQs for the 1998 cohort were 68.5, 40.1 and 46.3 ppt, respectively.

Total TEQ changes

Dioxin total TEQs decreased in 14 participants (64%), increased in 7 participants (32%), and remained the same in one participant (4%). Table 6 contains descriptive statistics for the change in mean total TEQ between samplings. Tables 7–10 provide statistical analysis results for changes in total TEQ. The mean total TEQ for all participants decreased from 62.5 to 61 ppt between the initial and follow-up samplings. This change was not significant according to both

parametric and nonparametric tests. Nonsignificant decreases occurred in serum total TEQ for males in both cohorts and a nonsignificant increase occurred in total TEQ for females.

Congener-specific TEQs

Tables 11–13 contain descriptive statistics for congener-specific TEQs in the 2001 sampling by sex and cohort. The highest contributors to the mean total TEQ in the 2001 sampling were 12378D (42.7%), 1234/678D (20.7%), 2378D (11.4%), 23478F (9.1%) and 33445P (7.4%). These five congeners contributed over 90% of the mean total TEQ in this population. Some differences appeared in the relative congener contributions to total TEQ by sex and cohort. Polychlorinated dibenzodioxins (PCDDs) contributed more to females' total TEQ compared with male participants (83.8% vs. 70.8%). Conversely, polychlorinated dibenzofurans (PCDFs) contributed more to the male's total TEQ (19.2% vs. 9.3%) as did the coplaner PCBs (9.9% vs. 6.9%). Compared to the 1998 cohort, participants from the 1997 cohort had higher contributions to their total TEQ from PCDFs (20.5% vs. 12.1%) and coplaner PCBs (10.2% vs. 7.7%) while at the same time having fewer PCDDs (69.2% vs. 80.1%).

Congener-specific TEQ changes

Table 14 provides descriptive statistics for congener-specific TEQ changes between sampling events. Between the initial biological samplings in 1997 and 1998 and the retesting conducted in 2001, some changes appeared in congener contributions to total TEQ. In general, most of the congener contributions to total TEQ decreased between sampling events. The contribution to total TEQ by contaminant class was similar between samplings, with PCDFs (13.4% vs. 13.3%) and coplaner PCBs (9.4% vs. 8.1%) decreasing slightly and PCDDs (77.1% vs. 78.7%) barely increasing. Only two congeners (1234/678D and 23478F) had an increased contribution to the mean total TEQ.

Environmental

Tables 15–18 provide mean congener-specific and total dioxin concentrations and TEQs for each environmental media tested. Table 19 displays the mean congener-specific contributions to total TEQ for each of the environmental media where dioxin was detected.

Total concentration

Tables 15–18 provide information on total dioxin concentrations detected in each environmental media, including the mean total concentration and the range of concentrations for each type of media sampled.

Soil, indoor dust and attic dust

Twenty surface soil samples were collected from 19 residential yards. In one case, two samples were collected from a participant's yard. When comparing outdoor surface soil sampling results to indoor dust and attic dust samples, total mean dioxin concentrations were markedly increased. The mean total concentration for the surface soil samples was 2,267.49 ppt, while indoor dust and attic dust mean concentrations where much higher at 12,408.99 and 44,843.81 ppt, respectively.

Well water

Well water samples were collected from three residences. Dioxin was not detected in any of these samples.

Fish

Three participants provided eight locally caught fish. The mean total dioxin concentration in the fish was 479.3 ppt and ranged from 154.6 to 825.7 ppt.

Fruits, vegetables and nuts

Two participants provided three homegrown fruits, including two persimmons and one lemon. The mean total dioxin concentration for the fruits was 109.6 ppt and ranged from 3.6 to 228.7 ppt. Two participants provided three homegrown vegetables including one red pepper and two turnips. The mean total dioxin concentration for the vegetables was 21.9 ppt and ranged from 1.1 to 61.1 ppt. Three participants provided three pecans. The mean total dioxin concentration for the pecans was 107.4 ppt and ranged from 1.5 to 225.4 ppt.

Congener-specific concentrations

Tables 15–18 provide information on congener concentrations detected in each environmental medium. For surface soil, indoor house dust, and attic dust samples, OCDD and 23445P had the highest and second highest mean concentrations, respectively. OCDD represented about half of the mean total dioxin concentration in soil and indoor dust samples, and slightly more than half in the attic dust samples. The congeners with the highest and second highest mean concentration in fruits, vegetables, and nuts were 23445P and 23344P, respectively. The 23445P congener accounted for more than half of the mean total concentration in these samples. In fish, 23445P had the highest concentration, followed by 33445P.

Total TEQ

Soil, indoor dust and attic dust

Dioxin total TEQs in the soil samples ranged from 0.09 to 19.26 ppt. The mean, median, and geometric mean for soil sample TEQs were 4.16, 3.19, and 1.79 ppt, respectively. Eighteen indoor floor dust samples were collected during the investigation. The total dioxin TEQs in the samples ranged from 0.26 to 83.13 ppt. The mean, median, and geometric mean for dust sample total TEQs were 16.78, 8.89, and 8.51 ppt, respectively. Attic dust samples were collected from 16 homes. The dioxin total TEQs in the attic dust samples ranged from 0.32 to 922.77 ppt. The mean, median, and geometric mean for attic dust samples were 105.74, 16.67, and 16.00 ppt, respectively.

Well water

Well water samples were collected from three residences. Dioxin was not detected in any of these samples.

Fish

The dioxin total TEQs in the fish ranged from 0.15 to 65.48 ppt. The mean and median for total TEQs were 20.55 and 15.14, respectively.

Fruits, vegetables and nuts

The dioxin total TEQs in the fruit samples ranged from 0.01 to 0.06 ppt. The mean and median total TEQs for fruit were 0.04 and 0.05 ppt, respectively. The dioxin total TEQs in the three vegetable samples ranged from 0.01 to 0.06 ppt. The mean and median total TEQs for these vegetables were both 0.03 ppt. The dioxin total TEQs in the three pecan samples ranged from

0.01 to 0.06 ppt. The mean and median values for the pecan samples were 0.03 and 0.02 ppt, respectively.

Congener-specific TEQs

As indicated in table 19, 1234678D contributed the most to the mean total TEQ in soil (22.9%), indoor dust (45.9%), and attic dust (35.0%). That said, however, two homes' attic dust results showed 1234/678D and 1234/678F as the main contributors to the total TEQ. In fish, one congener (33445P) contributed 74.9% to the mean total TEQ.

Associations between Biological and Environmental Data

Tables 20–30 report all statistically significant associations between congener-specific serum concentrations and environmental media concentrations. Spearman rank and linear regression analyses evaluated associations between congener-specific 2001 biological and environmental sampling data. GLM analyses tested for associations between congener-specific changes in serum concentrations and congener-specific environmental concentrations.

Associations between 2001 biological and environmental data

Table 20 provides results from Spearman rank analyses. These tests looked for associations between 2001 serum congener and total TEQ concentrations and the 2001 environmental congener concentrations. Linear regression results for congener-specific and total TEQ associations between 2001 serum and environmental sampling results are detailed in tables 21–25. Linear regression analyses looked at all participants combined as well as separate cohorts and sex.

Serum congener concentrations/total TEQ and surface soil

Spearman rank tests indicated significant positive correlations with 2001 serum concentrations and surface soil concentrations for two congeners (1234678D and 1234679D). Linear regression analyses for all participants indicated significant associations between serum and surface soil concentrations for three congeners (1234678D, OCDD, and 123789F). When analyzing associations between 2001 serum and surface soil concentrations by cohort using linear regression, one congener (1234679D) was significant in the 1998 cohort, and two congeners (1234/678F and 33445P) were significant in the 1997 cohort. Linear regression analyses for associations between 2001 serum and surface soil concentrations by sex indicated one significant congener for males (1234678D) and one for females (1234679D). Using analyses from both statistical tests, no significant associations were found between 2001 total TEQ and surface soil results.

Serum congener concentrations/ total TEQ and indoor dust

No congener-specific correlations were found between 2001 serum and indoor dust concentrations using Spearman rank tests with all participants combined. Similarly, linear regression analyses for all participants did not find any significant associations between congener-specific 2001 serum and indoor dust concentrations. When broken down by cohort and sex, however, a few significant associations appeared. For the 1997 cohort, four serum and indoor dust congener concentrations were significantly associated (1234/678D, 123789D, 1234678D, and 1234/678F). The 1998 cohort had one significant congener association (12378F). When analyzed by sex, males had one congener (234678F) with a significant association between serum and surface soil concentration, as did females (33445P). Analyses from both

statistical tests showed no significant associations between 2001 total TEQ and indoor dust results.

Serum congener concentrations/total TEQ and attic dust

Spearman rank tests indicated a significant correlation between 2001 serum and attic dust concentrations for one congener (33445P). Linear regression analyses for all participants found significant associations between congener-specific serum and attic dust concentrations for three congeners (123789D, 33445P, and 334455P). When analyzing the two cohorts separately, the 1997 cohort had a significant association between serum and attic dust concentrations for one congener (1234/678D), while the 1998 cohort had two significantly associated congeners (123789D and 1234789F). When testing for sex-specific associations, males had no significant results, while females had one significant congener association (123789D). Analyses from both statistical tests showed no significant associations between 2001 total TEQ and attic dust results.

Associations between the change in biological concentration and environmental data

Tables 26–30 display statistically significant associations between changes in total TEQ and congener-specific serum concentrations with environmental concentrations. Associations were evaluated using GLM repeated measures analyses. These analyses considered all participants combined as well as the two different cohorts and sexes separately. Many of the congener-specific analyses could not be performed since the log-transformation of "zero" values led to a sample size that was too small.

Serum congener concentrations/total TEQ and surface soil

Analyses of all participants, disclosed many congeners with significant associations between the change in serum concentration and surface soil concentration (123789D, 1234678D, OCDD, 3445P, and 33445P). Analysis by cohort found significant associations between changes in 1998 cohort members' serum and surface soil (123789D, 1234678D, OCDD, 2378F, and 123789F). Analysis by sex found significant associations between changes in females' serum and surface soil levels (2378F and 12378F). No significant associations were found for 1997 cohort members or males. No significant associations were found between the change in total TEQ and surface soil results.

Serum congener concentrations/total TEQ and indoor dust

A few associations were found between changes in serum levels and indoor dust congener concentrations. Analysis of all participants combined found a significant association between the change in serum 3445P and the level in indoor dust. The 1998 cohort serum changes in 1234679D and 2378F were significantly associated with levels in indoor dust. The 1997 cohort had insufficient data for many of the congeners. When analyzed by sex, males had a significant association between changes in serum 2378F concentration and the concentration in indoor dust, as did females for 12378F. The change in total TEQ and indoor dust results showed no significant associations.

Serum congener concentrations/total TEQ and attic dust

When all participants were considered together, changes in some serum congener concentrations were significantly associated with levels in attic dust (1234678D, OCDD, 12348F, and 3445P). When analyzed by cohort, the 1998 cohort had some significant associations (1234678D, 1234679D, OCDD, and 2378F) but data for the 1997 cohort comparisons was insufficient. When

analyzed by sex, males had only one significantly associated congener (12378F), while none of the congeners in attic dust were significantly associated with changes in female's mean serum concentration. The change in total TEQ and attic dust results showed no significant associations.

Associations between Biological and Demographic Data

Tables 31–41 report all statistically significant associations between congener-specific serum concentrations and demographic data. Spearman rank and linear regression analyses evaluated associations between congener-specific 2001 biological sampling data and demographic information. GLM analyses tested for associations between congener-specific changes in serum concentration and demographic information.

Associations between 2001 biological and demographic data

Tables 31–36 provide the significant associations between 2001 congener-specific serum dioxin concentrations and data gathered from participants. Table 31 reports all statistically significant results from Spearman rank tests. Tables 32–36 report all statistically significant associations obtained through linear regression analyses. Linear regression analyses tested all participants combined as well as considering the two cohorts and sexes separately.

Serum congener concentrations/total TEQ and age

Spearman rank and linear regression analyses showed a significant positive association between age and total TEQ. These significant associations with total TEQ were also present when using linear regression to analyze specific cohorts and sexes. For numerous congeners both statistical tests also indicated significant positive correlations between age and serum concentration (2378D, 12378D, 1234/678D, 123789D, 1234678D, OCDD, 23478F, 1234/678F, 234678F, 1234678F, and 334455P). The same congener-specific associations were present in all female participants as well as in the 1998 cohort. Still for some of these congeners (1234678D, 234678F, and 1234678F), males and the 1997 cohort did not have significant associations with age.

Serum congener concentrations/total TEQ and BMI

Body mass index (BMI) was not associated with serum total TEQ using either of the statistical tests. This lack of association was also evident when analyzing specific cohorts and sexes with linear regression. BMI was, however, significantly associated with three congeners (123789D, 234678F, and 1234678F) according to Spearman rank test results. Using linear regression, serum levels of two congeners (123789D and 1234678D) were found to be associated with BMI. BMI was not associated with any of the 2001 serum congener concentrations for either cohort. Similarly, when analyzed by sex no significant associations with male BMI and congener concentrations were found. But females had significant associations between BMI and two congeners (1234678D and 1234678F).

Serum congener concentrations/total TEQ and self-reported weight change

Spearman rank tests did not find any associations between weight change and total TEQ. Spearman rank tests did, however, indicate significant associations between self-reported weight loss and two congener-specific concentrations (12378F and 1234789F). Linear regression did not find the same associations between weight change and serum congener concentrations. Linear regression analyses reported a significant association with weight loss and serum concentration for one congener (1234679D). When analyzing by sex, males had no significant association

between weight change and serum congener concentrations or total TEQ. Females, however, had significant associations between weight loss and serum concentrations for two congeners (1234679D and 2378F). When analyzed by study cohort, the 1997 cohort had significant associations between weight loss and total TEQ as well as serum concentrations for many congeners (2378D, 12378D, 1234/678D, 123789D, 1234678D, 334455P). The 1998 cohort showed no significant associations between weight change and 2001 serum congener concentrations or total TEQ.

Serum congener concentrations/total TEQ and sex

Spearman rank tests indicated that sex was significantly correlated with only one serum congener concentration—males had a lower concentration of 1234678D than females. Linear regression results indicated that males had significantly lower mean serum concentrations of three congeners (2378D, 123789D and OCDD). Using either statistical test, no associations appeared between sex and total TEQ.

Serum congener concentrations/total TEQ and gardening

Spearman rank tests did not find significant correlations between 2001 serum congener concentrations or total TEQ and home gardening. Linear regression analyses found an association with home gardening and serum concentrations for two congeners (1234678D and 234678F). When male and female participants were analyzed separately, no serum congener concentrations or total TEQ results were associated with females and gardening. Males who gardened, however, had a positive association with total TEQ and some individual congeners (1234/678D, 123789D, 1234678D, 23478F, 334455P). Also, for males who gardened, there was a negative association with one congener (123789F).

Serum congener concentrations/total TEQ and fish consumption

Spearman rank analyses did not find any significant associations between total TEQ or congener-specific concentrations and fish consumption. Linear regression analyses found only one significant association with local fish consumption and serum congener concentration (234678F). When analyzed by sex and cohort, no significant associations were found between fish consumption and either total TEQ or serum congener concentrations.

Serum congener concentrations/total TEQ and crawfish consumption

Significant associations did not occur between crawfish consumption and congener-specific concentrations or total TEQ. Similarly, no significant associations were found when analyzing specific sexes and cohorts.

Serum congener concentrations/total TEQ and other demographic variables

Analyses for all combined participants, as well as analyses by sex and cohort, found no significant associations between

- total TEQ,
- or 2001 serum congener concentrations and
  - the age of the participant's home,
  - the length of residence in the home, or
  - the length of time between biological samplings.

Associations between the change in biological concentration and demographic data

Tables 37–41 display the statistically significant results of GLM repeated measures analyses. These analyses tested for associations between participant demographics and the change in either serum congener concentrations or total TEQ. Table 37 presents all significant results obtained when analyzing the entire combined EI population. Tables 38–39 report significant results by sex while tables 40–41 report cohort-specific, significant results.

Serum congener concentrations/total TEQ and age

A review of GLM analyses for all participants showed that age was significantly associated with a change in serum concentration for two congeners (123789F and 334455P). When analyzed by cohort, age was associated with concentration changes of two congeners in the 1997 cohort (OCDD and 23478F), and one congener in the 1998 cohort (334455P). Sex-specific analyses indicated age was significantly associated with the change in serum concentration for three congeners in males (OCDD, 2378F, and 23478F). The number of female participants was insufficient to evaluate associations between age and the change in serum congener concentrations.

Serum congener concentrations/total TEQ and BMI

No significant associations appeared between BMI and the change in congener-specific concentrations or total TEQ. Similarly, no associations appeared when analyzing sex and cohort for these relationships.

Serum congener concentrations/total TEQ and weight change

No significant association occurred between weight change and total TEQ. Participant's weight change between their first and second serum dioxin tests was, however, significantly associated with a change in serum concentrations for two congeners (2378D and 2378F). No significant associations were detected in sex-specific analyses. No associations were found for the 1998 cohort, but the 1997 cohort had one association between weight change and the change in congener concentration (334455P).

Serum congener concentrations/total TEQ and sex

GLM analyses indicated no significant associations between total TEQ changes and sex. Significant associations were, however, found between sex and the change in concentration for three congeners (2378D, 12378D and 123789D). These associations were not present when analyzing specific cohorts.

Serum congener concentrations/total TEQ and gardening

Home gardening was significantly associated with serum concentration changes for two congeners (1234678D and 1234678F). When analyzed by cohort, no associations appeared in the 1997 cohort but there were three significant congener associations for the 1998 cohort (1234678D, OCDD, and 234678F). When analyzed by sex, females had a significant association with gardening and serum concentration changes for one congener (2378D) while males had significant associations with many congeners (1234/678D, 123789D, 1234678D, 23478F, 123789F, and 334455P). Significant associations with gardening and total TEQ were not found.

Serum congener concentrations/total TEQ and fish consumption

No significant associations were identified between local fish consumption and changes in congener-specific concentrations or total TEQs. Also, no significant associations were identified between these variables when analyzing by sex or cohort.

Serum congener concentrations/total TEQ and crawfish consumption

ATSDR found no significant associations between the change in serum congener concentration and crawfish consumption for EI participants when analyzed as a group and also broken down by sex. When analyzed by cohort, however, some significant congener associations for the 1997 cohort (2378D and 12378D) appeared, as well as for the 1998 cohort (2378D, 1234/678D, 1234678D, OCDD, 1234/678F, and 234678F). No significant associations were found between total TEQ changes and crawfish consumption.

Serum congener concentrations/total TEQ and other demographic variables

GLM analyses for associations between the change in serum congener concentrations and the age of each participant's current residence indicated significant associations for only one congener (1234679D). When analyzed by cohort, ATSDR found no associations in the 1997 cohort, and the 1998 cohort had one significant congener (1234679D). When analyzed by sex, females did not have sufficient degrees of freedom to conduct this analysis. When the analysis was conducted for males, there was a significant association with the age of residence and changes in concentrations for three congeners (1234/678D, 23478F, and 1234678F). Associations between the change in total TEQ and the age of each participant's current residence were not statistically significant.

The amount of time between participants' first and second serum dioxin tests was significantly associated with changes in serum OCDD concentrations. And when analyzed by sex, a significant association appeared between the change in serum 3445P concentration and the time between tests for male participants. GLM analysis could not be conducted by cohort and for females because of the zero degrees of freedom for the "time between tests" variable. Associations between the change in total TEQ and the time between participants' serum samplings were not statistically significant.

GLM analyses for associations between the change in serum congener concentrations and each participant's residence time at their current location did not indicate any significant relationships when analyzing the EI group as a whole. When analyzing by sex, females did not have any associations between changes in serum concentration and residence time, but males did have two significant congener associations (2378F and 1234678F). When analyzed by cohort, associations for the 1997 cohort participants were not significant. For the 1998 cohort, however, residence time was significantly associated with changes in serum concentrations for three congeners (123789D, 12378F, and 1234678F).

Associations between Environmental Media Results

Table 42 displays significant congener-specific and total TEQ Spearman rank correlations between indoor and attic dust, indoor dust and surface soil, and age of house and attic dust results. Significant positive correlations between indoor dust and attic dust concentrations were present for many congeners (1234/678D, 123789D, 1234678D, 1234679D, OCDD, 23478F, 1234/678F, 234678F, 234678F, 1234789F, and 3445P). Indoor dust and surface soil also

indicated significant correlations for some congeners (2378F, 234678F, 3445P, and 33445P). Finally, significant correlations were found between attic dust concentration and age of home for many congeners (12345678D, OCDD, 2378F, 12378F, 23478F, 1234/678F, 123789F, 234678F, and 1234678F).

Reference Group Comparisons

Regional comparison

As discussed in the methods section, the population-based exposure study conducted by ATSDR in Lafayette Parish represented the most current index of regional blood serum dioxin concentrations. When comparing the 2001 EI group to the Lafayette reference population, all nondetect results were assigned values equal to one-half the analytical detection limit. The mean and median dioxin total TEQ values for the Lafayette population were 22.02 ppt and 15.56 ppt, respectively (Table 43). The mean and median total TEQ for the 2001 EI participants were 62.20 and 40.50, respectively. These central tendency statistics for the 2001 EI group exceeded similar measures in the Lafayette population.

Because age is a strong predictor for blood serum dioxin concentration, EI participants and the Lafayette reference population were evaluated by age quartiles (Table 43). 2001 EI participants between the ages of 30–44 had similar total TEQs to Lafayette participants in this age quartile. For the youngest age quartile (15–29 years) and the two oldest age quartiles (45–59 years and 60+ years), mean total TEQs for the Mossville group were, however, markedly higher than in Lafayette participants. The same trends were observed when comparing median total TEQ values for the Mossville EI and Lafayette age quartiles.

Congener-specific mean concentration and mean total TEQ comparisons between the Mossville EI group and the Lafayette reference population are presented in tables 44–45. Profiles were generated for mean concentration (Table 44) and mean total TEQ (Table 45) in the two populations and provide each congener's percentage contribution to these mean totals.

National comparisons

Three states meta-analysis

When comparing the 2001 EI group to the three states meta-analysis reference population, all nondetect results were assigned values equal to one half the analytical detection limit. The mean and median dioxin total TEQ values for the three states meta-analysis reference population were 18.25 ppt and 16.20 ppt, respectively (Table 46). The mean and median total TEQ for the 2001 EI participants were 62.20 and 40.50, respectively. These measures of central tendency for the 2001 EI exceeded similar statistics for the three states meta-analysis reference population.

Age is a strong predictor for blood serum dioxin concentration; therefore, the 2001 EI participants and the three states meta-analysis reference population were evaluated by age quartiles (Table 46). The youngest two age quartiles (15-29 years and 30-44 years) in the EI group and the reference population had similar mean and median total TEQ values. However, the EI group had higher mean and median total TEQ values in the oldest two age quartiles when compared to the three states meta-analysis reference population.

NCEH national data

As discussed in the methods section, NCEH's Second National Report on Human Exposure to Environmental Chemicals provided 95th percentile concentrations for six dioxin congeners.

These concentrations were compared to 95th percentile concentrations for the same six congeners in the initial 1997/1998 sampling as well as the follow-up 2001 EI sampling. As reported in Table 47, the 95th percentiles for the six congeners in the 1997/1998 initial sampling and the 2001 follow-up sampling all exceeded the 95th percentiles from the NCEH comparison population. The 95th percentiles for the six congeners in both the 1997/1998 and 2001 samplings also exceeded the confidence intervals for the NCEH data, indicating these increases were statistically significant. The frequency of 2001 EI participants who had congener concentrations exceeding the NCEH 95th percentiles varied from 13.6% to 31.8%.

NCEH's Third National Report on Human Exposure to Environmental Chemicals provided 95th percentile concentrations for 10 dioxin congeners. These concentrations were compared to 95th percentile concentrations for the same 10 congeners in the initial 1997/1998 sampling as well as the follow-up 2001 EI sampling. As reported in Table 48, the 95th percentiles for the 10 congeners in the 1997/1998 initial sampling and the 2001 follow-up sampling all exceeded the 95th percentiles from the NCEH comparison population. The 95th percentiles for the 10 congeners in both the 1997/1998 and 2001 samplings also exceeded the confidence intervals for the NCEH data, indicating these increases were statistically significant. The frequency of 2001 EI participants who had congener concentrations exceeding the NCEH 95th percentiles varied from 9.1% to 54.5%.

Congener Half-life Evaluations

2378D

The reported half-life for 2378D in humans ranges from 5.8 years to 8.7 years (Flesch-Janys et al. 1996; Michalek et al. 1996; Needham et al. 1994; Ott and Zober 1996). This range was obtained from studies of four different populations exposed to 2378D: Vietnam veterans exposed to Agent Orange, the BASF cohort, the German pesticide worker cohort, and Seveso, Italy residents.

Assuming 2378D had a half life of 5.8–8.7 years, the five participants from the 1997 cohort were expected to have concentrations decreased by 41.2%–29.9%, respectively. Four of these five individuals had actual decreases ranging from 15.7%–100.0% while one had a 38.1% increase. The mean decrease in 2378D for this group was 1.08 ppt, a decrease of 22.9%.

Assuming 2378D had a half life of 5.8–8.7 years, the participants from the 1998 cohort were expected to have concentrations decreased by 29.8%–21.0%, respectively. Of these 17 individuals, one remained the same, eight decreased, and eight increased. Decreases in 2378D concentration ranged from 1.2%–54.1%. The increases in concentration for eight individuals ranged from 8.5%–330%. The 1998 cohort had a mean increase in 2378D concentration of 0.26 ppt, an increase of 3.4%.

Considered together, the 22 participants had an average lipid adjusted 2378D concentration of 7.02 ppt in their initial sampling and an average concentration of 6.98 ppt in their follow-up sampling. This resulted in a mean decrease of 0.6% for 2378D.

12378D

Few studies have generated estimated half-lives for 12378D in humans. Two analyses, however, reported half lives for 12378D in the range of 9–16 years (Tuomisto 1999; Flesch-Janys 1996).

Assuming 12378D had a half life of 9–16 years, the five participants from the 1997 cohort were expected to have 12378D concentrations decreased by 29.1%–17.5%, respectively. Three of these five individuals had decreases in 12378D ranging from 0.5%–100%. The other two participants had increases of 1.5% and 74.4%. The mean decrease for 12378D in this group was 0.5 ppt, a decrease of 4.1%.

Assuming 12378D had a half life of 9–16 years, the participants from the 1998 cohort were expected to have 12378D concentrations decreased by 20.4%–12.0%, respectively. Of these 17 individuals, 11 decreased and 6 increased. Decreases in 12378D concentration for the 11 participants ranged from 7.5%–59.7%. Increases for the other six individuals ranged from 6.1%–240%. The 1998 cohort had a mean decrease in 12378D concentration of 0.1 ppt, a decrease of 0.4%.

Considered together, the 22 participants in this exposure investigation had an average lipid adjusted 12378D concentration of 26.26 ppt in their initial sampling and an average concentration of 26.06 ppt in their follow-up sampling. This resulted in a mean decrease of 0.7% for 12378D.

1234678D

The reported half-life for 1234678D in humans ranges from 3-7 years (Tuomisto 1999; Flesch-Janys 1996).

Assuming 1234678D had a half life of 3–7 years, the five participants from the 1997 cohort were expected to have concentrations decreased by 64.3%– 35.7%, respectively. Four of the five individuals had decreases ranging from 9.5%–65.5% while the other participant had an increase of 5.7%. The mean decrease in 1234678D concentrations for this group was 17.44 ppt, a decrease of 23.7%.

Assuming 1234678D had a half-life of 3–7 years, the participants from the 1998 cohort are expected to have levels decreased by 49.5%–25.4%, respectively. Of the 17 participants from the 1998 cohort, 14 decreased and 3 increased. The decreases in 1234678D concentrations ranged from 2.9%–83.3%. Increases for the other three participants ranged from 0.6%–7.5%. The 1998 cohort had a mean decrease in 1234678D concentrations of 24.36 ppt, a decrease of 20.8%.

Considered together, the 22 participants had an average lipid-adjusted 1234678D concentration of 107.2 ppt in their initial sampling and an average concentration of 84.4 ppt in their follow-up sampling. This resulted in a mean decrease of 21.3% for 1234678D.

Discussion

Dioxin is primarily produced as an unintentional byproduct of numerous industrial processes. Dioxin is generated during incineration, pulp and paper mill processes, and the chemical synthesis of trichlorophenoxyacetic acid, hexachlorophene, polychlorinated biphenyls, vinyl chloride, and pentachlorophenol (CDC, 2003). Since the 1970s, environmental releases of dioxin from industrial sources have decreased by approximately 76% (EPA 2000; IOM 2003). This decrease in environmental emissions has been accompanied by a decrease in the general population’s body burden (Aylward and Hays 2002; Lorber 2002).

Biological

Dioxin is a ubiquitous environmental contaminant and has been detected in human blood, adipose tissue and milk. With the current sensitivity of analytical methods, dioxin can be detected in almost all residents of industrialized countries. The major source of exposure to dioxin in the general population is from food—particularly beef, dairy products, and fish—with smaller exposures from contamination in air, water, and soil (EPA 2000). Dioxin concentrations in humans do not vary significantly by race or geographic region, but concentrations generally increase with age (EPA 2000). Humans are reportedly less sensitive to dioxin than many other species (Dickson 1993; Neubert 1997/98).

Concentration

Total concentration changes

When analyzing mean total dioxin concentrations, a significant decrease was observed between the two sampling events, one based on parametric, and the other on nonparametric analysis (Table 7). This decrease in concentration may indicate a decrease in exposure between sampling events. The 1998 cohort had a statistically significant decrease in mean total concentration; however, the decrease in mean total concentration for the 1997 cohort was not statistically significant. The small number of participants in the 1997 cohort may have precluded the ability to observe a significant mean total concentration decrease in this group.

Congener-specific concentrations

OCDD had the highest serum concentration for all congeners in both the 1997 and 1998 sampling events as well as in the 2001 follow-up EI (Table 4). OCDD significantly decreased between sampling events in the serum of the 1998 cohort; however, there was a non-significant decrease in the 1997 cohort. OCDD's presence as the highest concentration congener is consistent with dioxin sampling results in many human studies (Tepper 1997; EPA 2000). OCDD is the highest concentration congener in human tissue in most industrialized countries. (EPA 2000; Schecter 1994).

Congener-specific concentration changes by cohort

Three congeners (2378F, 123789F, 1234678F) had significantly decreased concentrations in both cohorts based on the parametric and nonparametric analyses (Table 7). 1234678F has a half-life of approximately 3 years (Flesch-Janys 1996). Because this investigation had a short re-sampling period of 3–4 years, the significant decrease in 1234678F concentration is consistent with its relatively short half-life.

Considering only significant concentration changes where parametric and nonparametric tests agree, no significant increases in blood dioxin levels were observed among the congeners with all participants combined (Table 8). The 1997 cohort, however, had a significant increase in 23478F, and the 1998 cohort had a significant increase in 3445P based on the nonparametric test. The exposure source associated with the significant increases in these two congeners is unknown.

Congener-specific concentration changes by sex and cohort

Congener 123789F decreased significantly in both cohorts and both sexes based on parametric and nonparametric analyses (Table 9). Linear regression indicated a positive correlation between the decrease in this congener's concentration and both soil levels and self-reported local fish

consumption. Still, questionnaires have only a limited ability to determine consumption rates and the types of fish consumed. These inherent limitations make difficult a direct inference regarding the association between fish consumption and the decrease in this congener. Although linear regression indicated an association between dioxin soil levels and the decrease in 123789F, the significance of this finding is not clear.

Females in the 1998 cohort had significant increases in both 1234/678F and 334455P (Table 10). Linear regression indicated that only age was significantly associated with both of these congener changes in females. Why these two congeners significantly increased in the 1998 female cohort is unknown.

With both parametric and nonparametric analyses, a nonsignificant decreasing trend in dioxin concentration is seen among most congeners for both cohorts and sexes. This indicates that current exposures above background are probably nominal for most of the EI participants.

TEQ

Total TEQ

Lipid-adjusted serum total TEQs in the 2001 sampling ranged from 4.1–245.2 ppt. The mean, median, and geometric mean for total TEQs were 61.0, 39.9, and 40.8 ppt, respectively. To better contextualize the total TEQ results, the 2001 follow-up EI participants' results were compared to reference groups and compared to levels at which health effects are likely to occur. Therefore, the relevance of dioxin total TEQ results is discussed in two sections later in this document—the reference group comparisons section and the health effects section.

Total TEQ changes

Although a slight decrease in mean total TEQ was observed between biological sampling events, this decrease was not statistically significant (Table 7). Some participants (7/22, 32%) had increases in their total TEQ values. Excluding, however, two elderly individuals, participants with increased total TEQs had very small proportional changes in these measures. The small, statistically insignificant decrease in mean total TEQ, as well as the few individual increases in total TEQ, could be due to many possible variables, including the long and variable half-lives of many of the congeners, body weight changes in participants, the short re-sampling period of 3–4 years used in this investigation, laboratory analytical variability, and ongoing exposures.

The significant decrease in mean total concentration and not in mean total TEQ could be explained by the toxicity weighting calculations used in determining total TEQs. OCDD was the predominant congener by concentration in the EI group and was the congener whose concentration decreased the most between sampling events. OCDD has, however, a very low toxicity. Therefore, significant changes in OCDD concentrations have a negligible impact on total TEQ calculations (Table 6).

Congener-specific TEQs

In the 2001 EI participants, congener 12378D contributed the most (42.7%) to the mean total TEQ (Table 11). This congener's significant contribution to the mean total TEQ is similar in both the 1997 and 1998 cohorts. Congener 12378D contributes substantially to overall dioxin toxicity because it is as toxic as 2378D. The half-life of 12378D is estimated to be 9–16 years (Flesch-Janys 1996). The mean 12378D TEQ for the 2001 investigation was 26.1 ppt. There was a minimal decrease between sampling events for 12378D among the 22 participants. The

prevalence of 12378D in the serum of participants may be a reflection of its long half-life, physiological factors, and historic or current exposure.

12378D is produced during combustion of municipal waste incinerators, cigarettes, wood and coal, waste oil and polyvinylchloride materials (Hazardous Substance Data Bank 2003). 12378D is also released in effluents from the pulp and paper industry and in sewage from municipal waste (Cruczwa 1986; Hazardous Substance Data Bank 2003). 12378D is found in 2,4,5-T and other pesticides and may be released during their use. The congener profile for 2,4-D salts and esters mimics a combustion source profile. That said, however, a major difference is the abundance of 12378D in 2,4-D (14%), which is not seen in any other combustion or non-combustion sources (EPA 2000).

Most dioxin literature focuses extensively on one congener, 2378D. The blood dioxin levels of 2378D in the 2001 participants contributed 11.4% to the total TEQ (Table 11). 2378D was the third highest contributor to the total TEQ, with 1234/678D being the second highest contributor (20.7%) to the total TEQ (Table 11). This pattern is similar in the initial sampling of the 1997 and 1998 cohorts. 2378D has the same toxicity as 12378D. The half-life of 2378D in humans is estimated to be 5.8–8.7 years (Flesch-Janys et al. 1996; Michalek et al. 1996; Needham et al. 1994; Ott and Zober 1996). The mean TEQ for 2378D in the 2001 investigation was 7.0 ppt. Among the 22 participants, minimal decrease appeared between sampling events for 2378D. The prevalence of 2378D in the serum of participants may be a reflection of its long half-life, physiologic factors, exposure to 2378D in the past, and current background exposure.

2378D is produced by incineration of municipal, medical, and industrial wastes. It is also formed in bleached wood pulp and paper production. 2378D is produced during combustion of coal-fired or oil-fired power plants, polyvinylchloride, wood burning, and home heating systems. It has been detected in automobile and diesel exhaust. It can be a contaminant of various pesticides and can be found in vegetation treated with phenoxy acetic acid herbicides. It is also formed as a byproduct in the manufacture of 2,4,5-trichlorophenol (Hazardous Substance Data Bank 2003; ATSDR 1998).

The general population is exposed to 2378D primarily from food ingestion, especially foods of animal origin such as milk, dairy products, meat, fish, and eggs. Food accounts for more than 90% of human exposure to dioxin (Dickson 1993; ATSDR 1998; Hazardous Substance Data Bank 2003). Secondary exposure occurs from ambient air and skin contact with materials contaminated with 2378D (Hazardous Substance Data Bank 2003). Historical information is not available to determine if a specific source could have contributed to the contribution of 2378D in the serum of participants.

Congener-specific TEQ changes

As discussed earlier, no significant change in the total TEQ was observed among specific cohorts and sexes. Most of the congener contributions to total TEQ decreased between sampling events. Only two congeners (1234/678D and 23478F) had appreciable increases between sampling events (Table 14).

Environmental

Dioxin is found everywhere in the environment, with low background concentrations found in the air, water, and soil. Lower concentrations are found in biological and environmental samples in less industrialized, rural regions compared to more industrialized, urban areas. Dioxin is

released to the environment during combustion processes (e.g., municipal solid waste, medical waste, and industrial hazardous waste incineration, and fossil fuel and wood combustion); during the production, use, and disposal of certain chemicals (e.g., PCBs, chlorinated benzenes, and chlorinated pesticides); during the production of bleached pulp by pulp and paper mills; and during the production and recycling of several metals. Highly chlorinated dioxins (1234678D, 1234679D, and OCDD) are the most common congeners found in environmental samples. Currently, atmospheric fallout of particulates and gases containing dioxin is the predominant source of dioxin in soil. Historically, dioxin was also deposited onto soil through pesticide applications, disposal of dioxin-contaminated industrial wastes, and via land application of paper mill sludge (ATSDR 1998).

Various man-made sources—current and historical—likely contributed to the congener patterns found in the environmental media tested in this follow-up exposure investigation. The congeners found in the highest concentrations in the surface soil, indoor dust, and attic dust samples included OCDD, 1234678D, and OCDF. This pattern is visually the most similar to the profiles of pentachlorophenol (PCP) and of municipal sewage sludge (EPA 2000). Insufficient information is available in the literature to determine if past use of PCP or other chemicals were widely applied in the Calcasieu area for weed or insect control. Whether sewage sludge has been used as a soil amendment is also unknown. Finally, until the 1980s, stack testing for dioxin was not required for industrial operations, making reconstruction of past combustion emissions difficult.

Except for attic dust, other environmental media were subject to weathering, erosion, and a more rapid breakdown of dioxin. Therefore, environmental concentrations may have been higher in the past. Sampling results from participants' yards and the interiors of their current residences indicated that current exposures to dioxin through these sources are not at levels of health concern. Still, exposure levels at previous residences may have been different. Since they were initially tested in either 1997 or 1998, the majority (59%, 13/22) of participants in the 2001 follow-up EI have relocated.

Soil, indoor dust, and attic dust

The slight differences in congener contributions in the different media may indicate differences in historical versus current sources of dioxin, differences in indoor versus outdoor contaminant breakdown, or a combination of the two. The small number of samples collected during the investigation does not allow for an in-depth analysis of differences in congener contribution to TEQ by medium.

Attic dust had the highest concentrations for all environmental media sampled. This was expected, given that attics act like passive air samplers. That is, particulates that enter the attic settle to the floor and remain until disturbed through remodeling, cleaning or other infrequent activities. Environmental weathering (e.g., wind, rain, sunlight) and human foot traffic are not applicable to the breakdown, dilution, or removal of contaminants in attic spaces (Rasmussen 2001; Ilacqua 2003). Because, however, no attic dust comparison values are available, it is difficult to evaluate the public health significance of these dioxin sampling results.

The mean surface soil TEQ for the 19 homes tested in this follow-up EI was 3.9 ppt. This concentration is well below the ATSDR soil TEQ screening guideline of 50 ppt. The screening guideline is based on ATSDR's chronic oral Minimal Risk Level (MRL) of 1 pg/kilogram body

weight/day. Screening guidelines are not available for indoor dust. Nevertheless, the mean indoor dust TEQ of 17.4 ppt was also less that the ATSDR soil TEQ screening guideline.

Well water

Dioxin was not found in private well water samples. Because dioxin strongly adheres to soil particles and has very low solubility in water, migration of this contaminant through the soil and into the groundwater is not likely. Dioxin may move down into the soil if organic solvents (e.g., alcohol, oils, gasoline) are also present in the soil (ATSDR 1998).

Fish

Participants who provided fish samples for analysis stated that they did not eat the fish. Instead, most participants were interested in finding out the dioxin content of the fish. One exception was a participant who reported eating fish caught in Toledo Bend. The fish provided for analysis were caught in the following locations: Toledo Bend, under the I-10 bridge, under the 210 bridge, Bayou D'Inde, and Moss Lake. The fish species included catfish, garfish, mullet, black drum, and redfish.

In general, fish bioconcentrate more highly chlorinated congeners such as penta-, hexa-, and hepta-chlorinated biphenyls. The fish samples collected in the follow-up EI were analyzed for many dioxins, including some coplanar PCBs. Unlike this investigation's other environmental samples, samples of fish contained higher concentrations of coplanar PCBs than dioxin or furan congeners. The highest mean concentrations detected were for PCB congeners (23445P, 33445P, 3344P and 2334P). Coplanar PCBs contributed over 75% of the mean total TEQ in the edible portions of the fish tested during this investigation.

No current comparison or guidance values are available for easily determining acceptable dioxin concentrations in fish. In the early 1980s, the U.S. Food and Drug Administration (FDA) issued tolerance levels for consumption of dioxin-contaminated fish. The FDA recommended limited consumption of fish with dioxin concentrations greater than 25 ppt, and no consumption of fish with dioxin concentrations greater than 50 ppt (ATSDR 1998). EPA promulgated the most recent guidance regarding dioxin contamination in fish. In 2000, the EPA recommended that fish should not be consumed if concentrations of dioxin are greater than 1.2 ppt-TEQ (EPA 2000). Unfortunately, EPA's guidance does not consider the contribution of coplanar PCBs—chemicals that have dioxin-like effects and contribute to the total TEQ. EPA's 1.2-ppt guidance value is of limited use in this investigation, given that coplanar PCBs account for over 75% of the mean total TEQ in the fish samples. Regardless, however, of the guidance values selected for evaluating the fish sampling data in this exposure investigation, most fish were above any acceptable level of dioxin contamination and therefore not fit for human consumption.

Fruit, vegetables, and nuts

Little evidence supports the suggestion that dioxin contamination in soil is absorbed into non-aquatic plants. Dioxin is lipophilic, adsorbs strongly to soil, and is not very soluble in water. The contamination of plants is mainly due to dioxin deposition onto plant surfaces from the air (ATSDR 1998).

Unlike the environmental samples, samples of food contained higher levels of coplanar PCB congeners than dioxin or furan congeners. Mean levels of 23445P, 23344P, and 3344P were the highest congener concentrations in all fruits, vegetables, and nuts tested. But total TEQ levels in all fruit, vegetable, and nut samples were well below any levels of concern.

Associations between Biological and Environmental Data

Serum congener concentrations/total TEQ and surface soil

Only one congener (1234678D) was significantly associated with serum and surface soil results in both statistical tests. This congener had the second highest mean concentration in serum. When analyzing all participants combined, significant associations were found between the change in serum concentration for some congeners and their concentration in surface soil (123789D, 1234678D, OCDD, 3445P, and 33445P). These associations were not present when participants' serum concentrations were analyzed by sex. When analyzing by cohort, the 1998 cohort had two congeners with the same significant associations (123789D and OCDD). Total TEQ in serum was not associated with surface soil TEQ.

Serum congener concentrations/total TEQ and indoor dust

Analyses of all participants combined showed no significant associations between 2001 serum congener concentrations and indoor dust. One congener was significantly associated with the change in concentration in serum and indoor dust (3445P). When participants were analyzed by sex or cohort, there were no significant associations with this congener. Total serum TEQ was not associated with indoor dust TEQ.

Serum congener concentrations/total TEQ and attic dust

As mentioned in the exposure investigation protocol, attic dust samples were collected to determine if historical air deposition of dioxin occurred. Attic dust samples cannot be used to determine or estimate human exposures to dioxin because no applicable exposure estimates are available for inhalation or ingestion of attic dust contaminants. To assume similar exposure to soil or indoor dust—because attics are infrequently accessed and not part of the typical indoor environment—is inappropriate.

Associations Between Biological and Demographic Data

Serum concentration/total TEQ and age

Dioxin is resistant to human metabolism and subsequently can bioaccumulate in people exposed over many years or decades (ATSDR 1998). Due to this relationship between exposure and metabolism, combined with the prevalence of historic environmental dioxin contamination in many industrialized countries, blood dioxin concentrations in the general population are higher in older individuals. Older exposure investigation participants who were long-term residents of the Mossville community or other unincorporated areas west of Lake Charles were selected for the 1998 investigation because they were at greater risk for cumulative exposure to dioxin.

During the 2001 follow-up investigation, participants ranged from 23 to 78 years of age, with an average age of 57. Older participants in these two investigations had higher blood dioxin concentrations and total TEQs. There were strong associations between 2001 total dioxin TEQs and age. The associations were present when analyzed using both statistical tests. These significant associations were also present when analyzing by sex and cohort. Many individual congeners had significant associations between increasing age and increasing concentration. These associations were present based on both parametric and nonparametric statistical tests. Associations between increasing age and increasing dioxin concentrations or total TEQs have been reported in numerous studies (ATSDR 1998; Falk 1999; Schecter 1996; Neubert 1997/98).

Therefore, these findings are not unusual or unexpected. In short, these findings correspond with our current understanding of serum dioxin concentrations and age in the general population.

No significant associations appeared between age and the change in total TEQs between sampling events. Some congener-specific concentration changes were, however, significantly associated with age in males and cohort membership. Studies have reported increased dioxin congener half-lives in older persons (Flesch-Janys D 1996). Therefore, the elevated average age of participants may be a major determinant in the association between the change in some congener concentrations and age.

The reason for the elevation in blood dioxin concentration and total TEQ in the older participants in this investigation is unknown. Older residents' elevated dioxin concentrations are possibly related to historical exposure to dioxin contamination in food or environmental media at levels higher than current background levels.

Serum concentration/total TEQ and BMI

According to both parametric and nonparametric tests, BMI was not associated with total TEQ. A few congener-specific concentrations were significantly associated with BMI, but no distinct trends surfaced.

Serum concentration/total TEQ and weight change

Spearman rank analyses found no relationships between 2001 participants' total TEQ and self-reported weight change. A few congeners, however, had significant negative correlations between congener concentration and weight gain. In other words, individuals who reported losing weight between serum tests had higher concentrations of these two congeners than those who reported either no change in weight or a weight gain.

Linear regression analyses indicated few significant associations between weight change and total TEQ or congener-specific concentrations. Results were not consistent when looking at individual cohorts or sexes.

In a steady state, dioxins equilibrate in different areas of the body based on the tissue's lipid content. Adipose tissue concentrations vary in a manner inversely proportionate to the mass of the adipose tissues (Sullivan and Krieger 2001). Therefore, increases in weight may be associated with decreases in dioxin concentrations. Some individuals who reported gaining weight between serum tests had lower congener concentrations than those who either lost weight or had no change in weight. This pattern was not found consistently when analyzing total TEQs in the 2001 EI participants. Therefore, self-reported weight change was not a large contributor to the total dioxin TEQ change or to the change in most congener-specific concentrations. Further analyses, such as physiologically based pharmacokinetic (PBPK) modeling, may provide useful insight to this relationship.

Serum concentration/total TEQ and sex

A review of results from all statistical tests showed no significant associations between total TEQ and sex. Linear regression and GLM analyses, however, identified a few congeners significantly lower in males.

Although no sex-specific significant statistical associations were found, in the 2001 sampling females tended to have higher dioxin TEQs than males. A similar trend was observed between the females and males in the 1997/1998 cohort. In 2001, females had mean and median total

TEQs of 89.9 ppt and 73.9 ppt. Males had mean and median total TEQs of 41.1 ppt and 33.5 ppt. In this investigation females were slightly younger (mean = 55.8 yrs) than males (mean = 58.5 yrs).

Similarly, by concentration alone, the females tested in both 1998 and 2001 had a higher mean dioxin concentration than did the males (Tables 3 and 5). Between the two sampling events, the men had a significant decrease (nonparametric and parametric analysis) in total dioxin concentration, and the females did not. The 1998 cohort had dioxin concentrations approximately two times higher than the1997 cohort. This finding may be a reflection of the small number of individuals in the 1997 cohort.

By concentration alone men had a significant decrease; this is supported by decreases in some congeners in the men only. For example, by GLM analysis the serum changes were greater in males than in females for three congeners (2378D, 12378D, and 123789D). Linear regression results indicated that in 2001 males had significantly lower mean levels of 2378D, 123789D and OCDD.

In comparison, in Seveso, Italy where a large population was exposed to quantities of 2378D following an industrial accident, women tended to have higher 2378D levels than did men. This difference persisted after adjustments for age, BMI, smoking, and other factors (Landi et al 1998). Repeated measurements in some residents have shown that the half-life of serum TCDD is longer for women than men (Needham et al 1997/98). While no evidence for sex differences in exposure was documented in the Seveso population, we do not know if the women in this investigation had different levels of exposure (Landi et al 1998).

Variations in metabolism, elimination, percent body fat or hormone-related factors may have accounted for this finding in the Seveso population (Landi et al 1998). Perhaps some of these factors may account for the significant mean decrease by concentration in men and not in the women between sampling events in the EI population. Women may retain dioxin for a longer time period because of differences in metabolism or elimination, and thus they may have higher average levels than men.

PCDDs contributed more to the female's total TEQ compared with males; and males had more PCDFs and coplanar PCBs. Perhaps this is due to different exposure sources or physiologic differences in metabolism and elimination. Most studies have not documented sex differences in congener patterns. Most study populations consist mostly of occupational exposure in men. This may explain the lack of sex differences in much of the dioxin literature.

Serum concentration/total TEQ and gardening

Little association was found between self-reported gardening and total TEQ or total TEQ changes in the EI population. Some congener-specific concentrations and concentration changes were associated with gardening, but there was little consistency in findings among all participants as well as by cohort and sex.

The pattern of degradation or breakdown of dioxin congeners differs in humans and in the environment. These differences, however, are not well understood. This lack of understanding of dioxin congener degradation, combined with the small sample size in the exposure investigation, had significant limitations in determining the effect of gardening on dioxin body burden. In addition, many participants (59%, 13/22) moved between their first and second serum dioxin test and therefore were not gardening in the same location. Nevertheless, current soil and indoor dust

dioxin levels in EI participants' homes are well below ATSDR's health-based screening guidelines. Thus the idea that current gardening practices are a significant dioxin exposure pathway in EI participants is unlikely.

Serum concentration/total TEQ and fish consumption

Total TEQ, or changes in total TEQ and self-reported consumption of locally caught fish, showed no significant associations. Only one congener was significantly associated with fish consumption. Using this limited information and our limited fish sampling, an association between self-reported consumption of locally caught fish and dioxin body burden cannot be addressed.

Serum concentration/total TEQ and crawfish consumption

Crawfish are frequently consumed by residents in the Mossville and greater Lake Charles communities. The majority of EI participants (68.2%, 15/22) reported consuming locally caught crawfish. Participants did not provide crawfish samples in the follow-up exposure investigation, so comparisons between total TEQ and congener-specific levels in crawfish and the participants was not feasible. The use of a crude demographic data to estimate actual dietary intake makes difficult any quantification of crawfish consumption's contribution towards total TEQ and congener-specific changes. GLM analyses indicated significant associations between increased congener concentrations and crawfish consumption in the 1998 cohort. Still, in the 1997 cohort some congener concentrations were significantly decreased in participants reporting crawfish consumption. A representative sample of dioxin levels in local crawfish would assist in ascertaining if crawfish are a significant current source of dioxin exposure in the community.

Serum concentration/total TEQ and other demographic variables

No significant associations were found between total TEQ or the change in total TEQ and other demographic variables, including the age of participants' homes, the amount of time between biological sampling, or participants' residence time at their current location. Very few congener-specific concentrations or concentration changes were associated with the age of participants' homes, the amount of time between biological sampling, and participants' residence time at their current location.

Associations between Environmental Media Results

Many significant associations were found among environmental samples taken from in and around participants' homes. Numerous congener concentrations in indoor dust, attic dust, and surface soil were strongly associated. These results fit with the assumption that soil contamination in the yard can be tracked in to the house.

Reference Group Comparisons

The 2001 EI serum dioxin results were compared to multiple reference populations. These included a regional group sampled in Lafayette Parish, Louisiana in 2002, as well as two national reference populations. National reference data were obtained from a meta-analysis of serum dioxin data gathered in three states during 1995–1997 and population-based samplings conducted by NCEH in 1999–2000 and 2001–2002. In all of these comparisons, the 2001 EI group generally had higher

- total dioxin concentrations,

- congener-specific concentrations,
- total TEQs, and
- age-stratified total TEQs.

Regional comparison

Because congener-specific and age-stratified data were available for all participants, the comparisons using Lafayette Parish resulted in the most robust evaluations. These comparisons indicated that mean total dioxin concentrations and mean total TEQs in the EI group were higher than in Lafayette Parish. The age-stratified total TEQ comparison (Table 43) showed similar total TEQs in the younger age quartiles (15–29 years and 30–44 years) and much higher levels in the older age quartiles (45–59 years and 60+ years). The notable differences in age-stratified results may reflect increased historical exposures in the EI participants age 45 years and older. The EI group had a higher frequency of participants in the older two age quartiles, while Lafayette participants were equally distributed among all age quartiles. This may partly explain the increased mean concentration and the total TEQ measurements in the EI population. Regardless, this comparison indicated that older EI participants have elevated blood serum dioxin levels when compared to Lafayette Parish residents. When analyzing congener-specific contributions to mean concentration and mean total TEQs in the EI and Lafayette populations, no striking patterns emerged. Generally, dioxin congeners were the primary contributors to mean total concentrations and mean total TEQs, while furan and coplaner PCB congeners had less influence (Tables 44 and 45). Differences in some mean congener concentrations and TEQ contributions were observed, but when considered individually, none explained the EI population increases.

National comparisons

One of the national comparisons used data collected during dioxin investigations conducted in three states. This evaluation compared total TEQs between the two populations using the same age quartiles as the Lafayette comparison (Table 46). The younger age quartiles (15–29 years and 30–44 years) in the 2001 EI group and the three-states comparison population had similar total TEQ levels. As with the Lafayette comparison, however, the 2001 EI group had higher total TEQs in the older age quartiles (45–59 years and 60+ years) than the three-states comparison population.

Finally, the 2001 EI group was compared to population-based dioxin congener concentration data compiled by NCEH. Due to low sample volumes, the 1999–2000 NCEH data only reported 95th percentile concentrations for six congeners. For these six congeners, all 95th percentile concentrations from both the initial sampling in 1997/1998 and the 2001 follow-up EI sampling were above the comparison population's 95th percentile concentrations (Table 47). These results indicated that mean concentrations for these six congeners were typically higher in the EI group than in the general population. Still, the extent of this elevation could not be quantified because low sample volumes and a high number of nondetects generated problems in calculating statistical distributions within the NCEH dataset. The 2001–2002 NCEH data reported 95th percentile concentrations for 10 congeners. For these 10 congeners, all 95th percentile concentrations from both the initial sampling in 1997/1998 and the 2001 follow-up EI sampling were above the comparison population's 95th percentile concentrations (Table 48). These results indicated that mean concentrations for these 10 congeners were typically higher in the EI group than in the general population. As with the 1999–2000 sampling data, the extent of this elevation

could not be quantified, given that low sample volumes and a high number of nondetects generated problems in calculating statistical distributions within the NCEH dataset.

Congener Half-life Evaluations

Three congeners were used to evaluate temporal changes in participants' blood serum dioxin concentrations. This evaluation quantified mean concentration changes for each congener and compared these changes to expected decreases based on half-life calculations. This was a crude method for quantifying expected concentration changes because it did not control for many variables that affect dioxin concentration in the body, and it also did not account for participants' background exposure to dioxin between sampling events.

In general and based solely on half-life calculations, participants' congener concentrations did not decrease at expected rates. The mean concentration decrease for two of the congeners with longer half-lives (2378D and 12378D) was less than 1%. Expected concentration decreases based on half-life estimates for these two congeners ranged from 12.0–41.2%. The congener with a short half-life (1234678D) had a mean concentration decrease of 21%, below the expected decrease range of 25.4–64.3%. Most participants had decreasing concentrations for the three congeners, but these decreases did not correspond with expected values based on reported half-lives in the body.

Many variables influence congener-specific blood serum dioxin concentration changes. Obviously, contributions from exposure to any background level of dioxin between sampling events altered participants' blood serum dioxin concentration. Other variables, however, impact the ability to effectively remove these contaminants and thus influence half-lives in the body. These variables include the extent of existing concentrations in the body, individual metabolism, percent body fat, smoking status, sex, age, and changes in body weight and body fat (Flesch-Janys 1996; Landi et al. 1998; Michalek et al. 1996; Michalek and Tripathi 1999; Ott and Zober 1996; Van der Molen et al. 1998; Wolfe et al. 1994). Also, some investigators have recently questioned the constant elimination rate assumptions used in this comparison [Michalek et al 2002; Van der Molen et al 1998].

The majority of dioxin contamination in most people is primarily attributable to dietary influences (Fries GF 1995; Fürst P 1993). Dietary exposures result from ingesting low-level quantities of dioxin in animal fats including fish, meat, and dairy products. Because of ubiquitous background exposures in the general population, the assumption that exposure investigation participants were not exposed to any dioxin since their first blood sampling is problematic. The inability to calculate the contribution of dietary dioxin to serum TEQ levels in the EI population was a limiting factor in this evaluation.

Limitations

Sampling

The 2001 follow-up exposure investigation did not sample all food sources—the most common route of dioxin exposure. Sampling was conducted in late November when several locally raised or locally caught shellfish, including crab, crawfish, and shrimp were not in season. The lack of data on these high-fat components of the local diet limited evaluations of their potential contribution as dietary dioxin sources. Sampling was conducted during the fall when many gardens were dormant, so the assessment of dioxin contamination in locally raised fruits and vegetables was limited. Most fruits and vegetables have, however, a very low fat content and

therefore represent a minimal source of exposure. This observation was supported by the extremely low concentrations detected in the few vegetable, fruit, and nut samples collected during the investigation.

Sampling of attic surface dust was undertaken to determine if it was an indicator of historic air dioxin deposition. Because historic air emissions were difficult to quantify retrospectively, attic dust provided some insight into past air emissions. Yet no comparison data or health guideline information for attic dust sampling were available, so subjects were informed prior to their participation that these results could not be used to determine risk or predict the potential for adverse health effects.

Some participants from the original 1997 and 1998 biological samplings were not included in the 2001 follow-up exposure investigation for various reasons. Of those eligible subjects who were not included in the follow-up investigation, one chose not to participate, a few died since their initial participation, and some had moved out of the area and could not be located. One person was willing to participate but was excluded because preexisting medical conditions precluded that person's ability to safely donate the required quantity of blood.

Analysis

Many problems were encountered in the statistical analyses of biological and environmental sampling data obtained during the 2001 follow-up EI. Some of the major obstacles included

- statistical analyses of a small data set,
- analyzing dioxin concentrations reported as nondetects,
- comparing environmental and biological sampling results that did not include the same set of dioxin congeners, and
- the transformation of log-normally distributed data.

The laboratories reported some dioxin congener concentrations as nondetects. For internal comparisons of initial and follow-up blood serum dioxin concentrations among EI participants, all nondetects were assigned a value of zero. But for external comparisons to various reference population data, nondetects were assigned values equal to half the limit of detection, given that this was how nondetects were treated in most of the reference data sets. These different substitution methods for nondetect values altered many individual results, as well as group measures of central tendency and variability.

A few dioxin congeners, specifically the coplanar PCBs, were quantified in environmental samples but were not analyzed in biological samples. This created problems when comparing congener patterns among environmental and biological samples. Another inherent difficulty in comparing congener patterns in environmental and biological samples is the dissimilar rates of congener degradation. That is, dioxin congeners have different half-lives depending on whether they are being metabolized in humans or degraded in the environment. Therefore, even if a single dioxin source had contaminated biological and environmental mediums simultaneously, over time the congener profiles for these mediums would become more and more dissimilar.

Many of the environmental sampling datasets obtained through this investigation were log-normally distributed. Therefore, these data were log-transformed prior to statistical analysis. Log transformation introduced dilemmas: concentrations with a value of zero could not be correctly

transformed. This problem was also apparent when substituting zero values for any nondetectable concentrations.

Interpretation

This exposure investigation was not conducted in a population-based sample of area residents. Therefore, ATSDR cannot use this information to make generalizations regarding blood serum dioxin concentrations in all residents of Mossville or Calcasieu Parish. The initial blood sampling events in 1997 and 1998 were intentionally biased to include individuals who were more likely to have elevated blood serum dioxin concentrations based on their age or proximity to potential industrial sources. Consequently the follow-up sampling of these participants was also biased by the initial selections.

Many epidemiological studies of dioxin's effects at low-level, chronic exposures are unfortunately, inconclusive. Studies on subjects with high exposure levels have reported weak or conflicting findings. Also, several of these analyses were based on occupational cohorts or acute events resulting from industrial accidents, making them inappropriate comparisons for this investigation. The lack of epidemiological evidence for low-level exposures makes difficult the assessment of the real public health impact associated with the concentrations observed in the exposure investigation participants.

In the original 1997 cohort and in both the 1998 and 2001 follow-up EIs, 80 milliliters of blood were collected from most participants. This large sample volume resulted in very low detection limits for each congener. Smaller blood sample volumes were collected for comparison or reference group populations. This difference in sample volumes resulted in higher congener-specific and overall dioxin detection limits for the comparison populations. Therefore, nondetects or so-called zero values were more frequently encountered in the reference populations. When total TEQ values were calculated for the population-based reference groups, the prevalence of nondetects artificially decreased these reference values. The amount of bias introduced by these differences in detection limits is unknown and not quantifiable.

Any results of statistical analyses on a small data set should be interpreted with caution. Many significant associations found in this report are considered exploratory or hypotheses-generating by ATSDR.

Health Effects

The health significance of the blood dioxin concentrations measured in this investigation is unclear. The two primary clinical health effects associated with human exposure to high dioxin concentrations through occupational or accidental exposures include chloracne and transient, mild hepatotoxocity (Dickson 1993; ATSDR 1998). Still, no participants in this investigation have dioxin concentrations at levels high enough to illicit these effects.

Most human epidemiological data are based on occupational exposures or accidental releases. These data are also usually related to elevated exposures to one dioxin congener, 2378D. The general population is typically exposed to a mixture of dioxin congeners; effects from specific congeners are, therefore, difficult to evaluate independently (Dickson 1993; ATSDR 1998). Many scientists believe, however, that the biological mechanisms mediating the effects of 2378D are similar for other dioxin congeners.

Non-cancer health effects

Humans appear to be less sensitive to dioxin than are other species (Dickson 1993; Neubert 1997/98). A number of non-cancer health effects have been associated with dioxin exposure. The EPA dioxin reassessment concluded that further study is needed before a causal relationship between dioxin and many adverse health outcomes can be established (EPA 2000). The health effects needing further study include circulatory and heart diseases, diabetes, reproductive and developmental problems, and immunologic disorders. Human studies have not demonstrated consistent findings for many of these adverse effects, and many of these studies are difficult to interpret due to inadequate exposure data or multiple chemical exposures.

Occupational

In studies for which exposure data are available, 2378D levels associated with chloracne were significantly higher than those observed in the EI population. For instance, in humans exposed to dioxin in the workplace, chloracne was observed at body concentrations of 95 to 3000 ng dioxin/kg body weight (DeVito 1995). This corresponds to lipid-adjusted, blood dioxin concentrations of 432 to 13,400 ppt (ATSDR 1999). All of the blood dioxin concentrations in the follow-up EI population were well below this range with a maximum total TEQ of 245.2 ppt and a mean total TEQ of 61.0 ppt.

Environmental

When studying environmental dioxin exposures in the general population, the industrial accident in Seveso, Italy provides some useful comparisons. The occupational literature often reports exposure to only male workers; therefore, comparisons to the general population can be difficult. The Seveso incident is particularly useful because it documented environmental dioxin exposure to residents of different ages and sexes. But one limitation of relying on the Seveso population for a comparison is the acute nature of the exposure, which differs from the presumed long-term, chronic exposure in the EI population.

In Seveso, Italy a large population was exposed to 2378D following an unintentional industrial release in 1976. Blood concentrations of 2378D in the exposed population ranged from 828 ppt to 56,000 ppt (Mocarelli et al. 1991). Chloracne was the primary health effect observed in this population, and it was the only clinical alteration positively associated with 2378D levels in soil. Severe chloracne was observed in six children, with 2378D levels ranging between 12,100–56,000 ppt while a milder form of chloracne was observed in 3 children with 2378D levels of 828 ppt, 1,690 ppt, and 7,420 ppt. That said, however, chloracne was not present in a 15 year-old boy with a 2378D level of 10,400 ppt, nor was it observed in adults with 2378D levels ranging from 1,770–9,140 ppt (Mocarelli et al 1991). These results indicate that 2378D-induced chloracne is not dose-dependent, and that chloracne may be a more sensitive endpoint for children. In the 2001 investigation, the maximum serum TCDD concentration was 25.5 ppt—orders of magnitude below any level at which chloracne was observed in Seveso adults. Even when using total TEQ as a potential exposure metric to predict the occurrence of chloracne, the highest value in the 2001 EI population was 245.2 ppt in an older adult, a concentration well below levels in Seveso adults who did not exhibit this condition.

Liver function tests analyzed in children 6 years after the Seveso accident found that most of the liver parameters were slightly elevated—but not abnormal—and returned to baseline within 3 years after the initial exposure (Mocarelli et al 1986). One finding of interest in the Seveso

population is not well understood; a larger number of females were born to parents who had been exposed to 2378D in Seveso (Mocarelli 1996). The mechanism for this observation is not known. This change in sex ratio was observed until 1984. Between 1984 and 1994 this difference was no longer significant (Mocarelli 1996).

Cancer health effects

2378D has been designated as a human carcinogen by the International Agency for Research on Cancer (IARC) [IARC 1997]. Other dioxin congeners have not been classified because of limited epidemiologic information. Because the other congeners are thought to have a similar mechanism of action, they are often discussed in a similar manner to 2378D. The IARC classification is based on sufficient evidence in animals, limited evidence in humans, and supporting evidence that 2378D has a common mechanism of action in various animals and humans. In general, 2378D is not considered a genotoxic carcinogen; instead, it is thought to be a cancer promoter (EPA 2000).

Occupational

In occupationally exposed workers, an increase in cancer incidence has been associated with dioxin body burdens of 109 to 7000 ng dioxin/kg body weight (DeVito 1995). These concentrations correspond to lipid adjusted blood dioxin levels of 495 to 31,800 ppt (ATSDR 1999). These levels exceed the blood dioxin levels in the EI population which had a blood dioxin range of 4.1–245.2 ppt.

Environmental

The Seveso population has been followed since the initial exposures in 1976. A 20-year mortality study did not find an overall increase in all-cause and all-cancer mortality (Bertazzi et al, 2001). No statistically significant increases in cancers were observed in the highest exposure area, Zone A. Exposure classification was based on soil concentrations in different zones at the time of the incident, not blood dioxin levels. In Zone B, where exposure was lower, rectal and lymphatic/hemopoietic cancers were significantly elevated. Some human studies document weak associations between 2378D and soft-tissue sarcoma and non-Hodgkin's lymphoma (ATSDR 1998). But many of these human studies do not provide adequate exposure data or are confounded by other chemicals. In particular, the increased risk for these cancers is usually associated with high exposures in occupational settings (CDC 2003). Continued, long-term follow-up of the Seveso population may provide further insights.

Although only one dioxin congener, 2378D, is classified as a human carcinogen, the risk of cancer in an individual cannot be predicted based on their body level. Cancer is not one disease. Each cancer has a different set of risk factors. And having a risk factor does not mean that a person will get cancer. Multiple factors play a role in a person getting cancer including genetics, infections, age, lifestyle (e.g., diet, smoking), and other health conditions. Current scientific information supports the conclusion that cancer cannot be predicted from the blood dioxin levels in the EI participants, both as a population and individually.

Summary

Mean dioxin concentrations in the EI population were elevated when compared to different reference populations. When evaluated individually, however, only older participants had elevated blood dioxin levels. The few younger participants less than 45 years of age had normal

blood dioxin levels when compared to various reference populations. The elevated dioxin levels documented in older participants do not approach concentrations at which the known clinical health effects of chloracne and liver function alterations occur. Many cancer and non-cancer health effects potentially associated with dioxin exposure cannot be predicted in the EI population. Similarly, an individual EI participant's risk of developing adverse health effects cannot be predicted from the blood dioxin levels measured in this investigation.

Excluding fish samples, significant dioxin contamination was not detected in the limited environmental sampling conducted during this investigation. The lack of elevated dioxin concentrations in participants' home environments, combined with the skewed age distribution of participants with elevated blood levels, supports the conclusion that elevated blood dioxin levels in older participants are likely associated with historical exposures. Therefore, current dioxin exposures in the Mossville community are most likely similar to background exposures in population of the United States generally.

Conclusions

- Blood dioxin concentrations were elevated in many of the 2001 follow-up exposure investigation participants.
- Blood dioxin concentrations decreased in most participants between their initial and follow-up samplings.
- Blood dioxin concentrations were primarily elevated in older participants.
- The elevated blood dioxin levels in older participants are likely attributable to historical dioxin exposures.
- The blood dioxin concentrations found in the 2001 follow-up exposure investigation participants are unlikely to produce the known clinical health effects of chloracne and elevated liver enzymes.
- Blood dioxin congener profiles differed from environmental congener profiles gathered during this investigation.
- Dioxin concentrations in some fish were at levels of concern.
- Dioxin concentrations in surface soil, indoor dust, well water, and homegrown fruit, vegetables, and nuts were not at levels of concern.

Recommendations

- Generate physiologically based, pharmacokinetic models to better understand changes in participants' blood dioxin concentrations.
- Encourage residents to follow fish advisories currently in effect in their areas.
- Continue investigating potential sources of historic and current dioxin exposure.

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