



Agency for Toxic Substances
and Disease Registry
Atlanta GA 30333

MAY 19 2004

MAY 13 2004

The Honorable John D. Dingell
House of Representatives
Washington, D.C. 20515-6115

Dear Mr. Dingell:

I am responding to your letter to Dr. Henry Falk, Director, National Center for Environmental Health/Agency for Toxic Substances and Disease Registry, regarding your interest in the Agency for Toxic Substances and Disease Registry's (ATSDR) public health activities at U.S. Marine Corps Base Camp Lejeune, North Carolina (Camp Lejeune). We share your concern that we consider every possible approach to provide the most thorough, evidence-based information about the potential for health effects from past exposures to contaminants in Camp Lejeune's drinking water.

The enclosures contain detailed responses to each of the specific questions in your letter. These responses consider the most current science on volatile organic compounds (VOCs), including the latest findings from the U.S. Environmental Protection Agency's (EPA) ongoing trichloroethylene (TCE) risk assessment and the information you cited in the California Environmental Protection Agency's *1999 Public Health Goal for TCE in Drinking Water*. Our responses also address the impact of current research on the conclusions in our 1997 public health assessment.

Regarding your request for a new public health assessment, ATSDR agrees that the information provided to the public must be based on up-to-date scientific information, and we are continuing to increase our understanding of the health risks at Camp Lejeune by monitoring the developments of the ongoing EPA TCE risk assessment and other new research. At this time, however, ATSDR does not believe a new health assessment is warranted. Should new information change our understanding about the risks from exposures to TCE and other VOCs, we would consider revisiting our conclusions, recommendations, and identified needs for further studies.

Our on-going efforts at the base continue. Recently, an ATSDR technical team returned from Camp Lejeune after meeting with staff there to coordinate logistics for the testing, planned for this summer, to develop more precise exposure dose estimates of the base's water-distribution system. Data from this and other planned tests will assist ATSDR scientists in conducting computer modeling of the water-distribution system. This information is essential to ATSDR's evaluation of health effects in children born to mothers who were pregnant while living on the base any time from 1968 through 1985.

ATSDR does recognize that gaps exist in the scientific information on health effects of VOC exposure. The Agency acknowledged this point in the 1997 Health Assessment for Camp Lejeune; and, as required under the Comprehensive Environmental Response, Compensation, and Liability Act, ATSDR has identified and endeavored to fill research needs related to the health impacts of TCE and other VOCs. Those data needs, and ATSDR's efforts to address them, are discussed in more detail in response to Question 12 and in accompanying documents. Further epidemiologic studies to determine potential links between human exposure to VOCs and health effects may address some of the concerns regarding health outcomes among children and adults exposed to contaminated drinking water at Camp Lejeune.

In addition, concerned individuals may obtain useful information from ATSDR's current study of *in utero* exposure. An important component of that study involves computer modeling to create a historic reconstruction of the water-distribution system. The modeling, similar to the approach ATSDR took in its investigation at the Toms River site in New Jersey, will provide more detailed information on which homes received contaminated water during which time periods. This information will allow ATSDR to determine whether an association exists between *in utero* exposures at Camp Lejeune and the health effects being studied. However, the modeling also will provide information on VOC exposures of populations, including children and adults, who are not part of the current study.

Again, I appreciate your interest in ATSDR's work at Camp Lejeune, and look forward to working with you in the future as we strive to answer these important questions on the potential health impacts of VOC exposure at Camp Lejeune.

Sincerely,


Julie Louise Gerberding, M.D., M.P.H.
Administrator

Enclosures

RESPONSES TO QUESTIONS

- 1. In Appendix E -1, the ATSDR lists the exposure factor for water ingestion for the population at Camp Lejeune as 0.57. This exposure factor is explained in the information below the chart as residents ingesting tap water four out of seven days per week or 208.6 days per year. However, the Environmental Protection Agency's policy for human health evaluation assumes that residents drink their tap water 350-365 days per year. This determination is found in Directive 9285.6-3, A Risk Assessment Guidance for Superfund. Furthermore, the ATSDR concurred with EPA's guideline of 350-365 days per year in other studies, including the 1999 Public Health Assessment of Iowa Army Ammunition Plant. Finally, when communicating with military families who lived at Camp Lejeune in the relevant housing areas, these individuals informed my staff that they remember using their taps every day of the year. Do you agree that a more conservative value should be employed with respect to the exposure factor in Appendix E-1? What would the exposure factor be, using the EPA assumption of drinking tap water 350–365 days per year?**

Response: ATSDR believes that the value in question, 0.57, is appropriate because it is based on site-specific data. EPA uses 350-365 days per year as a default value for quantitative risk assessment, setting “safe” levels for drinking water when more accurate, site-specific data is unavailable. In the case of Camp Lejeune, enough information was available to calculate a more accurate, yet still conservative, site-specific exposure factor of 0.57. This value adjusts for the four out of seven days per week that homes at Camp Lejeune may have received contaminated water.

Data on the water system at Camp Lejeune show that 1) not all of the wells that supplied the camp were contaminated; 2) not all of the wells available to the water system were always engaged; and 3) not all of the wells supplied the system at a constant rate.

At Tarawa Terrace, one of the seven wells contained contaminants and four of seven wells available were used on any given day. The water distribution system pumped and mixed water from four wells, then distributed it into the water lines and subsequently into the homes.

Statistically, random variation in the wells used on any given day suggests that the system used one of the contaminated wells less than four of seven days per week, or 57 percent of the time. Therefore, ATSDR’s use of 0.57 as a factor was actually a conservative measure.

ATSDR assumed that people at Camp Lejeune used their taps year round. The calculation was not that residents ingested tap water four days per week, but rather that they ingested *contaminated* tap water, at most, four days per week. Had there been any evidence to suggest that residents actually drank contaminated water seven days per week, 365 days per year, the exposure factor would have been 1.0. Please see the response to Question 7 showing ATSDR’s calculation of the worst-case cancer risk scenario using an exposure factor of 1.

- 2. The National Toxicology Program, within the U.S. Department of Health and Human Services, created a 10th Report on Carcinogens stating that "inhalation is the main route of potential environmental exposure to TCE (pg.3: TCE Information)." However, the ATSDR's Health Assessment only demonstrates calculations for ingestion of chemicals for Hadnot Point, Tarawa Terrace, and Holcomb Blvd (see appendix E-1). What would be the combined Cancer Risk if dermal and inhalation routes were included in the assessment?**

Response: The calculations in Appendix E-1 do account for inhalation as well as ingestion exposures. The document states, "Our VOC exposure estimates assume exposure to VOCs from ingesting 2 liters of water per day *and inhaling an equivalent concentration of VOCs during showering*" (pp. 24-25; emphasis added).

The further addition of the dermal exposure route to the cancer risk calculations does not significantly change the cancer risk numbers because its contribution is very small compared to the other two routes. See the response to Question 7, below, for calculation of cancer-risk estimates that also include dermal exposure.

- 3. On page 25 of the 1997 Public Health Assessment, the document asserts, "We also quantitatively consider the combined effects of the chemicals on the body when evaluating the likelihood of cancer," However, this evaluation does not appear to be present in the report. My staff asked the ATSDR's staff if a combined analysis had been done for each specific location (i.e., looking at the combined effects of TCE, DCE, Methylene Chloride, and Vinyl Chloride at Hadnot Point). The ATSDR's staff has responded that there was no combined evaluation of chemicals done. Do you agree that a combined assessment should be done for each location? If you do not agree, please explain your reasoning.**

Response: We agree that a combined assessment is necessary, and we conducted one for the 1997 Public Health Assessment.

ATSDR considers combined exposures to multiple chemicals and across all relevant exposure routes. At Camp Lejeune, ATSDR estimated exposure for each population exposed by different water supply systems. Even using conservatively high exposure estimates, the combined exposures to the multiple chemicals of concern did not result in adverse health effects.

The calculations for the quantitative combined effect of the chemicals on the body do not appear in the 1997 report. The 1997 report reads, "We also *qualitatively* consider the combined effects of the chemicals on the body when evaluating the likelihood of cancer." Thus, when asked by your staff whether we *quantitatively* assessed the mixtures, we responded that we did not.

In our 1997 assessment and our present reevaluation of combined effects of chemicals, we considered several studies that suggest as long as all of the components of any mixture are below their individual "no observed effect" levels, exposure to the mixture is unlikely to result in

adverse health effects (Wade et al. 2002; Gough 2002; Groten 2000; Seed et al. 1995; Feron et al. 1993). Moreover, adverse effects for these chemicals have been shown to occur only at exposure levels far higher than would have occurred at Camp Lejeune.

ATSDR's conclusions are based on all relevant factors collectively rather than by focusing only on mathematical estimates of theoretical risk. We have included combined chemical exposure calculations in the cancer risk estimates for our response to Question 7.

- 4. In Appendix E-1, the ATSDR lists a cancer slope factor for Vinyl Chloride as unavailable. However, on EPA's Integrated Risk Information System (IRIS) website, the Weight of Evidence Characterization shows that in 1986 Vinyl Chloride was listed as a Class A carcinogen in the U.S. EPA Guidelines. The dose response data used to derive a slope factor was published in 1981 (Feron et al. 1981). Why was the Cancer Slope Factor for Vinyl Chloride listed as Not Available in Appendix E-1? Do you agree that Cancer Risk from Vinyl Chloride should also be considered in the ATSDR Public Health Assessment? If not, please explain why not.**

Response: ATSDR chose not to use this slope factor because it had been withdrawn by EPA early in 1997, before completion of the health assessment. EPA has since published a proposed new slope factor with a ten-fold reduction in potency as compared to the prior cancer slope. Some scientific literature suggests that even further reductions in cancer potency estimates may be appropriate (Clewell et al. 2001).

Whether vinyl chloride was present at all is unclear. Levels of vinyl chloride were below the method detection limit. The qualitative analysis indicated that levels of vinyl chloride in Camp Lejeune's water (if present at all), even in combination with the VOCs actually detected, would not, under site-specific conditions of exposure, likely lead to adverse health effects. ATSDR believes that further evaluation of cancer risk associated with vinyl chloride is unlikely to produce a different result. We used EPA's proposed slope factor in our revised estimates of combined cancer risk for our response to Question 7.

- 5. (A) On Table 3 (page 26) of the 1997 assessment, the ATSDR lists the increased cancer risk for children as "unknown," No further analysis is presented in the corresponding Appendix E-1. In contrast the ATSDR conducted exposure and risk calculations for children for the Bourne Schools at the Massachusetts Military Reservation, Cape Cod, Massachusetts (*Bourne Schools Health Consultation 2000*). Why was the ATSDR able to calculate a risk estimate for children at the Bourne Schools but not for children at Hadnot Point, Tarawa Terrace, or Holcomb Blvd at Camp Lejeune?**

Response: We were able to calculate a cancer risk for the Bourne Schools and not at Camp Lejeune because of differences in the chemicals of concern and the disparity in the amount of available scientific literature on each. Information on the relationship between TCE exposure and childhood cancers, including acute lymphocytic leukemia, is scarce. In contrast, the

available literature on the chemicals of concern at the Bourne School — polychlorinated biphenyls (PCBs) in indoor air — and cancer is broader, reflecting the results of decades of research. In addition, the scientific information on PCBs is much different than that on TCE and cannot be applied to the situation at Camp Lejeune. Although we were unable to calculate a risk at Camp Lejeune, the Agency did address cancer in children on the basis of available animal and human studies.

(B) Furthermore, even though the cancer risk is listed as "unknown" in Table 3, on page 17 the ATSDR concludes, "Even though the ATSDR determined that cancerous health effects are *unlikely* in children, not enough scientific information is available to rule out the possibility of cancerous effects from low-dose exposures to VOCs such as those at Camp Lejeune." Please show the calculations that led you to the conclusion that health effects from the contaminated water at Camp Lejeune were unlikely for children.

Response: Specific to our conclusions about cancer being unlikely in children, Table 3 on page 26 indicates that increased cancer risks for children at Holcomb Boulevard were unlikely due to the extremely short exposure duration (approximately 12 days) to VOC-contaminated water supplied from Hadnot Point while repairs were made to the water distribution system. Page 24 describes the exposure situation in more detail. For children at Hadnot Point and Tarawa Terrace, Table 3 indicates that cancer risks were unknown.

ATSDR did not have adequate information to develop a quantitative estimate of cancer in children at Camp Lejeune. We based our conclusions about cancer in children by qualitatively evaluating possible adverse health outcomes in children exposed to contamination in Camp Lejeune's drinking water. We used conservative estimates of exposure to children and adults, including pregnant women, and information in the toxicological and epidemiological literature. Although existing studies exploring the association between oral exposure to VOCs in drinking water and childhood cancer were inconclusive and showed conflicting results, we believed available information was sufficient to warrant concern. This concern led to the recommendation to further study the potential for cancer in children exposed *in utero*.

(C) Based on the 1999 *Public Health Goal for TCE in Drinking Water* by the California Environmental Protection Agency, it is my understanding that certain cancers relevant to VOCs, including kidney or liver cancer, have cancer risks that are not relevant to the age of the individual. Would you agree that a cancer risk estimate should be assessed for non-age specific cancers and diseases relevant to the contaminants of concern? If not, please explain why not.

Response: When sufficient information is available ATSDR does assess non-age specific cancers and diseases relevant to the contaminants of concern and uses the quantitative risk estimates as part of the overall process of assessing adverse health outcomes of exposure. However, for the chemicals of concern that were in drinking water at Camp Lejeune, chemical-specific and age-specific information were insufficient to develop theoretical cancer risk calculations for children at various stages of development. For example, the mode of action for

TCE exposure and human cancer is not well understood. There is no recommended default process to settle the question of whether tumors arising through a hypothesized mode of action are relevant during childhood. Data gaps exist regarding differences in toxicokinetics between adults and children and how that would affect the dose response assessment for cancer in children. Also, dose-response assessment is limited by an inability to observe how developmental exposure can modify incidence and latency and an inability to estimate the ultimate tumor response resulting from induced susceptibility to later carcinogen exposures (EPA 2003).

- 6. Recent scientific research appears to indicate that children cannot be adequately assessed as "little adults." Therefore, do you agree that children who were exposed to VOCs at Camp Lejeune should be separately assessed because of their unique vulnerabilities (i.e., *Children's Health and the Environment: Public Health Issues and Challenges for Risk Assessment* by Landrigan et al (2004), *A Framework for Assessing Risks to Children from Exposure to Environmental Agents* by George Daston et al (2004), *Approaches to Environmental Exposure Assessment in Children* by Dr. Weaver et al (1998), *Chemical Wastes, Children's Health, and the Superfund Basic Research Program* by Dr. Landrigan et al (1999)? Please explain why a separate study focused on children exposed after childbirth should not be undertaken.**

Response: We agree that children are not "little adults. We also agree that children are particularly vulnerable to chemical exposures during gestation and the first few years of life.

ATSDR focused the current study on in utero exposure because the fetus is highly vulnerable to chemical exposures, and limited evidence in the scientific literature shows that maternal exposures to drinking water contaminated with TCE and PCE may lead to specific birth defects and childhood cancers. The evidence for this association is not conclusive. This fact is one of the major reasons we are studying specific birth defects and childhood leukemia — ATSDR's study will add to the scientific literature on the effects of maternal exposures to TCE and PCE.

In the current study of childhood leukemia and specific birth defects, we have to be able to identify and verify the cases of birth defects and childhood leukemia with nearly 100 percent completeness. Without a high percentage of verification, our study might be affected by selection bias that would impact the study's scientific credibility. The limited North Carolina birth defect registry data for the study period, as well as the unavailability of cancer registry data before 1990, has made it difficult to verify cases.

Nevertheless, we believe that identifying and verifying nearly 100 percent of the cases will be possible if we focus on neural tube defects, oral clefts, and childhood leukemia. Although ATSDR would like to have been able to conduct a more comprehensive study, studying other defects of interest — including heart, eye, and ear defects — was not scientifically feasible because we could not verify anywhere near 100 percent of the cases.

Problems with biases and statistical power would be much worse if we attempted to study preschool or school children. The following illustrates some of the limitations to adding other groups to the present study:

- A) We are studying all births and pregnancies that occurred at Camp Lejeune. The potential number of children born elsewhere but who lived at Camp Lejeune during their preschool or school years would be small because their parents, the soldiers training at the base and their spouses, were very young (late teens or early 20s) and unlikely to have many older children. Moreover, no listing of preschool children at the base is available.
- B) Which health outcomes should be evaluated is not obvious. We are already evaluating childhood leukemia. Most childhood leukemias are diagnosed before age 5, and the evidence in the scientific literature strongly indicates that exposures during gestation are the most important. Nevertheless, our study will obtain exposure histories from birth up to the time of diagnosis.
- C) For cancers other than childhood leukemia and for non-cancer endpoints, identifying and verifying cases with nearly 100 percent completeness is nearly impossible. For instance, for adult cancers caused by childhood exposures, ATSDR would need to assume a 10-20 year latency period, examine data from cancer registries in all 50 states, and link school data with data from these registries. For other endpoints, only mortality data would be available. During the latency period as the children grow towards adulthood, some may change their names and/or migrate out of the country.
- D) Exposures to other risk factors, such as other environmental pollutants, occupational exposures, and cigarette smoke, also may have occurred during the latency period. These other risk factors can be a source of confounding bias, and such bias can be extremely difficult to control for in a study.

ATSDR's focus at Camp Lejeune has been to study the highest risk group to determine the potential link between exposure and specific birth defects and leukemia. It has not been to survey the population to determine what health problems exist in those who lived on base. Instead, our purpose is to conduct a scientifically sound epidemiological study that can be an important addition to understanding the etiologic relationship between drinking water exposures to TCE and PCE and adverse birth outcomes and childhood leukemia.

- 7. **Table 3 on page 26 states that there is *no increase risk of cancer for adults due to any of the exposures at Camp Lejeune at Hadnot Point, Tarawa Terrace, or Holcomb Blvd. Please demonstrate how you reached this conclusion. Should this conclusion be re-assessed in light of new scientific studies that show an increase health risk for these contaminants (i.e., the California EPA's 1999 *Public Health Goal for Trichloroethylene in Drinking Water, Trichloroethylene and Cancer: Epidemiologic Evidence* by Dr. Wartenberg et al (2000), *Perchloroethylene - Contaminated Drinking Water and the Risk of Breast Cancer: Additional Results from Cape Cod, Massachusetts, USA* by Dr. Aschengrau et al)?***

Response: Since the Camp Lejeune public health assessment document was published in 1997, the role that TCE exposure plays in cancer has been explored further. TCE is clearly an animal carcinogen, although its potency appears to be relatively weak. Tumors develop in multiple organs of different rodent species at doses greater than 500,000 times higher than the worst-case exposure dose estimates a person would receive from drinking contaminated water at Camp Lejeune.

Recent human epidemiology studies come to different conclusions about TCE exposure and cancer. Some show a positive association but others conclude that the evidence does not support a causal relationship (Lee et al. 2003; Mundt et al. 2003, Bruning et al. 2003).

In general, ATSDR gives human epidemiological studies special attention. Two community-based studies have examined the relation between exposure to chlorinated solvents in drinking water and cancer (Ashengrau 1993, 1998; Paula 1999; Cohn 1994). Although some studies have suggested positive associations that support a causal relationship between chlorinated solvents (such as TCE and PCE) and cancer, the results remain inconclusive. Furthermore, the exposures studied were much longer than exposure durations experienced at Camp Lejeune. Nevertheless, on the basis of animal data and the suggestive — if inconclusive — human data, ATSDR concluded that cancer should be a *health effect of concern* for people exposed to TCE. Moreover, ATSDR considered this concern in depth for our 1997 document.

In 2001, EPA released the external review draft of its TCE risk characterization (EPA 2001). This document suggested that, in order to account for the significant uncertainty inherent in estimating cancer risk from TCE exposure, quantitative cancer risk assessments should use a range of oral cancer slope factors.

However, EPA's Science Advisory Board (SAB) later reviewed this risk assessment and issued their report in late 2002. The report identified several shortcomings and made several recommendations and requests for revision (EPA 2002). The final risk assessment is still undergoing revision and the TCE cancer potency factors remain in draft form.

Some of SAB's concerns involved a review article by Wartenberg (2000) and an occupational study by Henschler (1995). Both documents played prominent roles both in EPA's draft risk characterization and in the State of California's derivation of the public health goal for TCE in drinking water. Although these studies were important contributions to the scientific literature, SAB expressed several criticisms and concerns about both. Specifically, SAB has questioned the strength of the evidence for human cancer, the validity of the conclusions, and the significance of the results in light of the whole human epidemiology database (EPA 2002).¹

In drafting the response to this question, ATSDR recalculated our exposure assumptions to estimate worst-case conditions from residential use. This estimate combines all exposure routes, including direct ingestion, inhalation, and skin contact (e.g., while bathing) with water containing TCE and other volatile organic chemicals. ATSDR also assumed that contaminated

¹ See section 4.2.2, pages 11–13.

water was the only source of fluid intake every day of the year for the entire duration of duty at Camp Lejeune. As an added conservative, protective measure, ATSDR assumed that the TCE contamination remained at the maximum for the entire exposure (although actual levels dropped shortly after the initial maximum was detected, as described in the response to question 3).

The 1997 assessment applied the provisional TCE oral cancer potency factor of $0.011 \text{ (mg/kg/day)}^{-1}$ to conservative, but realistic, exposure estimates. The result was a total combined theoretical excess lifetime cancer risk of $5\text{E-}05$, equivalent to 5 cases in addition to those normally expected to occur (from all causes) in a population of 100,000.

In contrast, applying the more recent range of draft cancer potency factors ($0.02\text{--}0.4 \text{ (mg/kg/day)}^{-1}$) to worst case exposure estimates results in a theoretical excess lifetime cancer risk ranging from $8\text{E-}05$ to $2\text{E-}03$ (8 excess tumors in a population of 100,000 to 2 in a population of 1000). This is a roughly two to 40-fold higher estimate of theoretical cancer risk than estimated in 1997.

These are *theoretical* estimates of cancer risk based upon statistical models, which are distinct from *actuarial* risks based on actual data on the incidence of disease. By design, conservative assumptions about the cancer potency of TCE intentionally overestimate the true cancer risk, which is likely lower and may be as low as zero (EPA 2003).

ATSDR considers and uses quantitative cancer risks as one part of the screening process. Under Superfund risk assessment practice, theoretical cancer risks ranging from $1\text{E-}06$ to $1\text{E-}04$ typically do not lead to corrective actions. ATSDR uses a theoretical excess cancer risk of $1\text{E-}06$ as a target for screening, and when this level is exceeded, ATSDR scientists conduct a more refined exposure estimate and further evaluate the potential for adverse health effects from exposure. ATSDR made these estimates as part of the 1997 health assessment and, even without the more conservative cancer potency factors, performed the in-depth evaluation. In light of the breadth of the toxicological and epidemiological literature, applying the more conservative factors would not have changed the 1997 document's conclusions regarding the health hazards from exposure to contaminated drinking water at Camp Lejeune.

In addition to reviewing the risks derived through the application of quantitative risk assessments, ATSDR bases its health impact decisions on a qualitative review of both health and exposure data, as well as relevant site specific considerations. For example, we compare our site-specific estimates of exposure with levels found in the scientific literature that have actually been associated with health effects for each substance of concern. When making this comparison, we rely more strongly on the evidence from human studies than findings in animals. Also we take into consideration the likelihood that the community has been exposed through a completed exposure pathway.

- 8. The 1997 Public Health Assessment assumes a three-year exposure time frame for families that lived in the housing at Camp Lejeune. I am informed, however, that families could get permission to stay on the base while the service members served in Vietnam. Therefore, some military families may have resided at Camp Lejeune for a total of seven years: three years before a**

service member's tour in Vietnam, during the service member's one year tour, and three years after returning from Vietnam. Do you agree that this group's increased risk should be considered when making conclusions about the chance of increased cancer risk at Camp Lejeune? If not, please explain why not.

Response: ATSDR based its 1997 exposure assumptions and subsequent public health hazard conclusions on the best information available at the time. We understand that some military families may have been stationed at Camp Lejeune for a total period of seven years. Assuming seven years of daily exposure exclusively to the maximum concentrations of drinking water contamination approximately doubles the already highly conservative theoretical cancer risk estimates described in our response to Question 7. However, assuming a seven-year exposure duration would still not change ATSDR's original conclusions about the likelihood of developing cancer as a result of exposure to drinking contaminated water at Camp Lejeune.

9. The Hadnot Point water system supplied the Camp Lejeune Naval Regional Medical Center (prior to 1983). Why was there no occupational health assessment done for the doctors, nurses, and other hospital workers who were exposed at Hadnot Point? Should this group's increased risk be considered when making conclusions about the chance of increased cancer risk at Camp Lejeune?

Response: The exposure assessment did consider this group of people. Table 3 states the "Exposure Activity" as "People in the Hospital Point housing complex and *other buildings supplied by the Hadnot Point Drinking Water System* ingesting, inhaling, and having dermal contact with contaminated drinking water" (emphasis added). Although not listed as a separate group in the cancer risk estimate calculations, they were included in Table 3 and considered in our evaluation for likely health effects (cancer and noncancer). The exposures would not differ significantly from those of persons in housing areas.

10. Is there any scientific link between reproductive problems and exposure to VOCs as a child? If so, has this relationship been assessed in regards to Camp Lejeune?

Response: No known reports indicate adverse reproductive outcomes in adults as a result of childhood exposures to 1,2-DCE, PCE, or TCE. In addition, no studies have observed reproductive effects in experimental animals ingesting 1,2-DCE.

ATSDR has identified a priority research need for additional studies to investigate the potential for reproductive and developmental effects across multiple generations from oral exposures to PCE. Studies conducted in experimental animals have found no evidence for effects on mating, fertility, and reproductive performance in adults as a result of *in utero* exposures to TCE ingested by dams.

11. The Comprehensive Environmental Response Compensation and Liability Act (CERCLA), Section 104(i) requires the Administrator of the ATSDR to "maintain a national registry of serious diseases and illnesses and a national registry of persons exposed to toxic substances." Is there a national registry for TCE and PCE? Are military families who lived at Camp Lejeune during the period of contamination included in a national registry? Has the ATSDR considered whether to establish a Camp Lejeune specific registry of exposed persons as authorized by CERCLA section 104(i)(8)?

Response: Camp Lejeune families are not currently included in the National Exposure Registry (NER) for TCE. No specific registry for PCE currently exists.

At the moment, ATSDR is not adding new enrollees to NER, and the agency is deliberating how best to utilize or modify the NER in the future. The other major obstacle to including Camp Lejeune families in the registry is the fact that until computer modeling of the base's past water distribution system is complete, exposures to families there cannot be considered fully confirmed or documented. Documentation of exposure is required for enrollment in the registry.

Following the completion of the water modeling, however, ATSDR will evaluate the feasibility of enrolling those exposed to contaminated drinking water at Camp Lejeune in the existing registry or in a new registry, perhaps one that is site-specific.

12. The 1997 Public Health Assessment (page 15) states, "Because of the results of the epidemiological studies suggest a possibility of cancer from exposure to VOCs at low doses, more studies are needed to adequately address the issue of human cancer association with low-dose VOC exposure." Has the ATSDR recommended a program of research to address this issue? If not, why not? Has the ATSDR recommended any other research efforts or programs to address scientific gaps that have come to light as a result of the drinking water contamination situation at Camp Lejeune? If not, please explain why not.

Response: In developing the Agency's Toxicological Profile for DCE (1996), ATSDR found that no studies evaluating the carcinogenic effects of DCE in animals were available, nor were reports of cancer in humans exposed to this substance. Therefore, ATSDR identified a need for research in animals to determine the potential for carcinogenicity from exposures to DCE.

The Toxicological Profiles for PCE (1997) and TCE (1997) identified needs for additional epidemiological studies on these substances. Specifically, ATSDR recommended further evaluation of cancers associated with oral and inhalation exposures to these substances.

In addition to the toxicological profiles, ATSDR documented its "priority" data needs for TCE and PCE in a 1992 Federal Register notice. At that time, ATSDR considered additional epidemiology studies on effects from oral and inhalation exposures to TCE a priority, and cancer was among the endpoints requiring further study in any future epidemiological investigation.

Since then, several new studies on TCE's carcinogenic potential from high level occupational exposures have become available. The updated Toxicological Profile for Trichloroethylene (2000) discussed available studies. The profile also described the limitations of these studies for assessing health effects from low-level environmental exposures to TCE.

Thus, ATSDR still considered additional epidemiological studies a "data need," but no longer a priority. This reclassification is reflected in a January 2002 notice in the *Federal Register*, which lists the "priority data need" as "filled." The notice also explains, however, that "ATSDR continues to evaluate new data as they become available to determine if additional studies are needed" for understanding potential health risks from low-level environmental exposures.

On the question about recommendations for research to address data gaps at Camp Lejeune, ATSDR continues to work with the EPA to publish a test rule that will require private industry to conduct research on identified priority data needs for TCE and PCE. In addition, ATSDR is furthering collaboration with the Halogenated Solvents Industry Alliance to conduct studies of identified priority data needs for TCE and PCE.

These research efforts will address data needs for TCE and PCE and support agency efforts at sites where these substances have been found, including Camp Lejeune.

For your reference, we have attached the following documents:

- Announcement of final priority data needs for 38 hazardous substances. *Federal Register* Notice Publication. 1992 November 16.;57:54150-59.
- Letter from HSIA notifying ATSDR of interest in conducting voluntary research on TCE and PCE.
- Update on the status of the Superfund substance-specific applied research program." *Federal Register* Notice Publication. 2002 January 31;67:4836-54.

13. The Navy unsuccessfully attempted to reduce the scope of the ATSDR's proposed full epidemiological study of children exposed in utero. Please identify any issues raised by the Office of Management and Budget (OMB) with respect to the scope, methodology, timing, or funding of the ATSDR's proposed survey and epidemiological study. Please provide any documentation of OMB's comments with respect to the ATSDR's health assessment at Camp Lejeune or with respect to the proposed survey and epidemiological study for children exposed in utero.

Response: To assure completeness, ATSDR is continuing to gather information related to this response that will be provided in a separate communication.

References

Agency for Toxic Substances and Disease Registry. Toxicological Profile for 1,2-dichloroethene. Atlanta: U.S. Department of Health and Human Services; 1996.

Agency for Toxic Substances and Disease Registry. Toxicological profile for tetrachloroethylene (PERC). Atlanta: US Department of Health and Human Services; 1997.

Agency for Toxic Substances and Disease Registry. Toxicological profile for trichloroethylene. Atlanta: U.S. Department of Health and Human Services; 1997.

Ashengrau A, Ozonoff D, Paula C, Coogan P, Vezina R, Heeren T, Zhang Y. Cancer risk and tetrachloroethylene-contaminated drinking water in Massachusetts. *Archives of Environ Health* 1993;48:284–92.

Anshengrau A, Paula C, Ozonoff D. 1998. Tetrachloroethylene-contaminated Drinking Water and the Risk of Breast Cancer. *Environ Health Perspect* 1998;106 (suppl 4):947–53.

Bruning T, Pesch T, Wiesenhutter B, Rabstein S, Lammert M, Baumuller A, Bolt HM. Renal Cell Cancer Risk and Occupational Exposure to Trichloroethylene: results of a consecutive case-control study in Arnsberg, Germany. *Amer J Ind Med* 2003;43:274–85.

California Environmental Protection Agency. Public health goal for trichloroethylene in drinking water. Office of Environmental Health Hazard Assessment. February 1999.

Clewell HJ, Gentry PR, Gearhart JM, Allen B, Andersen M. Comparison of cancer risk estimates for vinyl chloride using animal and human data with a PBPK model. *Sci Total Environ* 2001;274:37–66.

Cohn P, Klotz J, Bove F, Fagliano J. Drinking water contamination and the incidence of leukemia and non-Hodgkin's lymphoma. *Environ Health Perspect* 1994;102:556–61.

Feron VJ, Jonker D, Groten JP, Horbach GJ, Cassee FR, Schoen ED, Opdam JJG. Combination technology: from challenge to reality. *Toxicol Tribune* 1993;14:1–3.

Gough M. Antagonism—no synergism—in pair wise tests of carcinogens in rats. *Regul Toxicol Pharmacol.* 2002 Jun;35(3):383-92.

Groten JP. 2000. Mixtures and interactions. *Food Chem Toxicol* 2000;38(1 Suppl):S65.

Lee LJH, Chung CW, Ma YC, Wang GS, Chen PC, Hwang YH, Wang JD. Increased mortality odds ratio of male liver cancer in a community contaminated by chlorinated hydrocarbons in groundwater. *Occup Environ Med* 2003;60:364–69.

ATSDR's Responses to Questions from Congressman Dingell

Mundt KA, Birk T, Burch MT. Critical review of the epidemiological literature on occupational exposure to perchloroethylene and cancer. *Int Arch Occup Environ Health* 2003;76:473–91.

Paula C, Anshengrau A, Ozonoff D. Tetrachloroethylene-contaminated Drinking Water in Massachusetts and the Risk of Colon-Rectum, Lung, and Other Cancers. *Environ Health Perspect* 1999;107:265–71.

Seed J, Brown R, Olin SS, Foran JA. 1995. Chemical mixtures: current risk assessment methodologies and future directions. *Regul Toxicol Pharmacol* 1995;22:76–94.

United States Environmental Protection Agency. Trichloroethylene health risk assessment: synthesis and characterization. External review draft. Washington, D.C.: US Environmental Protection Agency; 2001. EPA/600/P-01/002A.

United States Environmental Protection Agency (EPA). Review of draft trichloroethylene health risk assessment: synthesis and characterization: An EPA science advisory board report. Washington, D.C.: US Environmental Protection Agency; 2002. EPA-SAB-EHC-03-002.

United States Environmental Protection Agency. Draft final guidelines for carcinogen risk assessment final (external review draft): Risk assessment forum. Washington, D.C.: U.S. Environmental Protection Agency; March 2003. NCEA-F-0644A.

Wade MG, Foster WG, Younglai EV, McMahon A, Leingartner K et al.. Effects to subchronic exposure to a complex mixture of persistent contaminants in male rats: systemic, immune and reproductive effects. *Toxicol Sci* 2002;67:131–43.