Comment: Fourth full sentence, paragraph 1, page 3 is imprecise and misleading insofar as it implies that the dioxin levels in the Midland residential community were "elevated" above an applicable action level.

> **Response:** The word "elevated" has been removed from paragraph 1, page 3 of the consultation.

Comment: MDCH has mischaracterized the relevant and available data, First, numerous soil samples exists for the residential area north and east of the Dow plant site. The Dow Corporate Center is located within 3/4 of a mile of the northeast corner of the Dow plant perimeter, and it was tested extensively in 1998 as a surrogate for the community.

> **Response:** While the Corporate Center may be within ¾ of a mile of the northeast corner of the Dow plant site, there are other areas both north and east of the plant that have not been sampled to date. Additionally, dioxin TEQ concentrations ranging up to 584 ppt were found on the Corporate Center property. Additional sampling is needed in nearby neighborhoods to confirm if these concentrations are present on private, residential properties and to assess the resulting health risks to the residents.

Comment: The Kociba, et al, 1978 bioassay in Sprague-Dawley rats has been the basis for most quantitative and qualitative assessments of the potential carcinogenic action of TCDD. In particular, the excess of liver tumors in female rats (the most responsive tumor site) has provided the basis for EPA's quantitative estimate of the cancer potency of TCDD. However, MDCH's assessment of the Kociba et al., 1978 bioassay ignores many other relevant aspects of this bioassay. Three dose levels were used in that bioassay: 0.001, 0.01, and 0.1 ug/kg-day. Although the study found some increase in tumors in the highest dose group, it also found statistically significant decreases in several tumor types. The lowest dose group had fat tissue levels of 540 ppt TCDD - more than 50 times typical human TCDD fat levels - and yet experienced no increase in any tumor type. Further, total tumor burden was lower in all dose groups compared to the control rats. Thus, the picture MDCH paints of TCDD as a potent rat liver tumorigen distorts TCDD's overall properties.

Perhaps most significantly, however, even the rat liver tumor response in this bioassay is of little predictive value for human exposure situations. Human studies do not show any statistically significant increase in liver cancers as a result of TCDD exposure. The increases in liver tumors in the bioassay occurred only at dose levels that resulted in severe liver toxicity. Mechanistic studies of the effect of TCDD on rat liver tumor growth indicate that even when administered in conjunction with a known tumor initiator, TCDD produces increases in liver tumor precursors only at the highest dose levels tested, with lower exposures producing no increase or a decrease in the indicators for liver tumors. Thus, the animal bioassay data, while providing a basis for regulatory assessments of theoretical cancer potency of TCDD under worst-case assumptions, do not provide data to indicate a cancer risk due to exposures to low levels of TCDD in animals or in humans (e.g. 10 to 20 times background soil concentrations).

> **Response:** While the Kociba, et al, 1978 rat bioassay is used by both the U.S. EPA and the MDEQ to calculate an oral cancer slope factor for dioxins, it is not in any way the

only study of the carcinogenic effects of dioxins, nor is liver cancer the only carcinogenic effect noted in the vast amount of literature available. In particular, the Kociba study noted a significantly increased incidence of squamous-cell carcinomas of the tongue, hard palate, nasal turbinates and lung in both sexes of rats. The calculated cancer slope factor is based on the incidence of liver cancer in female rats because this effect of dioxin exposure showed the strongest response (i.e., had the highest rate of tumors) in this study. While it is true that endocrine-related tumours of the reproductive system and mammary glands were lower in the group of female rats most exposed to dioxin, the lower incidence of these tumours was likely attributable to a significant decrease in body weight seen in this group. A similar reduction in tumor incidence was not seen in female rats exposed to lower doses of dioxin or in male rats. So, at the highest dose used in this study, female rats showed less tumors of the reproductive and mammary glands, but more tumors of the liver. At these same doses, male rats showed increased tumors of the tongue, nasal passages, and lung without showing any reduction in any other type of tumor.

Most of the human data available to assess the carcinogenic potential of dioxins is from adult male workers. These studies of adult male workers indicate a significant increase in all cancers combined and in lung cancer among the more highly exposed groups. Animal studies suggest the possibility of a protective hormonal effect of dioxins and the risk of lung cancer in females. Conversely, adult male workers showed no evidence of developing liver cancer even in the workers exposed for the longest time to the highest levels of dioxin. This is consistent with the data from the Kociba, et al, 1978 bioassay, where the liver tumors were observed only in female rats. In addition, while it is true that female rats that developed liver cancer also showed evidence of significant liver toxicity, the livers of male rats also showed evidence of toxicity, but did not progress to liver cancer. The available data, viewed in its totality rather than focusing on one study or one result in a single study, indicate that dioxins are a potent carcinogen, that the effects appear to be hormonally mediated, and that human response to dioxin exposure cannot be assumed to differ from the animal models.

Comment: In other recent health assessments and consultations, ATSDR has described the health effects of dioxins in a much more balanced fashion (see excerpts from a 2000 Public Health Assessment and a 1999 Health Consultation). MDCH should revise the passage from page 7 of the Draft Midland Consultation warning of "adverse health effects,...including cancer" to include, as ATSDR has in other consultations and assessments, a balanced discussion of the current scientific uncertainty as to whether dioxin is carcinogenic to humans.

While the MDCH Draft Midland Consultation is not an appropriate forum to critique ATSDR's interim policy guidelines for dioxin, note that certain aspects of the De Rosa, et al., 1997b guidelines are extremely conservative. For example, the guidelines rely on incorrect assumptions regarding the relationship between animal studies and human health effects. In the De Rosa guidance, "[a] n uncertainty factor of 10 was used for extrapolation from animals". ATSDR has recognized in other health assessments and consultations, humans are believed to be 10 to 100 times less susceptible to dioxin than animals typically used in laboratory studies - not 10 times more as De Rosa et al., suggest. Accordingly, and especially in light of the site-specific

study that has been conducted for Midland, the ATSDR action level of 1ppb should be considered highly protective of human health.

> **Response:** While the potency of dioxin as a human carcinogen may be debated, the US EPA, the World Health Organization, the International Agency for Research on Cancer, and the U.S. National Toxicology Program have all concluded that 2,3,7,8-TCDD is a human carcinogen. MDCH will continue to use and cite the ATSDR dioxin policy as a basis for assessment of the human health risks of dioxin contamination in soil.

Comments Pertaining to the Health Outcomes Data Section

Numerous comments were received by MDCH concerning the Health Outcomes Data section of the Consultation. MDCH has removed this section from the Consultation and has not, therefore, addressed each individual comment here. Health data and a review of the available epidemiological studies will be comprehensively presented in future Public Health Assessment documents. Comments on the health outcomes section are provided below.

Comment: Ample studies of humans have been conducted based upon workers who have been occupationally exposed or residents who have been accidentally exposed to dioxins. These studies do not show any increased cancer risk or mortality rates among those exposed to even high levels of dioxins.

Comment: A comprehensive, community-approved new monitoring system should be set up to collect data on relevant health effects for the Midland and downriver communities. A special form should be designed for health practitioners specific to this region to collect data. Consideration should be given to providing a control population.

Comment: The Midland County Health Department claims three "studies," --actually reviews of available databases on disease incidence -- give the community of Midland a clean bill of health. Unfortunately, the data show a more complicated picture.

- Note the birth defects reference categorized as "integument" shows a statistically significant higher incidence in Midland 1992-96 when compared to the rest of Michigan. The report characterizes it as not significant but it is. The 95% CI is 1.01-2.61. (integumentary defects are important because this is what was seen in the PCB exposed kids in Taiwan, etc). Further, 6 of the 8 birth defect categories monitored showed increases over expected numbers. Again, with a small population and rare disorders, statistical significance is hard to achieve.

- The birth defects registry is notorious for underreporting. In addition, the exposed population is relatively small and the effect would have to be many times above the background level in order to be statistically significant, given the rarity of the disorder. It is important to communicate this point to the public. Further, it is unclear that children sent to specialty clinics are properly categorized in the registry.

- Again, gross birth defects are the ones that get reported. More subtle losses or defects are not reported.

- The four primary cancer sites -- prostate, lung, breast and colo-rectal are not considered primarily dioxin-related (although a recent report in Environmental Health Perspectives[2] suggests a link with breast cancer -- Breast cancer incidence went up marginally in Midland from 1985-99 (age adjusted rate 7.4-7.9/10,000). Dioxin-related cancers would be a better measure to review. However, those cancers are very rare and therefore statistical significance is difficult to achieve with such a small exposed population. Again, this point must be communicated to the public.

Comment: In addition, no such reviews of the data have been conducted for the potentially most exposed population along the Tittabawassee and Saginaw Rivers.

Comment: Although gross disorders more directly attributable to dioxin contamination are rare, and the population impacted is relatively small, it is therefore even more remarkable that Midland has experienced statistically significant elevated rates of a number of these conditions over the years. Those conditions include soft tissue sarcomas, cleft palate, and other dioxin exposure related birth defects. Diane Hebert notes these in her comments, and we incorporate those citations by reference here.

Comment: Media reports have pointed to more than 20 "studies" purporting to show no health effects, primarily to workers, from dioxin. A close review of Dow's web site, which includes over 20 "papers" shows these papers are actually a mix of scientific papers and letters to the editor or commentaries. Only ten are actually journal articles, primarily from the same cohort. All of the papers discuss only cancer mortality, not incidence, or other relevant health effects related to dioxin (with the exception of chloracne, a condition associated with very high levels of exposure).

Comment: These papers are not new data and have been reviewed and considered by the EPA in their reassessment of dioxin, and by other expert bodies when weighing evidence on the hazards of dioxin. Even with Dow's data, those expert bodies have agreed dioxin is a potent toxin to humans, and dangerous for workers.

Comment: Further, the papers do not include a more recent review by Dow, which did find additional excess cancers, although that study's results were initially characterized otherwise. Dow has indicated they have submitted the recent paper for publication but it was rejected. It is unclear whether Dow has submitted that paper to ATSDR/MDCH for review, but it certainly should be reviewed as part of the health consultation.

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[2] Environmental Health Perspectives Volume 110, Number 7, July 2002

Serum Dioxin Concentrations and Breast Cancer Risk in the Seveso Women's Health Study
Marcella Warner,1 Brenda Eskenazi,1 Paolo Mocarelli,2 Pier Mario Gerthoux,2 Steven Samuels,1,3 Larry Needham,4 Donald Patterson,4 and Paolo Brambilla2

Comment: Given that dioxin's toxicity can be more likened to the contaminant lead (in the importance of non-cancer effects and developmental and functional losses), Dow's overwhelming emphasis on cancer (and specifically, cancer mortality) in its comments is strange. They unscientifically take issue with the findings of several international agencies that dioxin is carcinogenic, yet point to their worker cancer mortality studies as evidence of dioxin's safety. Dow does seem to agree that cancers with strong associations to dioxin are rare, and their rarity makes statistical significance difficult.

Comment: Numerous reports have surfaced from surgeons, pediatricians, and other health professionals about the anomalous health effects from Midland area residents. One report from a surgeon in Saginaw suggested more surgery for cleft palate (associated with dioxin exposure) in the area than he had ever encountered in a practice that spanned a number of regions. Numerous reports from physicians at Mott Children's Hospital in Ann Arbor suggest Midland children are over-represented in the state with rare conditions. These reports have persisted over the years. Attempts to quantify these problems are frustrated by deficiencies in data collection and the likelihood that rare conditions are often not treated in the Midland area. Anecdotal reports of elevated rates of disease conducted by independent citizen reviews have also been reported. Those comments seem to warrant an investigation of the reports that do not appear to have ever been compiled and evaluated.

Comment: Anecdotal reports from veterinarians suggest anomalous birth defects and other problems in farm animals born downwind of Midland. Small populations, and lack of data tracking impede an understanding of any trends or anomalies here.

Comment: While anecdotal reports are, by definition, not rigorous reviews, and can be misleading, they can also be early warning systems for problems that may be escaping official data collection systems for a variety of reasons.

Comment: There is more than ample evidence that Midland and downriver residents have been exposed to elevated levels of dioxin. Biological sampling of the population, however, has not been done to answer the most important question – do the residents of Midland have elevated levels of dioxin in the bodies and breast milk. We urge biological sampling of wildlife and humans to determine if area residents have elevated levels of dioxin. Sampling protocols and plans should be developed in consultation with the community. Sampling of humans should focus on those most likely to have elevated levels, including fishers, long-terms residents, those in closest proximity to contaminated soils, and those directly downwind from dioxin sources. Sampling should include breast milk.

Comment: If biological sampling reveals elevated levels of dioxin, further public health interventions should be considered. For instance, additional screening to determine if thyroid levels in women of childbearing age have been altered will be critical in order to determine if routine screening should be part of regular prenatal care. Dioxin is known to alter thyroid levels in those exposed, even at relatively low levels of exposure. Thyroid is critical to development for the fetus. A simple test for pregnant women can determine if thyroid levels are adequate for fetal health. Interventions to address imbalances are possible. Ongoing monitoring of this program, and regular evaluation, can serve to determine its usefulness.

Comment: A new Environmental Health Perspectives article indicates that circulating levels of thyroid might not be the best predictor of thyroid function, so appropriate tests may need to be found, but in any case, this should be further explored.

Comment: There may be other proactive public health interventions to address the impacts of dioxin exposure that should be explored.

Comment: Please consider an independent comprehensive study of the overall health of Midland before issuing a new report.

Comment: I believe the Midland area needs a comprehensive health study done. I do not believe there are any studies to date regarding the synergistic effects of dioxin with other chemicals such as PBB, marathon or any of the numerous other chemicals with which Midland residents are bombarded, permitted and intermitted.

Comment: "I know that soil was moved to new subdivisions from flood plain areas and fields, so soil may have been moved back and forth between the two zip codes." (Comment addressing the zip code study – may explain why it seems inconsistent with expectations)

Comment: The MDCH study is incomplete, misleading and incorrect – omits previous soil and epidemiological studies. One error example - the zip code areas that MDCH report indicates a potential health concern are upwind from the Dow facility.

Comment: The MDCH report ignores 20 years of past studies concluding that Midland residents are as healthy or healthier than the average person in the state of Michigan.

Comment: Since it is already known that cancer incidence and birth defect rates in the Midland area are the same or lower than the rest of the state, what is the MDCH expecting to find from its study?

Comment: The 48640 zip code area was shown not to be as healthy as the 48642 area. Since the 48640 area is comprised of lower income residents, doesn't this have to be taken into account when making a comparative health assessment?

Comment: The zip code with the higher cancer rate (48640) has less dioxin than 48642.

Comment: Since Midland is a community with a high degree of population turnover, it would be important to study the health effects of lifelong residents. Previous studies that report Midland residents are healthier than the average state resident do not take the duration of time an individual has resided in Midland into account.

Comment: The Midland report should include a detailed discussion of specific, relevant health findings, such as the number of incidences of soft-tissue, prostate and lung cancer, as well as birth defects data, compared to State and county rates. Even findings that are not "statistically

significant" may be indicators of potential problems that could be investigated in a future health evaluation.

Comment: The public should be told that there are high incidences of certain cancers and birth defects in Midland and Saginaw.

Comment: Any evaluation should include all Midland zip codes that touch the plant site, not just the ones immediately north and south of the plant (48640 and 48642). Since the prevailing winds are west and northwest, the east and southeast zip codes would be relevant to the study.

Comment: An evaluation should also include all zip codes in downriver communities. These areas could be downwind and downriver so health problems could be air or water related.

Comment: Recommendations should include a means of identifying disease clusters, such as going door-to-door, to determine what diseases are present in the immediate population.

Comment: Impacts to children and females vs. males should be considered to determine differential effects.

Comment: Local medical and mental health professionals should be trained in the diagnosis, treatment, and reporting of health effects expected in this environment of contaminated air and soil.

Comment: The "Zip Code Study" dated July 23, 2001 reports that the 1998 rate for invasive bone and soft-tissue cancer for the 48640 zip code were significantly high but this is not noted in the Health Consultation.

Comment: Midland is the only county in the state in the "significantly high" category for chromosomal anomalies.

Comment: It would be helpful to know the Midland incidence of non-Hodgkin's lymphoma, as soft-tissue sarcomas are rare but elevated in the presence of dioxins.

Comment: How does our health data compare with other similarly contaminated communities?

Comment: The health data indicates that there could be a problem. The report should clearly state this.

Comment: I suggest that a map of the Midland area, emphasizing ZIP code areas, be included in the soil consultation report and the language be changed as follows: On page 10, 2nd paragraph under "Cancer Incidence for the Midland area", 2nd sentence "Zip code 48640 encompasses the southwest area of Midland including the Dow plant site, urban areas north and northwest of Dow, and a portion of Salzburg Road just east of Dow, while Zip code 48642 includes property to the north and northeast of the Dow plant site."

Comment: I would recommend that you delete the Dow study (occupational) from the Health Consultation until it has been submitted for peer review and published.

Comment: The Midland community needs to be told that there has never been a comprehensive health study in Midland and therefore it is impossible to suggest that Midland health has not been adversely impacted by dioxin and other chemicals.

Comment: Health issues that need to be studied or followed-up include soft tissue sarcoma, cleft palate, all other birth defects- please identify "other"-, and autism.

Comment: If this is such a huge health problem, why aren't some of the health effects showing up very clearly in public health data? Are the people in Midland healthy because the worst effects have been washed downstream into Saginaw?

Comment: Current and previous residents in any contaminated area should be interviewed about possible health problems that might have been caused by dioxin and tested for concentrations in their bodies.

Comment: Zip Code Study: MDCH imprudently relied on a "zip code study" that it knew to be flawed and, in fact, demonstrates an inverse correlation between the amount of dioxin in residential soils and incidence of cancer.

Comment: Epidemiology Studies: MDCH did not meaningfully address important epidemiology studies which found no consistent adverse health effects among Dow workers occupationally exposed to concentrations hundreds or thousands of times greater than the theoretical exposure from residential soils.

Comment: Please consider an independent comprehensive study of the overall health of Midland before issuing a new report.

Comment: I believe the Midland area needs a comprehensive health study done. I do not believe there are any studies to date regarding the synergistic effects of Dioxin with other chemicals such as PBB, malathion or any of the numerous other chemicals with which Midland residents are bombarded, permitted and unpermitted.

Comment: In the Summary section, the report suggests that there are no data regarding health risks in Midland Community. This is untrue and the summary section should be modified with this suggested language inserted after the second sentence as a replacement for third sentence.

"Over the years there have two birth defects studies, cancer studies, including a soft tissue sarcoma study and numerous studies by he Dow Chemical Company of their employees. None of these studies identified any health problems in Midland in excess of what one might in any other community in Michigan. Although no problems were identified in any health studies, because these were population based studies, some elevated problems may not have been detected from these studies. Therefore, it is our opinion that the site poses an indeterminate public health risk."

Comment: The use of the cancer incidence study conducted by the MDCH is disingenuous. "The greatest number of Midland residents that would be effected [sic] by dioxin live North East [sic] of the plant in zip code 48642 which had cancer incidence rates lower than 48640. The Plant location is on the Eastern [sic] edge of zip code 48640 boundary with the majority of the population in 48640 living north and West [sic] of the Plant.

"The only relevance of this study [is] to show that even with soil dioxin levels elevated above the ATSDR Screening level, there was no evidence of higher cancer rates in those areas. The cancer rates in the elevated dioxin areas were lower than the other comparables. Recommend if this study has little relevance to the issues of soil dioxins in Midland, it should be removed from the report. If it is included, a more complete description of its relevance and interpretation of the study results is warranted."

Comment: "The Report briefly mentions and quickly dismisses a Birth Defects Study conducted in 1999 by the MDCH as being irrelevant and unreliable. There have been two birth defects studies conducted by MDCH at the request of the Midland County Health Department in addressing the concern of possible elevated birth defects due to dioxins present in our community. In both studies no elevated birth defect rates were observed."

Comment: All current information we have about the Midland community is that our health status is similar to what one might find in any community in the State of Michigan. Our cancer rates and birth defects rates show no increased health problems as a result of dioxin in the soils in Midland.

Comment: August 6, 2001 – Midland County Health Department was contacted by the Dow Chemical Company requesting information about a cancer zip code study being conducted in Midland. MDCH had not contacted, involved or even informed the Midland County Health Department that the zip code study was being conducted.

Comment: August 30, 2001 - The Midland County Health Department...pointed out several flaws in the (zip code) study that still have not been addressed. MDCH representatives noted that what the study showed in that there is not indication of health problems in Midland because the higher soil dioxin areas had lower cancers.

Comment: Dow has commissioned numerous, extensive studies regarding the health effects of Midland workers who were occupationally exposed to hundreds or thousands of times as much dioxin as is the general Midland population from residential soil. Those studies have not found any adverse health effects at low-level exposures of the type to which certain Midland residents could potentially be exposed, and the results of studies of Dow and other workers exposed to very high levels of dioxin are inconsistent at best. In light of the extensive research of more exposed populations, including more highly exposed Midland workers, there is no scientific basis to believe that Midland residents exposed to orders if magnitude lower levels of dioxin in soils would face any discernible health effects whatsoever. MDCH should correct the Draft Health Consultation to reflect this reality.

Comment: As noted above, more than ample data exist to find the Midland residents face no apparent health risk based upon the small concentrations of dioxin above background levels found in Midland residential soils. MDCH should amend this statement accordingly, and in light of the extensive studies of the Dow worker cohort, including substantial data and analyses that MDCH did not consider, which show that there is no basis to believe Midland residents would experience any adverse health effects as a result of exposure to Midland residential soils.

Comment: MDCH should delete the entire discussion that comes under the heading "Cancer Incidence for the Midland Area" because it is based upon a highly unreliable "zip code study" that MDCH has acknowledged is of little or no scientific value. Indeed, ATSDR has noted the severe limitations of zip code studies under even the best of circumstances. Moreover, as explained more fully in Dow's main comments (see Section VI.A), the Midland zip code study, is seriously flawed because: (I) it relies on census data from 1990, even though the relevant zip code boundaries changed on July 1, 1996; (ii) some of the cancer causes in the registry likely have been misclassified based on post office boxes or places of treatment, as opposed to place of residence; and (iii) although MDCH mentions that the study found slightly elevated levels of cancer in zip code area 48640, it fails to note the proximity of the Dow plant site to the 48642 zip code area, the fact that the prevailing winds carry emissions in the direction of 48642, and the fact that the zip code (48642) with the higher dioxin levels (whatever their cause) has the lower cancer rates.

Accordingly, MDCH should delete all reference to the zip code study in its revised Health Consultation. If MDCH insists on including the zip code study, it would be irresponsible not to acknowledge all the substantial shortcomings of the study (including those noted by ATSDR with respect to an early zip code study) in revised Health Consultation. See Section VI.A.

Comment: MDCH improperly dismisses one of the Dow study's key findings in above-quoted passage. The finding is significant, however, insofar as the Dow worker cohort showed no association between exposure to high levels of dioxin and mortality rates. Moreover, total mortality rates for all causes of death were lower among Dow workers studies compared with white male cancer mortality rates for the general population in the U.S.. (See Section VII.) MDCH should replace the sentence that suggests the lower death rate is "not remarkable" and acknowledge the significance of these data in a revised Health Consultation.

Comment: MDCH fails to mention that the data show fewer than expected deaths with respect to a roughly equal number of other cancer sites (such as lung, liver, and brain). Moreover, all cancers combined are at expected levels. Further, the 245 workers in this study with chloracne- and presumably very high dioxin exposure- had a deficit of cancer. Rather than highlighting only those cancers where the incidence is slightly greater than expected, MDCH should present all of the foregoing data in a revised Midland Health Consultation. See Section VII.B.

Comment: As explained more fully in Dow's main comments, this statement is inconsistent with (I) the findings of the International Agency for Research on Cancer's ("IARC") recent review of dioxin health effect studies, (ii) the confounding factors present in the studies MDCH references, (iii) serum lipid level comparison; and (iv) the study of accidentally exposed residents in Seveso, Italy. MDCH should revise the above-quoted reference, as the body of

available scientific evidence does not demonstrate any "consistent" elevation of any particular cancers due to dioxin exposure

MDCH: *There were two cases of soft-tissue sarcoma in the cohort, an excess also reported in some other studies. (Dow 1997,1998)*

Comment: As explained more fully in Dow's main comments, MDCH has failed to note that the slightly higher than expected incidence of soft tissue sarcomas is not statistically significant. Moreover, the most recent update found that the SMR for these sub-cohorts had decreased compared with the original study, which indicates a decreased likelihood of a casual connection between dioxin exposure and STSs. See Section VII.B.2. MDCH should address these more recent data, and the statistically insignificant nature of the earlier data upon which it relied, in a revised Midland Consultation.

MDCH: *There are significant limitations in generalizing from the Dow study to the general population. First, the study is limited by the size of the exposed cohort, which is not sufficient to detect moderate increases in incidence rates for many of the cancer types of concern. Second, the individuals included in the cohort were all males. The effect of dioxin exposure on exclusively female cancer types cannot, therefore, be considered. Lastly, and of most importance, the assignment of workers to the "exposed" and "unexposed" groups and to the assumed level of exposure was based on job history, that is the work time spent in areas of the Dow plant where there was potential for dioxin exposure.*

Comment: These criticisms are unjustified. First, with respect to the size of the study, the Dow cohort of 2,187 workers represents the largest single plant mortality study of dioxin workers ever reported. Second, with respect to data on females, although admittedly not statistically significant, the Dow study did include five female workers with dioxin exposure, and all five are still alive, as reported in the most recent update. Third, with respect to the dioxin exposure characterization, this aspect of the study was based on comprehensive and reliable indicators of dioxin exposure, including industrial hygiene monitoring, analysis of historical plant operations, and detailed work histories of all cohort members.