

# **Attachment F**

## **Responsiveness Summary**

The MDCH presented the Pilot Investigation Protocol to the MDEQ CAP on December 3, 2003. Public comments were accepted through February 6, 2004. Comments and MDCH responses are provided in this Attachment.

## **PILOT EXPOSURE INVESTIGATION RESPONSIVENESS SUMMARY**

**1. Comment:** It is our understanding that both state and local agencies are obligated to reference Section 26 of the Public Health Code when conducting studies on human health subjects or environmental health needs. We recommend appraising stakeholder and the general public that not only are state and local public health agencies committed to investigation dioxin exposure to the residents along the Tittabawassee River downstream from the city of Midland, but by statute are required to conduct such investigations.

**Response:** The intent of this comment is not clear. The Michigan Department of Community Health (MDCH) is not aware of any specific requirement to conduct Exposure Investigations generally or specifically in the flood plain of the Tittabawassee River beyond the general requirements for the protection of public health contained in the Public Health Code. MDCH is not aware of any requirement to reference Section 26 in a protocol of this kind, but has complied with the general requirements contained in Section 26 in seeking a determination from the MDCH Institutional Review Board (please the response to the next comment).

**2. Comment:** We suggest that a statement indicating that the research will be conducted in accordance with MDCH Policy 0012 and the Code of Federal Regulations, 45CFR 46.101-0124 or other relevant policy be added. We suggest locating this statement on page 19.

**Response:** MDCH will conduct the Pilot Exposure Investigation (PEI) in accordance with all applicable State of Michigan and federal regulations and policies. The MDCH Institutional Review Board (IRB) exempted the PEI from review on the basis that it is a public health intervention rather than “research.” A copy of the IRB determination is provided in Attachment G. MDCH disagrees with the suggestion that a statement to this effect be included in the Informed Consent form in Attachment A. This document is intended to provide information to a potential participant in a way that is comprehensive yet easy to understand. References to State of Michigan policies or federal regulations would not contribute to this intent and no change has been made to the protocol.

**3. Comment:** We would suggest referenced of supporting data or studies be included that substantiates body burdens or health affects from dioxin as a result of skin absorption. Also, what have the supporting studies indicated regarding human exposure from skin absorption?

**Response:** A reference to the 1998 ATSDR Toxicological Profile for Chlorinated Dibenzo-*p*-dioxins has been added to the Soil Sampling section. The citation is provided in the PEI Reference section and the commenter is directed to pages 188-193 of the Profile.

**4. Comment:** With regard to the questionnaire: Combine questions 4 and 5.

**Response:** Questions 4 and 5 are consistent with the recommendations from the United States Office of Management and Budget published in the Federal Register July 9, 1997

(Vol. 62, No. 131: 36847-36946). In Directive 15, OMB recommended collecting race and ethnicity data through two separate questions, with ethnicity collected first. No change has been made in the questionnaire.

**5. Comment:** The eligibility questionnaire should ask whether the targeted participant has property that abuts to the Tittabawassee River or property that is frequently flooded.

**Response:** This question is not needed for the PEI since it is already known that all potential participants live in the flood plain of the Tittabawassee River and frequent flooding was a prerequisite for property selection. However, this a valid question for any future larger study that may be conducted in the area and will be added to the questionnaire before the conduct of such a study.

**6. Comment:** Eliminate questions 36 & 37 as irrelevant or combine questions 36 through 42 that would compile a work history resume, occupation disclosure, length of service but exclude the name of the company.

**Response:** MDCH does not agree that these questions are irrelevant. The answers will assist MDCH in understanding any ongoing occupational exposures to dioxins. No change has been made in the protocol.

**7. Comment:** Questions 43 through 52 should also exclude the company or employer name.

**Response:** See response above.

**8. Comment:** Questions 70 through 73 – change the wording of sport “caught” wild game to “kill” wild game. Hunters do not routinely catch prey.

**Response:** The wording “sport-caught” has been revised to “locally harvested” or “wild” as appropriate.

**9. Comment:** Add to the questionnaire, heating system type – forced air or hot water. Add to the questionnaire whether the home has central air conditioning. This could be useful to reducing the risk of exposure should elevated levels of dioxin in dust be attributed to open windows.

**Response:** While these may be valid questions, they are unnecessary because indoor dust sampling will provide actual measurements of dioxins in household dust to which people may be exposed. No change has been made in the protocol.

**10. Comment:** Add to the questionnaire, recreational activities of the participant in the river such as wading, swimming, skiing, tubing, etc. and frequency of activity. Add a time study of outdoors activities and what type of outdoors activities take place on the property.

**Response:** While questions concerning outdoor activities might yield useful information, the questionnaire is already long and potentially tedious for the participants. Therefore,

MDCH has not included additional questions concerning activities and instead chose to focus on fish/game consumption and occupational exposure since these activities are expected to have a greater effect on serum dioxin levels.

**11. Comment:** Add land type that surrounds the participants property, such as woods, meadows, pasture, agricultural production, etc.

**Response:** Consistent with the response above, no additional questions were added to the questionnaire.

**12. Comment:** Obtain additional information from the participants on the use and amount of pesticides, herbicides, or fungicides in or around the home.

**Response:** Consistent with the response above, no additional questions were added to the questionnaire.

**13. Comment:** How do we plan to determine if health effects are the result of exposure to the dioxin contaminants in the Tittabawassee River flood plain? What information or advice will be provided to the participants if health problems associated with dioxin exposure are discovered?

**Response:** The PEI will only tell us what level of dioxins each person has in his/her blood. The PEI is not intended to answer questions related to health effects. The commenter is referred to Attachment A, Informed Consent, What the Investigation Will NOT Tell Us, page 18).

**14. Comment:** What levels of body burdens will be used to determine if the participant is considered to be exposed?

**Response:** Upcoming NHANES data are expected later this year. If those data are not usable or not timely, MDCH and ATSDR have proposed to compare PEI results to data from other states where serum dioxin levels have been investigated in people with no known exposure to dioxins beyond background. The commenter is referred to the Biological Sampling section for a discussion of the interpretation of the data on page 13.

**15. Comment:** Will local health departments be informed of the results of the exposure investigation prior to its release?

**Response:** All individual sample results will be conveyed first in writing to the participants. The MDCH/ATSDR report that will summarize the results of the PEI will be provided to all stakeholders at the same time. As a courtesy to the local health departments, MDCH will provide advance notice of the release of the report.

**16. Comment:** Regarding the Scientific Advisory Group on page 2: Who will make the determinations of the nominated scientists? Why are only Dow Chemical and the Petitioners being asked to nominate scientists? How will you assure a good cross section of scientists who will base decisions solely on the scientific data?

**Response:** The Scientific Advisory Group referenced on page 2 will only be formed if MDCH or ATSDR move forward on a larger Exposure Investigation. These issues will be addressed at that time.

**17. Comment:** Are there specific actions levels or criteria for dioxins in indoor dust?

**Response:** No, there are no action levels for indoor dust. The commenter is referred to the Indoor Dust Sampling, Interpretation, on page 12.

**18. Comment:** The discussion regarding bioavailability of dioxin and the relationship to soils is well written and needs to be emphasized. Dioxin in soil or dust may or may not cause a relationship to dioxin in the body.

**Response:** Comment noted.

**19. Comment:** There are concerns about the nonrepresentative sample from five states. Are the background levels of this sample group consistent with those in Michigan?

**Response:** There are no data concerning background serum dioxin levels in Michigan. In the absence of such data, MDCH and ATSDR have proposed to compare PEI results to data from other states where serum dioxin levels have been investigated in people with no known exposure to dioxins beyond background.

**20. Comment:** What will the course of action be if body burdens are not found to be elevated?

**Response:** Participants will be notified that they do not have elevated serum dioxin levels. Residents will be advised to continue to follow the Michigan Fish Advisory as well as site-specific recommendations to limit future exposure.

**21. Comment:** Provide a place for “email address” in the Participant Information areas on page 37 of the Investigation Questionnaire.

**Response:** A place for an e-mail address has been added to question 8.

**22. Comment:** “Miscellaneous” is misspelled on page 38.

**Response:** Thank you for the correction

**23. Comment:** Under “Occupational History”, this section would be more useful if it was more like a job application and contained key job history (employer, from date, to date, position, duties). Suggest rewrite of questions 28-42.

**Response:** Questions 29-42 collect information on the participants "usual" or "longest-held" occupation and industry of employment. These questions are based on those used by the National Center for Health Statistics in the Occupational Health Supplement to the

National Health Interview Survey (Vital Health Stat 10(186) 1993), and are similar to questions used in the NHANES and the categories used on standardized death certificates. They have been used successfully in a number of occupational epidemiology studies.

The suggestion is to instead collect a comprehensive employment history for each individual. This was decided against because of the burden on the participant (it can take some time and effort to reconstruct an individual's lifetime employment) as well as the difficulty in processing and utilizing such information to estimate lifetime probability of exposure to dioxins due to occupation. Instead, it was decided to give the subject a list of occupations with high likelihood of dioxin exposure (questions 43-52), and to be comprehensive, to ask about "usual" occupation and industry. In this PEI, occupation is being treated as a potential confounder of the relationship of residential contamination to body burden of dioxin, and not to try to quantify how much of an individual's body burden is related to occupational history vs. residential exposure. Therefore, the level of detail from a lifetime occupational history was not felt to be necessary, given how burdensome it is to collect.

**24. Comment:** “Solid is misspelled in question 51.

**Response:** Thank you for the correction.

**25. Comment:** Question 88 appears confusing regarding eating home-raised meat. Suggest asking, “how often consumed” and “how much consumed.”

**Response:** MDCH agrees that the language in question 88 is somewhat awkward. However the suggested language does not provide clarification. Since one purpose of the PEI is to test the questionnaire, MDCH will administer the questionnaire as proposed but note whether participants have difficulty understanding the question.

**26. Comment:** The Pilot has apparently begun while the protocol is still open for public comment and before it has been finalized, which could imply that the protocol will not be followed and public input not considered.

**Response:** Consistent with the PEI protocol, soil samples were collected by the MDEQ in the summer and fall of 2003. These samples serve the dual purpose of furthering the MDEQ investigation into the extent of dioxin contamination in the flood plain of the Tittabawassee and providing data for participant selection for the PEI. MDCH has not yet begun additional PEI data gathering activities. Please see the revised Timeline on page 7.

**27. Comment:** The processes for decision-making needs to be better defined, and consider the limitations of background levels to be used for comparison and acknowledge the value of a regional control group.

**Response:** As per the stated purposes of this pilot exposure investigation (providing information on the levels of dioxin in soil, dust, and blood for 25 residents and testing the sampling criteria, questionnaire, and sampling methods prior to any larger effort), the processes outlined for decision-making are appropriate. MDCH will consider the limitations of background levels and acknowledges the value of a regional control group.

**28. Comment:** MDCH states that blood serum dioxin results greater than the 90<sup>th</sup> percentile of the normative data will be considered to be elevated. It is unclear how this value was chosen.

**Response:** The Pilot Exposure Investigation provides information on serum dioxin levels for 25 residents of the flood plain and evaluates the blood sampling and interpretation for the larger investigation. In absence of current age-specific reference levels for blood dioxin TEQs, the MDCH plans to define elevated serum dioxin TEQs as those levels greater than the 90<sup>th</sup> percentile of the best available normative data. Laboratories often establish their reference range by adding and subtracting two standard deviations to the mean. This results in a 5<sup>th</sup>, 50<sup>th</sup>, and 95<sup>th</sup> percentiles. The 90<sup>th</sup> percentile we propose to use as elevated is more conservative than the 95<sup>th</sup> percentile. This value will be evaluated in the Pilot Exposure Investigation before implementation of a larger investigation.

**29. Comment:** The NHANES report, published by the CDC in January of 2003, will not provide an adequate reference for comparison to the Pilot Studies.

**Response:** MDCH did not propose to use the January 2003 NHANES report (see page 13) and is aware that these data are not useable as a comparison. Upcoming NHANES data are expected later this year. If those data are not usable or not timely, MDCH and ATSDR have proposed to compare PEI results to data from other states where serum dioxin levels have been investigated in people with no known exposure to dioxins beyond background.

**30. Comment:** While comparison of background dioxin blood levels from other states may be useful, it would not include consideration of regional variability and may further result in misinterpretation of the results. Given regional variations have been reported in some studies and that there are differences in diet, it would be useful to have a local comparison group.

**Response:** The commenter does not define “local” when referring to a comparison group. People living in areas close to but outside of the Tittabawassee River flood cannot be considered to be unexposed to dioxin contamination in the river or near-by upland soils. People living in these areas may have visited parks where soil is contaminated or eaten game, fish, or domestic animal products that may contain dioxin contamination from the flood plain. No change has been made in the protocol.

**31. Comment:** An Institutional Review Board (IRB) should be consulted prior to the conduct of the study to ensure ethical treatment of human subjects.

**Response:** The PEI was exempted from review by the MDCH IRB on November 11, 2003 on the basis that it is a public health intervention rather than “research.” A copy of the IRB determination is provided in Attachment G.

**32. Comment:** Statistical measures to evaluate Type I and II errors, the underlying distribution and variance of the data, and other statistical considerations should be considered.

**Response:** MDCH will take this into consideration if any statistical tests are conducted on the PEI data. Since the sample size is small ( $n = 25$ ), statistical tests will likely have little value. General comparisons of whether the individual levels found during the PEI are higher or lower than background serum dioxin levels will occur. MDCH and ATSDR have proposed to compare individual PEI results to data from other states where serum dioxin levels have been investigated in people with no known exposure to dioxins beyond background.

**33. Comment:** It is recommended that the Pilot include an appendix and use a protocol for discussions with residents regarding blood dioxin levels. It is important that study subjects have an opportunity to discuss their results with a physician.

**Response:** The Consent Form provides the opportunity for participants to request that their serum dioxin test results be forwarded to their physician. MDCH does not agree that a protocol is necessary for discussions with residents. The results and situation for each individual will vary and preclude the use of a predetermined protocol for discussions

**34. Comment:** Curriculum vitae including credentials and a list of publications should be appended to the protocol for all investigators.

**Response:** The inclusion of curriculum vitae is appropriate for a health study, but not for a preliminary exposure investigation. Curriculum vitae are not going to be included at this time; however, the names and contact information of the investigators are provided.

**35. Comment:** The statement that “Soil particles can also be inhaled and then absorbed from the lungs into the blood” should be deleted. Inhalation of soil/dust into the deep lung and the subsequent absorption of dioxin into the blood are neither proven, nor physiologically relevant. A more relevant route of exposure would be a component of incidental ingestion, which is addressed in the State soil standards.

**Response:** The commenter is directed to pages 188-193 of the 1998 ATSDR Toxicological Profile for Chlorinated Dibenzo-*p*-dioxins. The citation is provided in the PEI Reference section.

**36. Comment:** It is recommended that the language in the Soil Sampling Justification section that indicates that exposure “...can occur through skin contact...” be deleted or clarified.



**Response:** The commenter is directed to pages 188-193 of the 1998 ATSDR Toxicological Profile for Chlorinated Dibenzo-*p*-dioxins. The citation is provided in the PEI Reference section.

**37. Comment:** In the Indoor Dust Sampling Interpretation section, the statement "...the results of the dust sampling could be used to estimate the contribution of dust to overall exposure" should be deleted. There is no explanation of how such exposure will be estimated relative to overall exposures. The last sentence of the Indoor Dust Sampling Interpretation section should be deleted. Comparison of "...dust-sampling results...where ATSDR has conducted indoor dust sampling" would be of limited use, as there are many other factors that may impact results.

**Response:** This section has been changed to read, "There are no specific action levels or criteria for dioxins in indoor dust. However, the results of the dust sampling will be used to determine if dioxin levels in indoor living spaces have been affected by outdoor soil contamination."

**38. Comment:** Reference to dioxin congener analysis to "identify similarities and/or differences" between blood, soil, and dust results should be eliminated. Comparisons between soil/dust and blood congener profile [are] inappropriate, due to changes in the congener profile that occur from degradation, metabolic, and pharmacokinetic processes.

**Response:** MDCH has evidence to suggest that profiles of soil samples and profiles for eggs taken from chickens living on contaminated soil are remarkably similar qualitatively. This evidence is being documented in a health consultation that is undergoing review at ATSDR. Given the persistence of dioxins in the human body, it is reasonable to conclude that there might be a similar effect seen in human biological samples. No change has been made to the protocol.

**39. Comment:** Conclusions regarding the source of an elevated blood level can only be determined after careful analysis of a number of factors; e.g. age, body weight, recent weight loss, occupation, lifestyle, lipid levels, smoking and diet, particularly consumption of local fish. Only after these considerations along with a careful analysis of possible exposure pathways can conclusions regarding possible exposure sources be reliably made. This level of evaluation is beyond the scope of this study from both a design and statistical analysis perspective.

**Response:** These limitations are acknowledged in the section titled Limitations of the Phase I Pilot Exposure Investigation.

**40. Comment:** The Protocol expresses intent to provide recommendations for behavior modifications based on study results that are beyond the bounds or scope of the study design. The protocol asserts, "If the investigation results suggest the need, residents can use this information to modify their behavior to limit exposure to impacted media." This and similar statements should be eliminated.

**Response:** MDCH does not agree with the comment. If participants are found to have elevated serum dioxin levels, MDCH will provide educational materials to help these

affected people limit their exposure to dioxins. For example, if such a participant indicates that he/she has been consuming fish from the Tittabawassee River without consideration of the Michigan Fish Advisory, MDCH will provide a copy of the Advisory and will discuss with the participant how best to limit their exposure.

**41. Comment:** The commenter agrees with the statement that "...the Pilot Investigation cannot be generalized to all people living in the flood plain" and that "it will provide the opportunity to test the survey questionnaire and blood and indoor dust sampling methods."

**Response:** Comment noted.

**42. Comment:** The commenter recommends that the sentence "Investigations may provide information about the relationship, if any, between dioxin blood levels and exposure to dioxin in soil..." be deleted from the Limitations section.

**Response:** The sentence has not been deleted. A general comparison of the blood serum dioxin levels, the house dust, and the soil results may provide insight as to whether further investigation via a larger study should be undertaken.

**43. Comment:** There is no discussion of how correlations between soil, household dust, and blood dioxin levels will be conducted, although the protocol indicates that such a correlation is one possible conclusion of the study. The commenter recommends eliminating references to anticipated conclusions about dioxin sources.

**Response:** MDCH does not intend to conduct any statistical correlations of the PEI data. Instead, the data gathered will be used to qualitatively evaluate whether further investigations may yield results that could be quantitatively analyzed for correlations between sources of exposure and serum dioxin levels.

**44. Comment:** Comparison of TEQ levels reported in eggs by MDEQ to an FDA standard for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in the Site Description section (page 6) should be corrected or eliminated. The protocol compares dioxin levels in eggs reported for 17 dioxin and furan congeners to an FDA standard for TCDD alone. A more appropriate comparison would be between the FDA standard for TCDD and the levels in the eggs of TCDD alone.

**Response:** Use of the TEQ approach to assess the hazard posed by exposure to the mix of dioxins, furans and co-planar PCBs is accepted scientific practice. The commenter is referred to the ATSDR Interim Policy Guideline cited in the PEI Reference section (De Rosa et al, 1997). No change has been made in the protocol.

**45. Comment:** The commenter requests removal of a listing of products historically produced at the Midland, Michigan site that do not related to or have any bearing on the question of possible dioxin and furan exposure. The commenter suggests alternate language.

**Response:** The word “napalm” has been removed from the noninclusive list of products produced at the Dow Chemical Plant in Midland. Otherwise, the sentence has not been changed.

**46. Comment:** The protocol should indicate the background dioxin [soil] concentrations in Michigan based on MDEQ statewide data.

**Response:** It is not clear why information about background soil concentrations is needed in this protocol. The soil concentrations of interest are those that exceed the MDEQ Residential Direct Contact Criteria of 90 ppt, which is about 10 times higher than the average “background” concentration of dioxin in Michigan soils. No change has been made to the protocol.

**47. Comment:** In both the Soil Sampling and Indoor Dust Sampling Justification section the statement “Concentrations of total dioxin TEQs in soil will be used to quantify exposure potential” should be modified to “...will be used to indicate the potential for exposure.”

**Response:** The recommended changes have been made in the protocol.

**48. Comment:** Remove the statement in the Biological Sampling Justification “In vivo tests in animals can be used to estimate bioavailability of dioxin in soil and dust, however this introduces uncertainty into the exposure assessment and does not provide information concerning dioxin exposure from other pathways.”

**Response:** The following language has been inserted into the protocol: “*In vivo* tests in animals can be used to estimate bioavailability of dioxin in soil and dust, and may be useful later in analyzing the relative contributions of various exposure pathways to the body burdens shown by these human measurements.

**49. Comment:** More clarity is needed in the Property Selection and Scoring section regarding the scoring process and use of scoring information. Inadequate information is provided on how soil sampling will be conducted. For the best evaluation of possible exposure, an evaluation of the property use patterns and conduct of sampling in high traffic areas, e.g. exposed soil, from gardens or other high use areas is recommended.

**Response:** Soil sampling was conducted by the MDEQ following standard sampling protocols. As indicated on page 11, preference was given to locations where the property owner indicated high use.

**50. Comment:** Data Quality Objectives (DQO) should be outlined in the protocol and a Quality Assurance Project Plan for soil, dust, and/or blood sampling and analysis should be provided as an attachment to the final protocol.

**Response:** DQOs and a Quality Assurance Project Plan (QAPP) are not required as specific components of an ATSDR Exposure Investigation. However, the elements of data quality objectives are clearly described in the statements of the PEI objectives,

design, and application of specific methods. Although there is not a separate QAPP document, the elements of a QAPP are also included in the description of the sampling methodology, the application of established MDCH and MDEQ guidance and procedures, the citation of standard EPA analytical methods for analysis of dioxins in soil and dust, and description of CDC methods for analysis of dioxins in blood samples.

**51. Comment:** the questionnaire should include basic questions that are necessary to understand the results. There is no indication that previous residence locations outside the study area will be evaluated. No information is collected about dietary pathways that are documented to contribute to body burdens of dioxins (e.g. milk, cheese, other dairy products, pork, beef, chicken, fish, etc.).

**Response:** With the exception of home-produced foods, the levels of dioxins in these foods and individual consumption rates are expected to be similar to “background” levels in the normative populations. All “basic questions” MDCH believes necessary to understand the results of the PEI have been included in the questionnaire.

**52. Comment:** The Pilot is not adequately robust to make conclusions ...or comments regarding the broader community of residents.

**Response:** This limitation is acknowledged on page 14 of the PEI protocol.