ATSDR
AGENCY FOR TOXIC SUBSTANCES AND DISEASE REGISTRY

Public Health Assessment for

Camp Lejeune Drinking Water Public Health Assessment
U.S. Marine Corps Base Camp Lejeune, North Carolina

MAY 3, 2016

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
Agency for Toxic Substances and Disease Registry

Comment Period Ends:

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THE ATSDR PUBLIC HEALTH ASSESSMENT: A NOTE OF EXPLANATION

This Public Health Assessment-Public Comment Release was prepared by ATSDR pursuant to the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA or Superfund) section 104 (i)(6) (42 U.S.C. 9604 (i)(6), and in accordance with our implementing regulations (42 C.F.R. Part 90). In preparing this document, ATSDR has collected relevant health data, environmental data, and community health concerns from the Environmental Protection Agency (EPA), state and local health and environmental agencies, the community, and potentially responsible parties, where appropriate. This document represents the agency's best efforts, based on currently available information, to fulfill the statutory criteria set out in CERCLA section 104 (i)(6) within a limited time frame. To the extent possible, it presents an assessment of potential risks to human health. Actions authorized by CERCLA section 104 (i)(11), or otherwise authorized by CERCLA, may be undertaken to prevent or mitigate human exposure or risks to human health. In addition, ATSDR will utilize this document to determine if follow-up health actions are appropriate at this time.

This document has previously been provided to EPA and the affected state in an initial release, as required by CERCLA section 104 (i)(6) (H) for their information and review. Where necessary, it has been revised in response to comments or additional relevant information provided by them to ATSDR. This revised document has now been released for a 60-day public comment period. Subsequent to the public comment period, ATSDR will address all public comments and revise or append the document as appropriate. The public health assessment will then be reissued. This will conclude the public health assessment process for this site, unless additional information is obtained by ATSDR which, in the agency's opinion, indicates a need to revise or append the conclusions previously issued.

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PUBLIC HEALTH ASSESSMENT

Camp Lejeune Drinking Water Public Health Assessment
U.S. Marine Corps Base Camp Lejeune, North Carolina

Prepared by:

Central Branch
Division of Community Health Investigations
U.S. Department of Health and Human Services
Agency for Toxic Substances and Disease Registry

FOREWORD

The Agency for Toxic Substances and Disease Registry, ATSDR, was established by Congress in 1980 under the Comprehensive Environmental Response, Compensation, and Liability Act, also known as the *Superfund* law. This law set up a fund to identify and clean up our country's hazardous waste sites. The Environmental Protection Agency, EPA, and the individual states regulate the investigation and clean up of the sites.

Since 1986, ATSDR has been required by law to conduct a public health assessment at each of the sites on the EPA National Priorities List. The aim of these evaluations is to find out if people are being exposed to hazardous substances and, if so, whether that exposure is harmful and should be stopped or reduced. If appropriate, ATSDR also conducts public health assessments when petitioned by concerned individuals. Public health assessments are carried out by environmental and health scientists from ATSDR and from the states with which ATSDR has cooperative agreements. The public health assessment program allows the scientists flexibility in the format or structure of their response to the public health issues at hazardous waste sites. For example, a public health assessment could be one document or it could be a compilation of several health consultations - the structure may vary from site to site. Nevertheless, the public health assessment process is not considered complete until the public health issues at the site are addressed.

Exposure: As the first step in the evaluation, ATSDR scientists review environmental data to see how much contamination is at a site, where it is, and how people might come into contact with it. Generally, ATSDR does not collect its own environmental sampling data but reviews information provided by EPA, other government agencies, businesses, and the public. When there is not enough environmental information available, the report will indicate what further sampling data is needed.

Health Effects: If the review of the environmental data shows that people have or could come into contact with hazardous substances, ATSDR scientists evaluate whether or not these contacts may result in harmful effects. ATSDR recognizes that children, because of their play activities and their growing bodies, may be more vulnerable to these effects. As a policy, unless data are available to suggest otherwise, ATSDR considers children to be more sensitive and vulnerable to hazardous substances. Thus, the health impact to the children is considered first when evaluating the health threat to a community. The health impacts to other high risk groups within the community (such as the elderly, chronically ill, and people engaging in high risk practices) also receive special attention during the evaluation.

ATSDR uses existing scientific information, which can include the results of medical, toxicologic and epidemiologic studies and the data collected in disease registries, to determine the health effects that may result from exposures. The science of environmental health is still developing, and sometimes scientific information on the health effects of certain substances is not available. When this is so, the report will suggest what further public health actions are

needed.

Conclusions: The report presents conclusions about the public health threat, if any, posed by a site. When health threats have been determined for high risk groups (such as children, elderly, chronically ill, and people engaging in high risk practices), they will be summarized in the conclusion section of the report. Ways to stop or reduce exposure will then be recommended in the public health action plan.

ATSDR is primarily an advisory agency, so usually these reports identify what actions are appropriate to be undertaken by EPA, other responsible parties, or the research or education divisions of ATSDR. However, if there is an urgent health threat, ATSDR can issue a public health advisory warning people of the danger. ATSDR can also authorize health education or pilot studies of health effects, full-scale epidemiology studies, disease registries, surveillance studies or research on specific hazardous substances.

Community: ATSDR also needs to learn what people in the area know about the site and what concerns they may have about its impact on their health. Consequently, throughout the evaluation process, ATSDR actively gathers information and comments from the people who live or work near a site, including residents of the area, civic leaders, health professionals and community groups. To ensure that the report responds to the community's health concerns, an early version is also distributed to the public for their comments. All the comments received from the public are responded to in the final version of the report.

Comments: If, after reading this report, you have questions or comments, we encourage you to send them to us.

Letters should be addressed as follows:

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Acronyms

ADAF	age dependent adjustment factor
AL	action level
AST	above ground storage tank
ATSDR	Agency for Toxic Substances and Disease Registry
BMDL	benchmark dose lower bound
BTEX	benzene, toluene, ethyl benzene, xylene
BLL	blood lead levels
CAP	Community Advisory Panel
CLW	Camp Lejeune water document
CREG	cancer risk evaluation guides (defined in Appendix A)
CSF	cancer slope factor
CDC	Centers for Disease Control and Prevention
CTE	central tendency exposure
DCE	dichloroethylene
DPH	Division of Public Health
EMEG	environmental media evaluation guide (defined in Appendix A)
gpm	gallons per minute
HB	Holcomb Boulevard
HEC	human equivalent concentration
HED	human equivalent dose
HI	hazard index
HP	Hadnot Point
IQ	intelligence quotient
IARC	International Agency for Research on Cancer
IEUBK	Integrated Exposure Uptake Biokinetic
IRIS	Integrated Risk Information System
IRP	installation restoration program
IUR	inhalation unit risk
LCR	Lead and Copper Rule
LOAEL	lowest observed adverse effect level
MBW	mean birth weight
µg/dL	micrograms per deciliter
MC	Monte Carlo
MCAS	Marine Corps Air Station
MCB	Marine Corps Base
MCL	maximum contaminant level (defined in Appendix A)
MRL	minimal risk level (defined in Appendix A)
NHANES	National Health and Nutrition Examination Survey
NMCPHC	Navy and Marine Corps Public Health Center
NOAEL	no observed adverse effect level
NPL	National Priorities List
NTP	National Toxicology Program
ODW	Office of Drinking Water
PBPK	physiologically-based pharmacokinetic
PCE	tetrachloroethylene, sometimes referred to as perchloroethylene
PLPPP	Pediatric Lead Poisoning Prevention Program
ppb	parts per billion
ppm	parts per million
PRP	potentially responsible party

RfC	reference concentration (defined in Appendix A)
RfD	reference dose (defined in Appendix A)
RME	reasonable maximum exposure
RMEG	reference dose media evaluation guide (defined in Appendix A)
SDWA	Safe Drinking Water Act
SGA	small for gestational age
SI	site investigation
SIRS	Site Investigation and Restoration Section
trans-1,2-DCE	trans-1,2-dichloroethylene
TCE	trichloroethylene
TLBW	term low birth weight
TT	Tarawa Terrace
TTHM	total trihalomethanes
USEPA	United States Environmental Protection Agency
UST	underground storage tank
VC	vinyl chloride
VOC	volatile organic compounds
WTP	water treatment plant

MCB Camp Lejeune Public Health Assessment Summary

Introduction

The Agency for Toxic Substances and Disease Registry (ATSDR) is a congressionally mandated agency of the U.S. Department of Health and Human Services. ATSDR conducted this public health assessment to:

1. Evaluate whether past exposure to the following chemicals (referred to here as contaminants of concern) in drinking water at the Marine Corps Base (MCB) Camp Lejeune were likely to have resulted in adverse health impacts related to that exposure:[1]
    a. Benzene,
    b. Tetrachloroethylene (PCE),
    c. Trichloroethylene (TCE),
    d. Trans-1,2-dichloroethylene (DCE), and
    e. Vinyl chloride.
2. Assess additional exposure scenarios requested by the Community Assistance Panel.
3. Evaluate more recent exposure to lead in drinking water based on sampling data collected at Camp Lejeune (2005–2013).

In a 1997 public health assessment (PHA), ATSDR concluded that people were exposed to contaminants of concern in MCB Camp Lejeune drinking water. Although ATSDR declared those past exposures a public health hazard, it did so on the information that was available at the time, which was limited. Since publication of the 1997 PHA, additional scientific analyses and studies have expanded the knowledge base regarding contaminants of concern in MCB Camp Lejeune drinking water. This assessment evaluates exposures based on these new analyses and studies, particularly the findings from ATSDR's historical reconstruction modeling efforts.

For this public health assessment, ATSDR developed estimates of exposure doses for the following groups who lived or worked at—or lived and worked at—MCB Camp Lejeune:

- Children who lived onbase with their families
- Adults who lived onbase (inclusive of pregnant women)
- Workers employed at the base, but who lived off-base
- Marine personnel who trained and lived onbase

This PHA also investigates how MCB Camp Lejeune is preventing lead exposure. The lead exposure assessment is conducted separately from the historical reconstruction contaminants of concern because the timeframes of exposure do not overlap and are separated by approximately 20 years. If lead is present in the drinking water, the contamination occurs after the water leaves the treatment plant. Groundwater is not the source of lead in the drinking water. The discussion of the lead evaluation begins in the section titled Lead in Drinking Water and is separate from this PHA's discussions on the other contaminants of concern.

[1] Using ATSDR historical reconstruction estimates, the potential exposure period varied depending on the MCB area: Hadnot Point (early 1950s–1996); Tarawa Terrace (late 1950s–1987); and Holcomb Boulevard (intermittently from 1972–1985; before 1972, Hadnot Point wells supplied Holcomb Boulevard drinking water).

In the past as well as today, groundwater is MCB Camp Lejeune's sole drinking water source. Researchers first identified groundwater contamination and, consequently, MCB Camp Lejeune drinking water contamination in 1980 at the Hadnot Point and Tarawa Terrace water treatment plants (WTPs) (MCB Camp Lejeune Water Documents CLW #438, #441, and #443). Because base operations and waste handling practices resulted in contaminated groundwater, sediment, soil, and surface water, USEPA added Camp Lejeune to its National Priorities List (NPL) on October 4, 1989. Researchers found that historical hazardous material handling and disposal practices led to environmental contamination at several base areas. Base-wide environmental investigations continue under MCB Camp Lejeune's Installation Restoration Program.

Drinking water samples taken in the early 1980s confirmed that MCB Camp Lejeune's Hadnot Point and Tarawa Terrace water treatment plants were distributing water that contained PCE and TCE; however, these contaminants were unregulated in drinking water at that time. MCB Camp Lejeune started removing the highest-contaminated wells at the Hadnot Point WTP in November 1984 and by February 1985 had switched to using uncontaminated wells altogether (Maslia et. al. 2013). Today the Hadnot Point WTP supplies MCB drinking water from uncontaminated, routinely monitored wells.

An offsite drycleaner contaminated the Tarawa Terrace water supply. In February 1985, MCB shut down the Tarawa Terrace WTP's two most contaminated wells, which reduced drinking water contaminant concentrations below current ATSDR levels of health concern. In March 1987, MCB Camp Lejeune closed the Tarawa Terrace WTP altogether.

Thus the historical record shows that in the past, people living and working at MCB Camp Lejeune were exposed to contaminated drinking water. However, because during the early 1980s these contaminants were unregulated, base officials took relatively few drinking water samples to measure chemical contaminants at the base's water treatment plant; therefore, the extent and duration of exposure was unknown. ATSDR conducted historical reconstruction modeling to estimate the past contaminant concentrations in MCB Camp Lejeune's water supplies (Maslia, et al., 2007, 2009, 2013). This drinking water public health assessment uses the concentrations generated by ATSDR's historical reconstruction modeling effort published in 2013 to complete a new exposure evaluation that estimates potential exposure doses, upper-bound cancer risks, and potential noncancer health effects.

ATSDR has conducted several investigations of potential health effects among Marine and naval personnel and their families from exposure to MCB drinking water. Refer to Appendix F for additional information on the ATSDR health studies. Studies include

1. Birth Defects and Childhood Cancer study published in December 2013,
2. Adverse Birth Outcomes study published November 2014,
3. February 2014 Mortality Study of active duty personnel stationed at MCB Camp Lejeune anytime between April 1975 and December 1985, compared with the mortality rates of active duty personnel at MCB Camp Pendleton,

4. A second mortality study published in August 2014 that compared the mortality rates of MCB Camp Lejeune workers with the mortality rates of MCB Camp Pendleton workers, and
5. A Male Breast Cancer Study published in September 2015, of Marines[2] born before January 1, 1969 and whose diagnosis, treatment, or both are recorded in the U.S. Department of Veterans Affairs Central Cancer Registry.

Ongoing ATSDR investigations include

1. A health survey of active duty personnel stationed at MCB Camp Lejeune anytime between April 1975 and December 1985, civilian employees who worked at the base anytime between October 1972 and December 1985, and parents and children surveyed from 1999 to 2002 for a birth defects/childhood cancer case-control study. This study will also include comparison groups from MCB Camp Pendleton.
2. A vapor intrusion evaluation, which—to the extent possible—will assess whether past or current building occupants were or are exposed to harmful levels of contaminants in indoor air originating from groundwater or soil contamination.
3. A cancer incidence study of Marine and Naval personnel who began active duty on or after April 1975 and were stationed at Camp Lejeune anytime during the period April 1975 to December 1985, and civilian employees who worked at Camp Lejeune anytime during the period October 1972 to December 1985. This study will evaluate specific causes of cancer that will involve cancer registries nationwide as well as federal cancer registries. This study will also include comparison groups from MCB Camp Pendleton.

[2] The term "Marines," as used in this public health assessment, includes naval personnel.

Conclusions

For those exposed to contaminated drinking water at MCB Camp Lejeune, the Agency for Toxic Substances and Disease Registry made the following conclusions:

Conclusion 1- Hadnot Point

Residents, workers, Marine and naval personnel, and Marines-in-training at MCB Camp Lejeune were in the past exposed to contaminants in drinking water supplied by the **Hadnot Point** WTP. And, using the estimates described in our report, this contaminant exposure was at levels that could have harmed their health. **The estimated levels to which all the above-mentioned groups of people were exposed would have resulted in an increased cancer risk and increased potential of experiencing adverse, noncancer health effects.**

Trichloroethylene (TCE) and vinyl chloride were the chemicals that contributed most to the increased cancer risk. The magnitude of the cancer risk estimated in this public health assessment depends on the period during which people were on the base and their ages while there. Using a 3-year exposure duration, the increased, upper-bound cancer risk exceeds the USEPA's Superfund target cancer-risk range (1 excess case for every 10,000 exposed persons to 1 excess case for every 1,000,000 exposed) during the years 1964–1985 (Figure 9). Specifically,

- Children living on-base from the early 1970s to the mid-1980s had an estimated, upper-bound cancer risk up to about 50 excess cases of cancer for every 10,000 exposed persons. This exceeds the USEPA's Superfund target cancer-risk range by about 50 times.
- Workers from the mid-1960s to the early-1980s had an estimated, upper-bound cancer risk of about three excess cases of cancer for every 10,000 exposed persons.
- Marines-in-training from the mid-1960s to the early-1980s had an estimated, upper-bound cancer risk of about four excess cases of cancer for every 10,000 exposed persons.
- Other adults living on-base from the late 1970s to the early-1980s had an estimated, upper-bound cancer risk of about one excess case of cancer for every 10,000 exposed individuals. This is within EPA's Superfund target cancer-risk range.

TCE was the main contributor to potential noncancer health effects. All exposure groups evaluated had exposures in the range of those that caused health effects in animal studies, increasing the risk of experiencing adverse noncancer health effects. Specifically,

- Pregnant women using Hadnot Point drinking water from 1972 to 1985 would have been exposed to TCE levels that could have resulted in effects to a developing fetus. Women in the first trimester of pregnancy are one of the most sensitive populations for exposure to TCE, primarily because of concerns associated with fetal heart malformations that could occur from exposure during that critical period of development.
- Children and all adults exposed to TCE during the years 1972–1985 were at an increased risk for immune system effects.

Conclusion Basis	TCE exposure is associated with an increased risk for kidney cancer, liver cancer, and non-Hodgkin lymphoma. Vinyl chloride exposure is associated with angiosarcoma of the liver and variable associations with lung and brain cancer. TCE and vinyl chloride are both considered known human carcinogens by the National Toxicology Program (NTP). The ATSDR mortality study of military personnel stationed at MCB Camp Lejeune found elevated hazard ratios for several cancers, including kidney cancer, liver cancer, esophageal cancer, cervical cancer, multiple myeloma, and Hodgkin lymphoma. Exposure to vinyl chloride is mainly associated with increased risk of liver cancer. For noncancer health effects, Hadnot Point area TCE exposure estimates of the dose for residents and workers not only exceeded the EPA Reference Dose (RfD) and ATSDR Oral Minimal Risk Level (MRL), but were in the same range as the human equivalent doses in laboratory animal studies that found associations with developmental and immune effects. These developmental health effects could include cardiac malformations and altered function of immune systems that could occur in children whose mothers were exposed during pregnancy. In addition, children and adults exposed to estimated TCE levels during the years in question might have resulted in increased risk for autoimmune disease and an increase in the delayed hypersensitivity response of the immune system.
Next Steps	ATSDR will conduct a cancer incidence study and continue to provide health education and followup materials to persons concerned about the potential magnitude of the increased risk of developing cancer or of the likelihood of noncancer health effects. ATSDR will work with the Community Assistance Panel[3], and the U.S. Department of Veterans Affairs to communicate health information to military personnel, workers, and families who were located at Camp Lejeune. This will include providing educational materials on the ATSDR Camp Lejeune Web site at http://www.atsdr.cdc.gov/sites/lejeune/index.html. Concerned persons can discuss any health concerns with their own healthcare providers, who may refer them to an Association of Occupational and Environmental Clinic (AOEC), which has doctors who specialize in occupational and environmental medicine. A list of AOEC locations is available at http://www.aoec.org/.
Conclusion 2- Tarawa Terrace-	Past exposure to contaminants of concern in drinking water supplied by the **Tarawa Terrace** WTP might have harmed the health of young children and Marines in training. **The estimated levels to which young children were exposed would have resulted in an increased cancer risk and increased potential of adverse, noncancer health effects.** Vinyl chloride contributed most to any increased cancer risk for those using the Tarawa Terrace water supply. The estimated magnitude of that risk as measured in this public health assessment depended on the time persons

[3] ATSDR created a community assistance panel (CAP) for the Camp Lejeune site for the purpose of having a forum to voice the concerns of the affected community of Marines and their families and to provide input for health studies. The CAP consists of community members, one representative from the Department of Defense (DoD), independent scientific experts, and ATSDR staff.

occupied the base and their ages while there. During 1956–1984, for those who used Tarawa Terrace water system drinking water, the cancer risk for children below age 6 did exceed the USEPA target risk range (Figure 10). Specifically,

- Children who lived on-base during 1956–1984 had an estimated, upper-bound cancer risk of up to about seven excess cases of cancer for every 10,000 exposed persons.
- For adults, workers, and Marines-in-training who were only exposed to water from Tarawa Terrace, the estimated, upper-bound cancer risk was within the EPA Superfund target risk range. However, Marines who were exposed to water from the Hadnot Point system during training may have had cancer risks similar to Marines who lived in Hadnot Point housing, which is described in Conclusion 1.

Regarding potential noncancer health effects associated with TCE exposure,

- Young children and Marines-in-training who lived on-base during the years 1956–1984 may have had an increased risk for adverse immune system effects.
- Children born to women who were pregnant when they lived at Tarawa Terrace and exposed to water from Hadnot Point system during training during the years 1956–1984 may have been at a greater risk for developmental and immune system effects resulting from exposures to peak concentrations.

Conclusion Basis

Vinyl chloride exposure has been associated with an increased liver cancer risk. The mortality study of military personnel stationed at MCB Camp Lejeune found elevated hazard ratios for several cancers, including liver cancer. For instance, during early 1982, hazard ratios for children 0–3 years of age exposed to drinking water contaminants were estimated to result in up to seven excess cancer cases per 10,000 persons. Children would have an increased cancer risk, while adults would have a low increased cancer risk. The cancer risk for Tarawa Terrace was almost completely associated with vinyl chloride exposure.

Regarding potential noncancer health effects, at Tarawa Terrace the maximum estimated ingestion of PCE and TCE exposure doses and inhalation concentrations were only slightly above the ATSDR and USEPA health guidelines (Figures 4 and 6). The estimated level of TCE exposure for women who had contact with Tarawa Terrace drinking water during the early stages of pregnancy, particularly those in training, could have resulted in adverse effects on fetal cardiac development, based on the results from an animal study.

Based on our current understanding from animal studies, noncancer and cancer health effects from exposure to even the peak PCE concentrations would not be expected to be associated with adverse health effects to residents, workers, or Marines at Tarawa Terrace. However, that conclusion is limited by the available dose-response information about all possible health outcomes. An ATSDR epidemiologic study found a suggested association between PCE exposure at the highest concentrations in the water supply and preterm birth (Ruckart et al., 2014). Although there are limitations in using this type of study to attribute such

	an effect to a specific chemical and exposure level, we acknowledge that there is uncertainty in the conclusion of no expected adverse effects. The maximum estimated ingestion exposure doses and inhalation concentrations of trans-1,2-dichloroethylene (trans-1,2-DCE) and vinyl chloride at Tarawa Terrace were below the ATSDR and USEPA health guidelines. Exposure to even the highest trans-1,2-DCE and vinyl chloride concentrations in the drinking water would unlikely be associated with health effects to the residents, workers, or Marines living at Tarawa Terrace.
Next Steps	ATSDR will continue to provide health education and followup materials to persons concerned about the potential magnitude of the increased cancer risk by working with the Community Assistance Panel, U.S. Department of Veterans Affairs, and by providing educational materials on the ATSDR Camp Lejeune Web site at http://www.atsdr.cdc.gov/sites/lejeune/index.html. Concerned persons can discuss any health concerns with their own healthcare providers, who may refer them to an AOEC, which has doctors who specialize in occupational and environmental medicine. A list of AOEC locations is available at http://www.aoec.org/.
Conclusion 3– Holcomb Boulevard	During brief periods (in June, 1978 and from January 28 to February 4, 1985), women in their first trimester of pregnancy exposed to TCE in drinking water from the **Holcomb Boulevard** water supply area could have had an increased risk for fetal cardiac effects and other adverse birth outcomes. At other periods, the levels of contaminants of concern in the water supply serving the Holcomb Boulevard housing areas were highly variable. **Still, the average levels of contaminants of concern over a 3-year residency are not considered to have been a health concern for children, men, or nonpregnant women.**
Conclusion Basis	For Holcomb Boulevard area drinking water, TCE was the only contaminant of concern whose historically reconstructed, estimated concentrations exceeded health-based screening values. The average levels over a 3-year residency did not result in exposures considered capable of adverse health effects. Still, during two periods the Holcomb Boulevard water system used exclusively contaminated Hadnot Point drinking water. For several weeks, this exclusive use resulted in drinking water TCE levels over 50 ppb. Developmental toxicology studies in animals indicate that TCE exposure is associated with an increased occurrence of fetal cardiac effects. Exposure of Holcomb Boulevard residents to TCE from water ingestion and inhalation of vapors during showering/bathing were estimated at levels similar to those associated with fetal cardiac effects in animal studies. Women exposed during the period when TCE concentrations exceeded 50 ppb and who were in their first trimester of pregnancy (i.e., when the fetal cardiac system is developing) could have had an increased risk for fetal cardiac effects.
Next Steps	Any Holcomb Boulevard resident concerned about drinking-water related exposures should visit the ATSDR Camp Lejeune Web site at http://www.atsdr.cdc.gov/sites/lejeune/index.html. Concerned persons can discuss any health concerns with their own healthcare providers, who may refer them to an Association of Occupational and Environmental Clinic (AOEC), which has doctors who specialize in occupational and

	environmental medicine. A list of AOEC locations is available at http://www.aoec.org/.
Conclusion 4- Other Exposures	**Persons working in laundry facilities or dining operations and persons who used Hadnot Point area indoor training pools from the early 1950s to February 1985 were exposed to contaminants of concern at levels that might have harmed their health.**
Conclusion Basis	ATSDR developed conservative (health-protective) models to estimate exposure for three different scenarios presented by the Community Assistance Panel. Model results produced concentrations that exceeded comparison values of concern. The three exposure scenarios were 1) Marines and civilians training and recreating at indoor swimming pools, 2) civilians working at laundry facilities, and 3) Marines and civilians working in dining halls. In all three scenarios, TCE and benzene exceeded their ATSDR intermediate and chronic minimal risk level (MRLs), and PCE exceeded its acute, intermediate, and chronic MRL. According to the applicable air studies in ATSDR's TCE toxicological profile, estimated TCE exposures also exceeded study effect levels.
Next Steps	ATSDR will conduct a cancer incidence study and continue to provide health education and followup materials to exposed persons by working with the Community Assistance Panel, U.S. Department of Veterans Affairs, and by providing educational materials on the ATSDR Camp Lejeune Web site at http://www.atsdr.cdc.gov/sites/lejeune/index.html. Concerned persons can discuss any health concerns with their own healthcare providers, who may refer them to an AOEC, which has doctors who specialize in occupational and environmental medicine. A list of AOEC locations is available at http://www.aoec.org/.
Conclusion 5- Lead	**Based on 2005–2013 sampling data, ATSDR concludes that past exposure to lead found in tap water at 14 locations could have harmed people's health. ATSDR also concludes that for current and future exposures the potential remains for elevated lead levels in drinking water throughout the base that could harm people's health because MCB Camp Lejeune's building's water lines contain copper piping and lead-containing solder that may leach lead into the tap water, especially hot water**. Drinking lead-contaminated water, along with exposure to lead from other sources such as lead paint, could cause harmful health effects, especially to children and to a pregnant woman's developing fetus. Because ATSDR recognizes that even low levels of lead in blood have been shown to have harmful effects, we support the additional efforts MCB Camp Lejeune began in 2013 to 1) increase monitoring frequency, 2) collect an immediate followup sample whenever lead is detected, and 3) follow the USEPA 3T guidance[4] as the base's school and daycare sampling strategy. These are voluntary actions undertaken by the base that go beyond regulatory requirements.

[4] USEPA's 3Ts (Training, Testing, and Telling) help schools use simple strategies for managing the health risks of lead in school drinking water

Conclusion Basis

Although lead can affect almost every organ and system in the body, the main target for lead toxicity is the nervous system. In general, the level of lead in a person's blood gives a good indication of recent exposure to lead and correlates with harmful health effects. ATSDR notes that for some of the more sensitive health effects associated with lead exposure, no clear threshold is available.

The 2005–2013 site-specific lead data show 14 of 382 drinking water samples exceeded USEPA's 15 ppb action level[5] for lead in the past. ATSDR finds there was a past potential for elevated blood lead levels (BLLs) above 5 micrograms per deciliter[6] (µg/dL) in children who drank water from the tap at these 14 locations. In addition, tap water from these 14 locations indicated the potential for elevating BLLs in the developing fetuses of pregnant women in the past. The length of time 9 of the 14 locations had elevated lead levels is unclear. At 8 of the 14 locations, tap water sampling data were unavailable before the lead level became elevated. At the Marine Corps Air Station (MCAS) New River location 458 AS 4025, a followup sample had not been collected as of 21 March 2016.

The site-specific lead data show 284 of the 382 drinking water samples (about 75%) did not detect lead at the minimum level of detection (3 ppb). However, MCB Camp Lejeune personnel found buildings with copper pipes and lead-containing solder indicating the potential for lead to leach into base tap water. Therefore, ATSDR finds the potential for elevated BLLs above 5 µg/dL in children who drink base water.

In October 2015, the Navy and Marine Corps Public Health Center (NMCPHC) reviewed BLL tests ordered at medical treatment facilities in the Camp Lejeune area (Camp Lejeune and Cherry Point) for Department of the Navy beneficiary children (NMCPHC 2015). Although the evaluation has limitations, from March 30, 2004 through October 1, 2015, only a few elevated BLLs[7] in children (i.e., 5 of 4,354 children tested) were found. These data may not necessarily be representative of all children in the site area because 1) the BLL program endeavors to test children with the highest risk for elevated blood lead levels and not all children, and 2) the evaluation did not include data from all sources like purchased care providers.

Other indoor and outdoor lead sources (e.g., lead-based paint) might also result in elevated BLLs. Therefore, ATSDR considers that people's (especially children's) daily exposure to drinking water with elevated lead

[5] USEPA's regulation to control lead in drinking water is known as the Lead and Copper Rule (also referred to as the LCR or 1991 Rule). If lead concentrations exceed an action level of 15 ppb in more than 10% of customer taps sampled, the system 1) must take a number of additional actions to control corrosion, 2) must inform the public about steps they should take to protect their health, and 3) may have to replace lead service lines under their control.

[6] Until 2012, children were identified as having a blood lead level of concern if the test result was 10 µg/dL or more of lead in blood. Experts now use a reference value of 5 µg/dL based on the U.S. population of children 1 to 5 years of age in National Health and Nutrition Examination Survey (NHANES) (ACCLPP 2012; CDC 2012b).

[7] Elevated BLL is based on the reference level in place at the time of testing. NMCPHC used a BLL reference value of 10 µg/dL for the years 2004 through 2013 and found two children with elevated BLLs. NMCPHC used the current BLL reference value of 5 µg/dL for the years 2014 through 2015 and found 3 children with elevated BLLs (NMCPHC 2015).

concentrations could have in the past and could currently harm their health.

Next Steps After its review of available information, ATSDR recommends

- People take measures to reduce exposures to lead in drinking water by using cold water for consumption and running the cold water 1–2 minutes before using it for drinking water purposes (CDC 2013d).
- People take steps to reduce lead uptake (see Figure 17, Appendix I).
- People take measures to reduce exposure to lead from other possible sources (see Table 12 and Figure 18, Appendix I).
- Parents follow the American Academy of Pediatric Guidelines and have their children tested for blood lead at 1 and 2 years of age (AAP 2012).
- MCB Camp Lejeune follow its 2013 Environmental Standard Operating Procedure (MCB Camp Lejeune 2013), USEPA's 3T guidance (USEPA 2013b), and USEPA's Lead and Copper Rule (USEPA 2012c).
- MCB Camp Lejeune retest MCAS New River location 458 AS 4025.

Overall Limitations of Conclusions

ATSDR attempted to assess accurately the potential health effects that contamination had on the MCB Camp Lejeune community. However, limitations exist in the environmental data sets used to make that assessment. When such data limitations appeared, ATSDR chose conservative (health-protective) data-interpretation options that were estimates of exposure in the upper end of the range of recommended values.

Limitations related to VOCs include the lack of water sampling data prior to 1982, uncertainty about when contamination first occurred in water supplies, reliance on the testing of finished water for leaving the treatment plant rather than at the point of exposure (i.e. the faucet or shower) for estimating exposure, limited information about site-specific exposure parameters, lack of indoor air samples, uncertainties that are intrinsic to the use of models to predict inputs to the assessment, uncertainties about the combined effects of exposure to the specific mixture of chemicals in the water systems, limitations in the available toxicological data to predict the health impacts of exposure, and lack of specific health outcome data, specifically incidence data for cancer and cardiac defects to confirm the potential effects that are described in this assessment.

Lead-related limitations include a lack of information on exposure duration and other site-specific exposure parameters, as well as uncertainties that are intrinsic to the use of a model to estimate BLLs in children. For more detailed information, see the discussion in the Data Limitations sections of the document.

Background

Site Description and History

Marine Corps Base Camp Lejeune (MCB Camp Lejeune) is in Onslow County, North Carolina, southeast of Jacksonville and about 70 miles northeast of Wilmington, North Carolina. The base covers an area in southeastern North Carolina's Coastal Plain: approximately 151,000 acres (233 square miles), with 14 miles of beach on the Atlantic Ocean. Camp Lejeune began operations in late 1941 (Watson 1995). The military base has been densely populated throughout its history, with approximately 43,000 active duty military personnel and 51,000 dependents as current occupants.

Over the years, contaminants from unlined landfills and leaking, aboveground and underground storage tanks migrated into soil and groundwater at locations across MCB Camp Lejeune. In 1983, MCB Camp Lejeune conducted an initial assessment of the potentially contaminated areas. Since that time, base-wide environmental investigations have been ongoing and continue under MCB Camp Lejeune's Installation Restoration Program. Because of proven environmental contamination, on October 4, 1989, USEPA added Camp Lejeune to its National Priorities List. Under the Comprehensive Environmental Response, Compensation, and Liability Act of 1980, as amended, (CERCLA), commonly known as the Superfund Law, the Agency for Toxic Substances and Disease Registry (ATSDR) was then required to conduct a public health assessment of the MCB Camp Lejeune site.

ATSDR's 1997 public health assessment found that people had been exposed to contaminants of concern in the MCB Camp Lejeune drinking water. ATSDR declared those past exposures a public health hazard, and ATSDR maintains that position today. Since the 1997 PHA, additional scientific information has expanded the knowledge base related to exposures to contaminants of concern in drinking water at MCB Camp Lejeune. This public health assessment will use this new information to evaluate these exposures, particularly the findings from ATSDR's historical reconstruction modeling efforts.

As of 2015, MCB Camp Lejeune's eight water-distribution systems had supplied or currently supply drinking water to base family housing and other facilities (Figures 1 and 2). Three of the eight distribution systems were contaminated and therefore were evaluated in this public health assessment: Tarawa Terrace, Hadnot Point, and Holcomb Boulevard. The Hadnot Point and Tarawa Terrace water-distribution systems operate independently of each other and were contaminated from different sources. Trichloroethylene (TCE), vinyl chloride (VC), tetrachloroethylene (PCE), and refined petroleum products such as benzene were most of the groundwater contaminants in the Hadnot Point Water Treatment Plant service area. Except for intermittent supply by contaminated Hadnot Point water between 1972 and 1985, groundwater in the Holcomb Boulevard WTP service area remained largely uncontaminated. Researchers have identified historical base operations and disposal practices at MCB Camp Lejeune as responsible for contamination of groundwater and drinking water supplies in the Hadnot Point-Holcomb Boulevard study area (Faye et al., 2010, 2012b). PCE and its degradation products [TCE, trans-1,2-dichloroethylene (trans-1,2-DCE), and VC] were the contaminants found in the Tarawa Terrace drinking water. ABC One-Hour Cleaners, an off-site drycleaner, was the source of the contaminants found in the Tarawa Terrace Water Treatment Plant (Shiver, 1985).

Because each water treatment system had many more wells than were necessary to supply water on any given day, operators rotated wells in and out of service. Thus, water from contaminated and uncontaminated wells mixed at WTPs before delivery to housing areas and other base facilities. As a result, contamination levels in the drinking water systems varied depending on the number, amount, and specific wells used at a particular time. By February 1985, MCB Camp Lejeune had removed from service the most highly contaminated wells in the Hadnot Point and Tarawa Terrace systems.

Figure 1. The Hadnot Point-Holcomb Boulevard Water Distribution Areas, U.S. Marine Corps Base Camp Lejeune, North Carolina

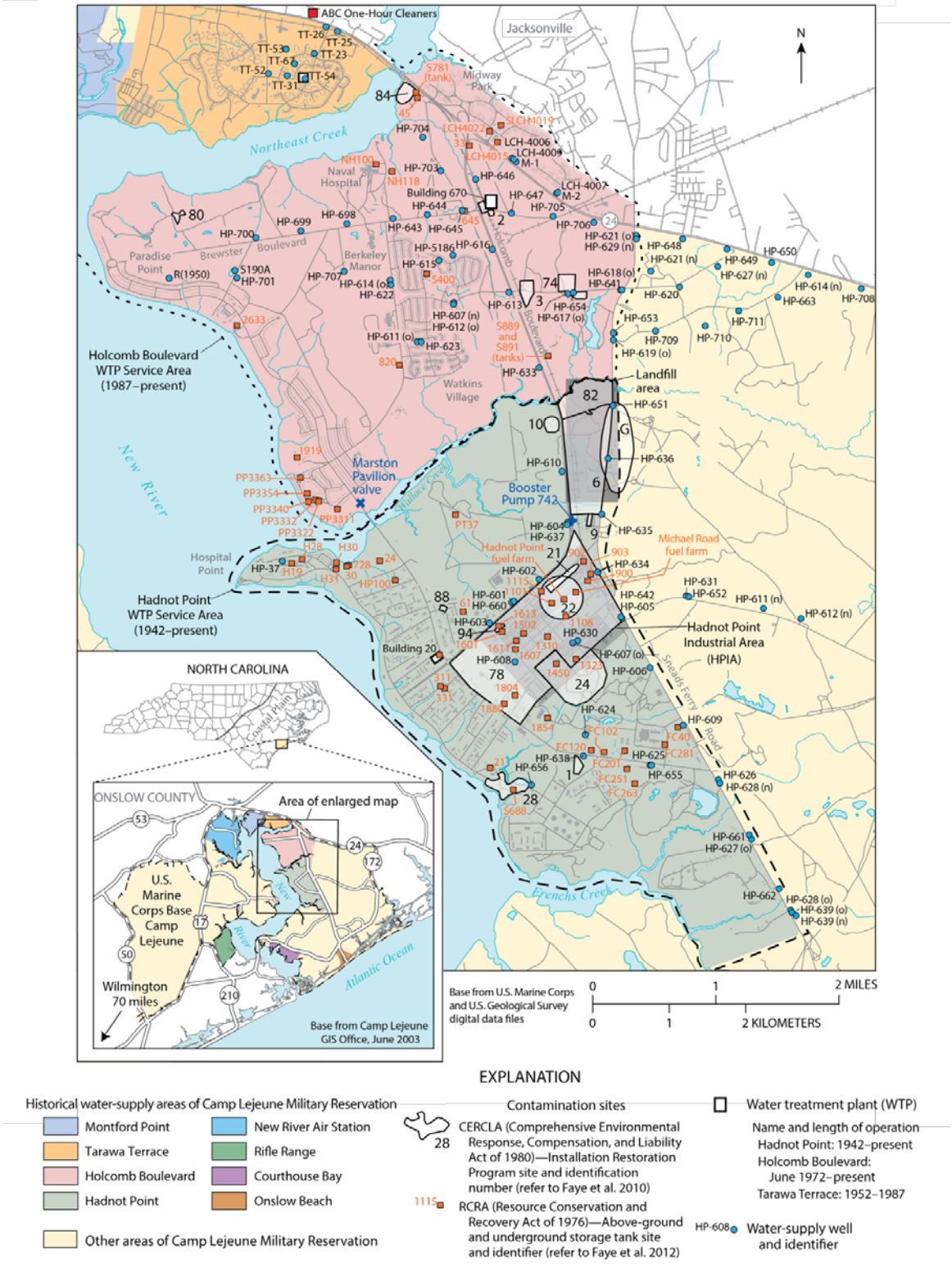
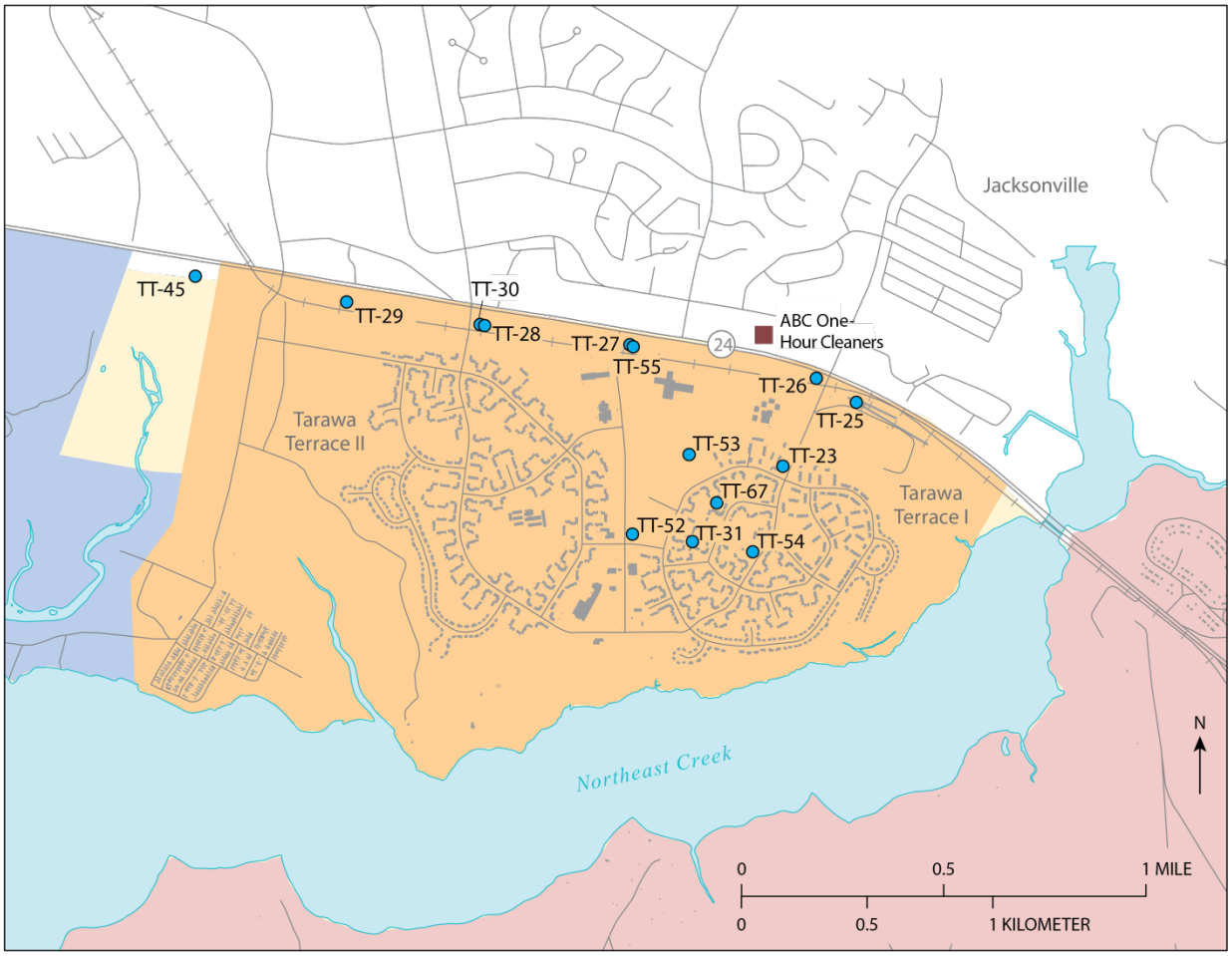


Figure 2. The Tarawa Terrace Water Distribution Area, U.S. Marine Corps Base Camp Lejeune, North Carolina



Base from U.S. Marine Corps Base Camp Lejeune geospatial files

EXPLANATION

Historical water-supply areas of Camp Lejeune Military Reservation

- Montford Point
- Holcomb Boulevard
- Tarawa Terrace
- Other areas of Camp Lejeune Military Reservation

TT-54 Water-supply well and identifier

Refer to Figure 1 for a map of the area surrounding Tarawa Terrace

Investigations of Groundwater Contamination

The Safe Drinking Water Act (SDWA of 1974) — established national permissible contaminant levels in large and municipal drinking water systems. But the SDWA also protected small water supply wells and sole-source aquifers. Acting under SDWA authority, the U.S. EPA set national primary drinking water regulations that included U.S. EPA's maximum contaminant levels (MCLs) (Pontius 2003). With the promulgation of the 2nd national interim public drinking water regulation on November 29, 1979 (also referred to as the total trihalomethanes [TTHM] rule), U.S. EPA set an interim MCL for TTHMs of 0.1 mg/L as an annual average (USEPA 1979).[8] This rule applied to any community water system that served at least 10,000 persons and that added a disinfectant to drinking water during any part of its treatment process. Thus to comply with USEPA's TTHM rule, in October 1980 the MCB Camp Lejeune water utility began testing its drinking water for TTHMs (Camp Lejeune Water Documents CLW #436). None of the THMs are chemicals of concern at Camp Lejeune.

Discovery of contaminated water supplies at MCB Camp Lejeune initiated a series of groundwater contamination assessments. The MCB Camp Lejeune Installation Restoration Program (IRP) conducted groundwater contamination assessments under the auspices of CERCLA. Additional assessments under the authority of the Resources Conservation and Recovery Act (RCRA) surveyed groundwater contamination from aboveground and underground storage tanks (AST/UST) that had leaked refined petroleum products into soil and groundwater. Faye et al., (2007, 2010) described soil and groundwater at IRP-CERCLA sites contaminated by PCE, TCE, and their degradation products, as well as benzene, toluene, ethyl benzene, and xylenes (BTEX) components. In a companion report, Faye et al., (2012) summarized investigation results for 64 designated RCRA study areas and described the occurrence and distribution of BTEX components within groundwater in the Hadnot Point/Holcomb Boulevard study area.

ATSDR Epidemiological Health Studies

Thus far, ATSDR has completed five health studies at MCB Camp Lejeune. A 2013 study (Ruckart et al. 2013) evaluated whether *in utero* and infant (up to 1 year of age) exposures to contaminants of concern in MCB Camp Lejeune drinking water were associated with specific birth defects (i.e., neural tube defects and oral clefts) and childhood hematopoietic cancers. The birth outcomes that are related to the effects of TCE exposure *in utero* in animals (e.g., cardiac abnormalities and altered immune system development) could not be evaluated because of limited ability to ascertain this information from parental surveys and in lack of a health registry that would have been needed to quantify those outcomes. Although limited in statistical precision because of wide confidence intervals, the study findings suggested an association between drinking water contaminants and neural tube defects (i.e., spina bifida and anaencephaly), published in *Environmental Health* in December 2013. The study found a weaker association with childhood hematopoietic cancers.

The second health study (Bove et. al. 2014) was an evaluation of mortality among Marine and naval personnel stationed at Camp Lejeune. These study findings were also limited in statistical precision, but nonetheless did find for several causes of elevated mortality rates compared with MCB Camp Pendleton personnel, including multiple myeloma, Hodgkin lymphoma, and cancers of the kidney, liver, esophagus, and cervix. This study also appeared in *Environmental Health* in February 2014.

The third health study (Bove et al., 2014) was an evaluation of mortality among civilians who worked at Camp Lejeune from 1973 to 1985. Again limited in statistical precision, the study findings still showed elevated mortality hazard ratios for kidney cancer, leukemias, multiple myelomas, rectal cancer, oral

[8] Total trihalomethanes or TTHMs is the sum of chloroform ($CHCL_3$), bromoform ($CHBr_3$), bromodichloromethane ($CHBrCl_2$), plus dibromochloromethane ($CHBr_2Cl$), which are disinfection byproducts formed by chlorination of drinking water (Singer 1993).

cavity cancer, and Parkinson's disease. *Environmental Health* published this study in its August 2014 issue.

The fourth health study (Ruckart et al., 2014) evaluated adverse birth outcomes for children whose mothers lived at MCB Camp Lejeune at the time of delivery from 1968 to 1985. The findings suggested associations between TCE exposure during pregnancy and small for gestational age, term low birth weight, and reduced mean birth weight. The study also found an association between PCE exposure during pregnancy and risk of preterm birth, particularly during the 2nd trimester, and between benzene exposure and term low birth weight. *Environmental Health* published this study in its November 2014 issue.

The fifth health study (Ruckart et al., 2015) is a case-control study to determine whether male Marines who served at MCB Camp Lejeune during periods of contaminated drinking water have elevated rates of breast cancer. The findings suggested possible associations between exposure to PCE, DCE, and vinyl chloride at Camp Lejeune and male breast cancer. Exposures to TCE, PCE, DCE, and vinyl chloride were also observed to possibly accelerate the onset of male breast cancer. *Environmental Health* published this study in its September 2015 issue.

ATSDR is also analyzing data from a health survey of Marines, Navy personnel, and civilian workers at MCB Camp Lejeune and at MCB Camp Pendleton in San Diego, California.

ATSDR intends to evaluate specific causes of cancer in a planned cancer incidence study that will involve cancer registries nationwide as well as federal cancer registries.

To learn more about ATSDR's health studies, please refer to Appendix F, read the respective study, or visit ATSDR's Camp Lejeune Web site (http://www.atsdr.cdc.gov/sites/lejeune/qa_healthstudyactivities.html).

ATSDR Evaluation of Environmental Exposures

ATSDR's 1997 public health assessment found that some past exposures to contaminants of concern and lead in certain MCB Camp Lejeune drinking water sources were a public health hazard. This current public health assessment updates with new data the 1997 assessment for Hadnot Point and Tarawa Terrace, particularly the findings from ATSDR's historical reconstruction modeling efforts. We included the evaluation of exposures to benzene in the update for the Hadnot Point water system.

The few available drinking water sample results prevented a thorough exposure analysis for the time the contaminated wells were actually in use. To estimate the historical concentration of contaminants in Tarawa Terrace and Hadnot Point-Holcomb Boulevard drinking water supplies, ATSDR used water-modeling techniques and historical reconstruction to estimate concentrations of particular contaminants in drinking water and to determine the level and duration of human exposure to contaminated drinking water. During 2007–2009, ATSDR published historical reconstruction results for contaminants in drinking water supplied to Tarawa Terrace family housing areas and vicinity. During 2013, ATSDR published historical reconstruction results for drinking water supplied to Hadnot Point, Holcomb Boulevard and the vicinity. This current public health assessment uses the modeled, historical contaminant concentrations from the 2013 ATSDR report to estimate the exposures. A brief summary of these reports, as they apply to this evaluation, is included in Appendix G.

For a detailed description of the historical reconstruction process, please refer to the ATSDR reports titled

- "Analysis of Groundwater Flow, Contaminant Fate and Transport, and Distribution of Drinking Water at Tarawa Terrace and Vicinity, U.S. Marine Corps Base Camp Lejeune, North Carolina: Historical Reconstruction and Present-Day Conditions" (Maslia, et al., 2007)[9] and

[9] Report available at http://www.atsdr.cdc.gov/sites/lejeune/docs/ChapterA_TarawaTerrace.pdf.

- "Analysis and Historical Reconstruction of Groundwater Flow, Contaminant Fate and Transport, and Distribution of Drinking Water within the Service Areas of Hadnot Point and Holcomb Boulevard Water Treatment Plants and Vicinities – U.S. Marine Corps Base Camp Lejeune, North Carolina" (Maslia, et al., 2013)[10].

Because volatile chemicals contaminated the MCB Camp Lejeune groundwater, vapors from these chemicals possibly migrated through the soil into nearby buildings and affected indoor air quality, a process known as vapor intrusion. This is a contaminant-migration pathway that can lead to the type of exposure that ATSDR is evaluating in a separate public health assessment.

Environmental Data Screening Process

This section contains the results of reconstructed contaminant concentrations in the drinking water for Hadnot Point, Holcomb Boulevard, and Tarawa Terrace and a comparison of those results to environmental and health guidelines. The information provided includes concentration trends over time, comparison to screening levels and federal drinking water standards, and determination of whether the chemicals could have been detected by taste and odor in the water. To identify the contaminants that required further investigation, ATSDR screened or compared contaminant concentrations with the ATSDR Environmental Guidelines discussed below.

Environmental Guidelines are media-specific substance concentrations ATSDR derives from health guidelines (MRLs, RfCs, RfDs), which integrate default exposure assumptions and dose-response criteria from toxicological studies. ATSDR environmental guidelines include available environmental media evaluation guides (EMEGs), reference dose media evaluation guides (RMEGs), and cancer risk evaluation guides (CREGs). Health assessors use these guidelines to evaluate potential health hazards associated with exposure to chemicals in water, soil, and air. MCLs and maximum contaminant level goals (MCLGs) are criteria used in the EPA Drinking Water Program.

- **EMEGs** represent concentrations of substances in water, soil, and air to which humans might be exposed during a specified period (acute, intermediate, or chronic) without experiencing adverse, noncancer health effects. Acute exposures are those of 14 days or less, intermediate exposures are those lasting 15 days to 1 year, and chronic exposures are those lasting longer than 1 year. They incorporate default, conservative (health-protective) exposure assumptions for adults and children. EMEGs are based on ATSDR minimal risk levels (MRLs).
- **RMEGs** are based on USEPA's reference doses (RfDs) and on default exposure assumptions for adults and children. U.S. EPA's reference concentrations (RfCs) serve as RMEGs for air exposures. Like EMEGs, RMEGs represent concentrations of substances (in water, soil, and air) to which humans might be exposed without experiencing adverse, noncancer health effects. Because RfDs and RfCs, which are the basis of the RMEGs consider lifetime exposures, RMEGs are used to evaluate chronic exposures.
- **CREGs** are media-specific comparison values. CREGs help to identify concentrations of cancer-causing substances unlikely to result in an increase of cancer risk in an exposed population. ATSDR develops CREGs using U.S. EPA's cancer slope factor (CSF) or inhalation unit risk (IUR), a target risk level (1×10^{-6}), and default exposure assumptions. The target risk level of 1×10^{-6} represents a theoretical risk of one excess cancer case in a population of 1 million exposed people.
- **MCLs** are enforceable EPA drinking water standards and are the highest level of contaminant allowed in a water supply system. MCLs are set as close to the MCLG as feasible using the best available analytical and treatment technologies and taking cost into consideration.

[10] Report available at http://www.atsdr.cdc.gov/sites/lejeune/docs/chapter_A_hadnotpoint.pdf.

- **MCLGs** are non-enforceable EPA health benchmark goals, which are set at a level at which no known or anticipated adverse effect on human health is expected to occur and which allows for a margin of safety. For chemicals that are carcinogens, EPA policy is that the MCLG is zero.

Table 1: Comparison Values and Drinking Water Standards for Water Ingestion (parts per billion (ppb))

Chemical	EMEG-Chronic	EMEG-Intermediate	RMEG	CREG	Current MCL
Benzene	5 (child) 18 (adult)	-	40 (child) 140 (adult)	0.64	5
PCE	80 (child) 280 (adult)	80 (child) 280 (adult)	60 (child) 210 (adult)	17	5
TCE	5 (child) 18 (adult)	5 (child) 18 (adult)	5 (child) 18 (adult)	0.76	5
trans-1,2-DCE	-	2,000 (child) 7,000 (adult)	200 (child) 700 (adult)	-	100
VC	30 (child) 110 (adult)	-	30 (child) 110 (adult)	0.025	2

"-" indicates no value available

EMEG – ATSDR environmental media evaluation guide

RMEG – ATSDR reference dose media evaluation guide

CREG – ATSDR cancer risk evaluation guide

MCL – EPA maximum contaminant level

PCE – tetrachloroethylene

TCE – trichloroethylene

DCE – dichloroethylene

VC – vinyl chloride

Boldfaced values in the table above were the guidelines used in the following comparisons.

Chemical Background Information

Detection of benzene in groundwater is usually an indication of contamination from refined petroleum products (e.g., gasoline, jet fuel, diesel fuel).

PCE is a chemical most widely used for dry cleaning of fabrics and for metal-degreasing operations. Consequently, PCE is also a common groundwater contaminant. PCE has chemical properties very similar to TCE. Both TCE and PCE can persist in groundwater for long periods, but microbial activity can also degrade them both.

Because of its widespread use as a solvent, degreasing agent, and dry cleaning chemical, TCE is a common groundwater contaminant in areas of industrial activity. Because of TCE's physical properties, releases from storage tanks or spills onto a ground surface can pass easily through the soil into underlying groundwater. TCE can persist in groundwater for long periods, but microbial activity can degrade it.

Trans-1,2-DCE is a degradation product of TCE and PCE and is also found in some industrial solvents. Detection of DCE in groundwater is an indication that soil and groundwater conditions support microbial metabolism of these solvents. DCE can metabolize further into VC (ATSDR 1996a).

The detection of VC in groundwater can be the result of the microbial-degraded TCE and PCE. VC can persist in groundwater for long periods.

Hadnot Point Water Supply Area

The monthly concentrations for PCE, TCE, trans-1,2-DCE, VC, and benzene in the drinking water were estimated for the period from 1942 to 2008 (Maslia et al., 2013; Appendix A7 and A8), as shown in Figure 3. TCE was estimated as present in the drinking water above its current MCL of 5 parts per billion (ppb), as early as 1953. At later times, there were detections of trans-1,2-DCE and then VC, PCE, and benzene. The use of wells contaminated with TCE, trans-1,2-DCE, PCE, and VC is estimated to have continued until 1985. The presence of benzene at relatively low concentrations (up to 12 ppb) in the drinking water supply is estimated to have continued until 1996.

- The comparisons in this section are against the historical maximum, monthly-reconstructed concentrations. Figure 3 is a plot of the historical reconstructed concentrations for Hadnot Point.
- For the dose calculations presented later in the Health Effects Evaluation Section, the monthly concentrations were averaged over a 3-year period and then used to provide a basis for determining the exposure concentration for residents and workers at MCB Camp Lejeune. For example, the concentration at January 1972 is the average of the monthly estimated concentrations for the 3 years that follow January 1972, or the average from January 1972 to January 1975. This procedure was followed for each month to calculate the rolling averages used in the Health Effects Evaluation Section. Using 3 years is consistent with the ATSDR health studies' exposure duration. The exception to the 3-year rolling average for assessing exposure levels is for TCE, for the reasons described below.
- The contaminant of primary concern at Hadnot Point is TCE, which has been associated with adverse effects on the cardiac system of the developing fetus. However, 3-year average concentrations would not be appropriate to evaluate pregnant women's exposures (as short-term monthly peaks may not be accounted for) because of concerns associated with fetal heart impacts occurring in as little as 3 weeks of exposure. This duration is based on the gestational time for human cardiac development, which is 3-6 weeks after conception (Sadler, 2000; Dhanantwari, 2009). To evaluate exposure to a pregnant woman, ATSDR used the monthly concentrations estimated from historically reconstructed modeling (Maslia et al., 2013; Appendix A7 and A8) for the estimated dose, rather than the 3-year average concentration. Assuming that any adult population could include a pregnant woman, this approach was applied for any of the scenarios for individuals 16 years of age or older.

Below is a summary of estimated contaminant concentrations in the drinking system compared with federal drinking water standards and health-based screening values:

- **Benzene**–Within the Hadnot Point Industrial Area (Figure 1), significant volumes of liquid hydrocarbon fuels were lost because of leakage to the subsurface resulting in groundwater contamination. Six active water-supply wells were located in this area. Water from the contaminated wells mixed with water from other uncontaminated wells in the Hadnot Point WTP system, reducing the final concentrations in the drinking water at the point of exposure. From 1979 to 1984, the estimated drinking water concentrations of benzene exceeded the 5-ppb chronic EMEG for children or the current 5-ppb MCL (Figure 3). The chronic 18-ppb EMEG for adults was not exceeded. But from 1963 through 1996, the ATSDR 0.64-ppb CREG was consistently exceeded. The maximum reconstructed monthly concentration of 12 ppb of benzene occurred during April 1984. Two higher readings were reported in 1985 for actual measured levels of benzene at the Hadnot Point WTP: November 19, 1985 (2,500 ppb) and December 10, 1985 (35 ppb). Concern remains, however, about the accuracy of the reported 2,500 ppb level.[11] The

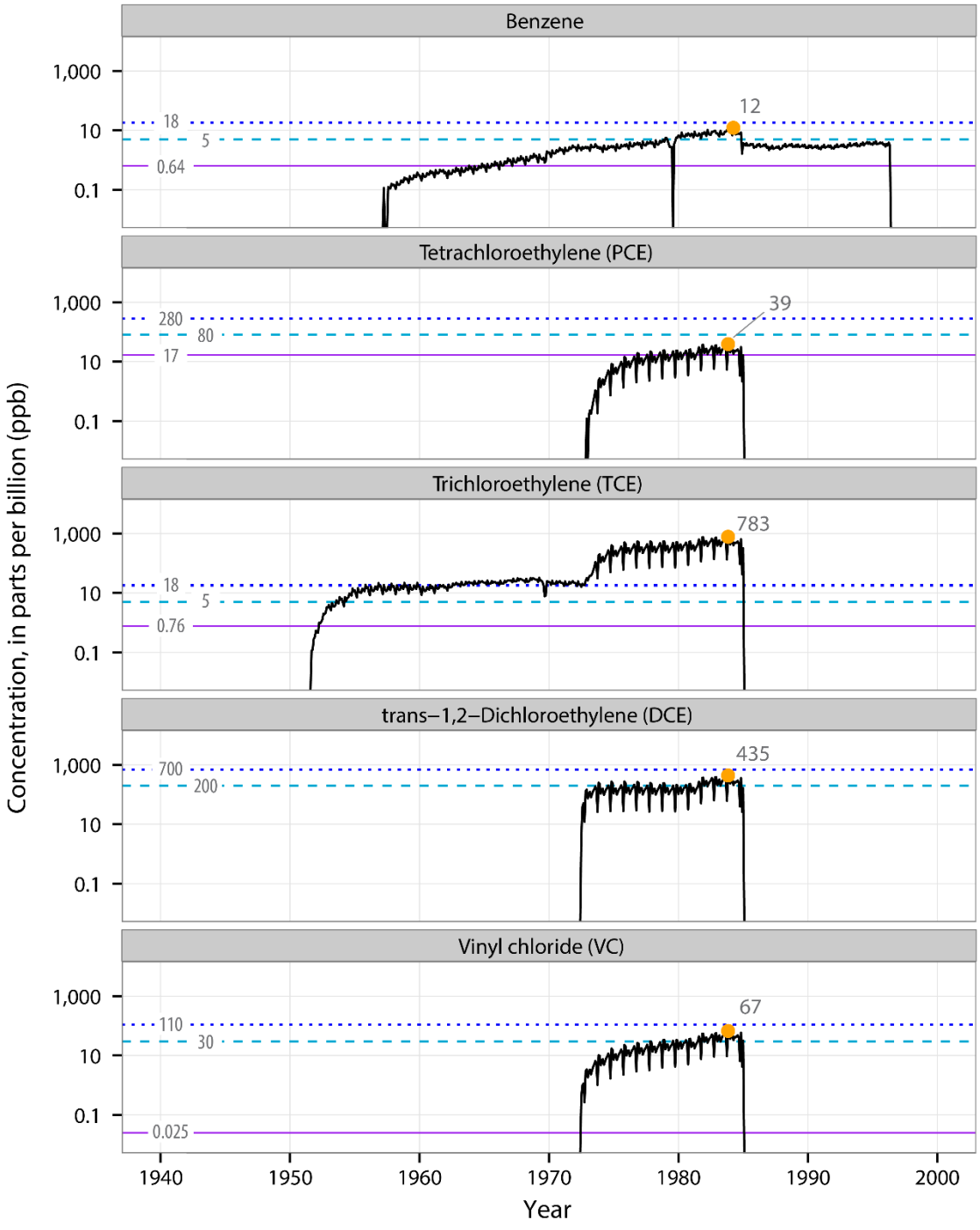
[11] Maslia et al. (2013) discusses sampling issues with this specific reported benzene value and with all historical water-quality sampling data at USMC's Camp Lejeune. The laboratory analysis noted that the 2,500 µg/L benzene sample "appears to have been contaminated with benzene, toluene, and methyl chloride" (JTC

taste/odor threshold for benzene in water is 500 ppb (ATSDR 2007b). The estimated benzene levels in the Hadnot Point water supply system never reached a concentration where taste or odor would have detected them.

- **Tetrachloroethylene (PCE)–**From 1976 to 1985, although the estimated PCE levels in the Hadnot Point water supply system exceeded the ATSDR 17-ppb CREG intermittently, the estimated PCE levels did not exceed ATSDR's 60-ppb RMEG for children nor the 80-ppb EMEG for children. Estimated PCE concentrations first exceeded the current 5-ppb MCL during 1974, then continued to exceed the current MCL through most of 1975 through 1985, and reached a maximum reconstructed monthly concentration of 39 ppb during November 1983. The taste/odor threshold for PCE in water is 300 ppb (ATSDR 2014b). The estimated PCE levels in the Hadnot Point water supply system did not reach a concentration at any time where taste or odor would have detected them.
- **Trichloroethylene (TCE)–**From the early 1950s through January 1985, the estimated TCE levels in the Hadnot Point Water Supply System exceeded the ATSDR 5-ppb EMEG for a child and the 18-ppb EMEG for an adult. During November 1983, TCE levels reached a maximum reconstructed concentration of 783 ppb. The maximum TCE level that actually measured in the Hadnot Point water supply system was 1,400 ppb in May 1982. The adult 18-ppb EMEG for TCE was exceeded consistently from the early sixties through January 1985. Based on water-model results (Maslia et al., 2013), the 0.76-ppb CREG for TCE was exceeded from the early 1950s through January 1985. The taste/odor threshold for TCE in water, described as a sweet, chloroform-like odor, is 310 ppb (ATSDR 2014a). Estimates showed this concentration was present in the Hadnot Point water supply system intermittently from 1974 until 1985.
- **Trans-1,2-Dichloroethylene (trans-1,2-DCE)**–The estimated levels of trans-1,2-DCE exceeded the current 100-ppb MCL for most of the early 1970s through January 1985, and levels reached a maximum reconstructed concentration of 435 ppb in November 1983. The ATSDR 200-ppb child RMEG was exceeded intermittently throughout that period, but the adult 700-ppb RMEG was not exceeded. The taste/odor threshold for DCE in water is 26 ppb (ATSDR 1996a). This concentration was estimated as present at the Hadnot Point water supply system from 1972 to 1985. DCE has been described as having a sweet, slightly acrid odor.
- **Vinyl chloride (VC)**–The estimated levels of VC exceeded the current 2-ppb MCL for most of the early 1970s through January 1985, with the maximum reconstructed VC concentration of 67 ppb. The child 30-ppb EMEG was exceeded intermittently from the late 1970s through January 1985. Estimated VC concentrations did not exceed the ATSDR 110-ppb adult EMEG. The ATSDR CREG 0.025-ppb value was exceeded from the early 1970s through 1985. The taste/odor threshold for VC in water is 3,400 ppb (ATSDR 2006). The estimated levels of VC in the Hadnot Point water supply system did not reach a concentration where taste or odor would have detected them.

Environmental Consultants 1985). Further, it was noted that this data point is "not representative" (U.S. Marine Corp Base Camp Lejeune Water Document CLW #1356).

Figure 3. Summary of the Historical Reconstruction Monthly Contaminants of Concern Concentrations in Hadnot Point Drinking Water (1942–1999); relative to health-based comparison values



Agency for Toxic Substances and Disease Registry (ATSDR) adult and child noncancer comparison values for benzene, tetrachloroethylene, and vinyl chloride are chronic environmental media evaluation guides (EMEGs). Noncancer comparison values for trichloroethylene and trans-1,2-dichloroethylene are reference dose media environmental guidelines (RMEGS).

Tarawa Terrace Water Supply Area

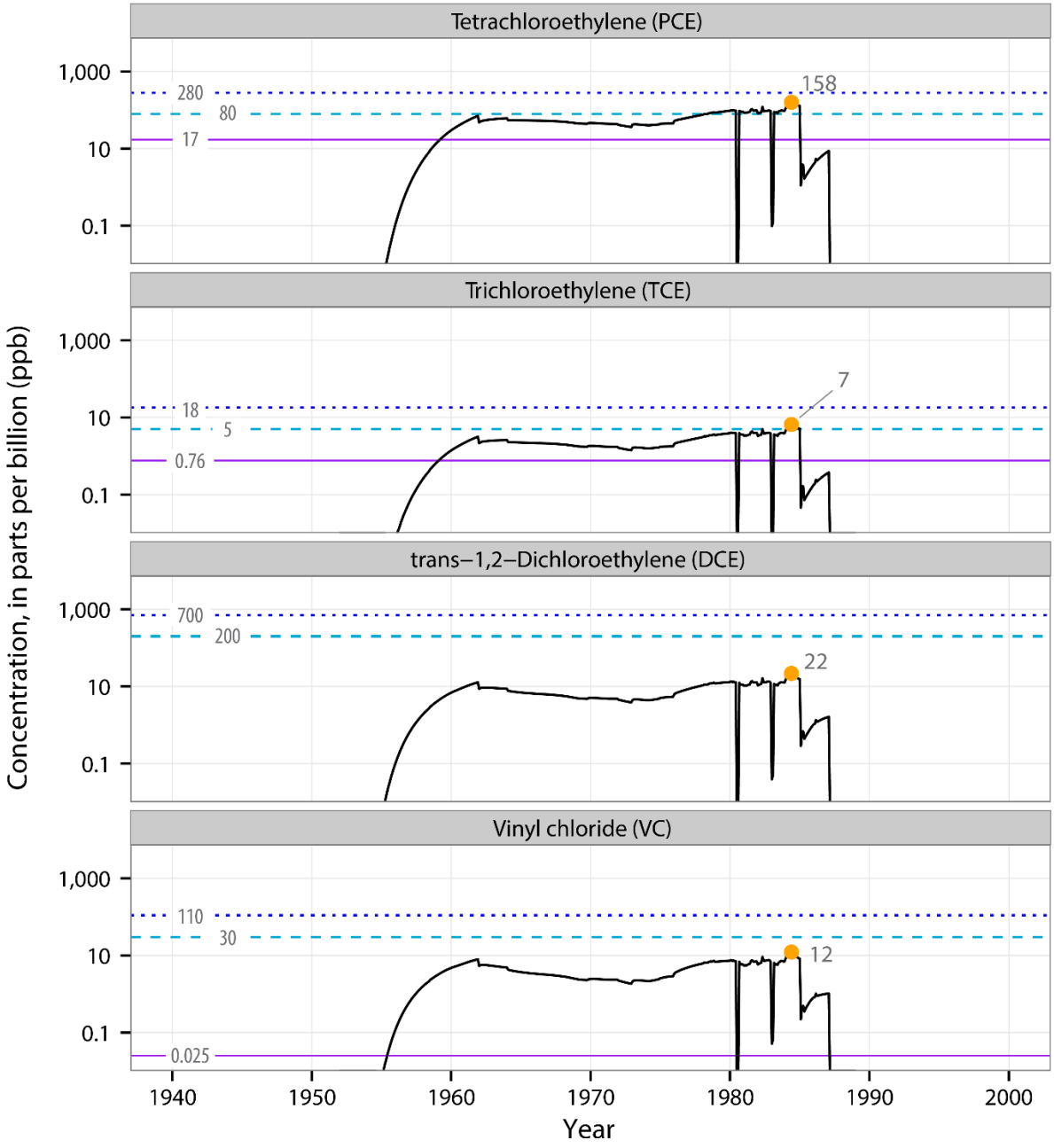
ATSDR reconstructed monthly mean drinking-water concentrations for PCE, TCE, trans-1,2-DCE, and VC from 1952 to 1990 (Maslia, 2008; Appendix I5). Figure 4 shows the historical reconstruction concentrations for each chemical during that period. Using the ATSDR multispecies simulation values (Maslia et al., 2007, Appendix A2), PCE was estimated as present in the Tarawa Terrace drinking water above its current 5-ppb MCL beginning in 1958, followed in time by VC, then TCE. Trans-1,2 DCE did not exceed its MCL. By the end of February 1985, MCB Camp Lejeune removed from service the most highly contaminated Tarawa Terrace wells. The treatment plant was closed by March 1987.

A summary of the estimated concentrations in the drinking system, compared with federal drinking water standards and health-based screening values, appears below. Note that Marines-in-training and on-base workers who lived at Tarawa Terrace would have been exposed to contaminants in the drinking water at their residences, but would have also been exposed to contaminants from the Hadnot Point water supply system during training and at their workplaces.

- **Tetrachloroethylene (PCE)**–During June 1984, the estimated PCE levels in the Tarawa Terrace water supply system reached a maximum reconstructed monthly concentration of 158 ppb.[12] During most of 1958 through 1985, levels exceeded the current 5 ppb MCL. But from 1986 until water system closure in February 1987, estimated levels barely exceeded the MCL (ranging from 4–9 ppb). The maximum PCE level measured in the Tarawa Terrace water system was 215 ppb in February 1985. The PCE concentrations exceeded the ATSDR 17-ppb CREG from 1959 to 1985. For children, from July 1978 through January 1985, readings mostly exceeded ATSDR's 80-ppb EMEG. The taste/odor threshold for PCE in water is 300 ppb. The estimated levels of PCE in the Tarawa Terrace water supply system did not reach a concentration at any time where taste or odor would have detected them.
- **Trichloroethylene (TCE)–**From February 1984 through January 1985, estimated TCE levels in Tarawa Terrace drinking water—with a maximum 7-ppb reconstruction monthly concentration—exceeded the ATSDR 5-ppb Chronic EMEG for a child and U.S. EPA's 5-ppb federal drinking water standard (MCL). The 18-ppb adult EMEG was not exceeded. But the 0.76-ppb CREG for TCE was exceeded from 1959 through January 1985. The taste/odor threshold for TCE in water is 310 ppb. Estimates did not show this concentration was present at any time in Tarawa Terrace drinking water.
- **Trans-1,2-Dichloroethylene (trans-1,2-DCE)**–Estimated levels of trans-1,2-DCE in Tarawa Terrace drinking water—with a maximum reconstruction monthly concentration of 22 ppb—did not at any time exceed the current 100-ppb MCL. Neither the 200-ppb ATSDR child nor the 700-ppb adult RMEG were exceeded during this period. The maximum estimated 22-ppb concentration was below the 26-ppb odor threshold for trans-1,2-DCE in water.
- **Vinyl chloride (VC)**–From 1958 to January 1985, estimated VC levels—with a maximum 12-ppb reconstruction monthly concentration—exceeded the current 2-ppb MCL. Neither the child nor the adult EMEGs were exceeded. However, from 1955 to 1987, the 0.025-ppb ATSDR CREG value was exceeded. The taste/odor threshold for VC in water is 3,400 ppb. The estimated VC levels in Tarawa Terrace drinking water did not at any time reach a concentration where taste or odor would have detected them.

[12] Two types of historical reconstruction simulations were conducted for the Tarawa Terrace area: 1) single species PCE, and 2) multispecies degradation of PCE. The maximum values reported here are from the multispecies degradation of PCE (Maslia et al. 2007, Appendix A2)

Figure 4. Summary of Historical Reconstruction Monthly Contaminants of Concern Concentrations in the Tarawa Terrace Drinking Water (1952–1987); relative to health-based comparison values



Agency for Toxic Substances and Disease Registry (ATSDR) adult and child noncancer comparison values for tetrachloroethylene and vinyl chloride are chronic environmental media evaluation guides (EMEGs). Noncancer comparison values for trichloroethylene and trans-1,2-dichloroethylene are reference dose media environmental guidelines (RMEGS).

Holcomb Boulevard Water Supply Area

Intermittently from 1972 to 1985, the Holcomb Boulevard housing area received contaminated Hadnot Point drinking water. During such periods, only TCE was identified as a contaminant of concern because it routinely exceeded its current MCL (Maslia et al., 2013; Appendix A8). For example, during the month of June 1978, when contaminated water from the Hadnot Point WTP supplemented Holcomb system water, the maximum reconstructed TCE concentration exceeded the drinking water standard at Midway Park (23 ppb), Berkeley Manor (51 ppb), and Watkins Village (38 ppb) housing areas. During an 8-day period from January 28 through February 4, 1985, use of Hadnot Point water resulted in a maximum reconstructed-mean monthly TCE concentration that exceeded the drinking water standard at Paradise Point (66 ppb), Midway Park (53 ppb), Berkeley Manor (54 ppb), and Watkins Village (56 ppb) housing areas. The maximum TCE level actually measured in the Holcomb Boulevard water system was 1,148 ppb on January 31, 1985 at the Berkeley Manor Elementary School. Before June 1972, Holcomb Boulevard housing area received its drinking water exclusively from Hadnot Point water supply wells. Residents who lived in the Holcomb Boulevard housing area before June 1972 should refer to the Hadnot Point sections of this document to determine any possible exposures to them. A complete listing of all mean concentration of contaminants within the Holcomb Boulevard water supply area are provided in Maslia et al., 2013; Appendix 8.

Exposure Pathways Analysis

A critical step in ATSDR's evaluation process is assessment of exposure pathways. The goal of exposure pathway assessment is to identify likely site-specific exposure situations and answer the following questions (ATSDR 2005):

- Is there a source of contamination?
- Is there a release into the environment?
- Who is exposed to environmental contamination?
- How are people exposed?

"Completed" exposure pathways represent those where all five "elements" of exposure exist (a population who could be exposed, the existence of contaminated media, a contaminant source, and an exposure point and route). Table 2 lays out these elements. In the case of past situations, the pathway has been labeled complete because contamination was detected in well water that we know people were using for drinking and bathing purposes. ATSDR has designated future exposures as "potential" because groundwater contamination plumes could possibly migrate to active wells.

Water Treatment Plants

ATSDR evaluated exposure pathways to determine where people contacted drinking water (Table 2). ATSDR also determined that past completed pathways applied to MCB Camp Lejeune. Before MCB Camp Lejeune took the contaminated wells offline, the only exposure to the contaminants of concern was through the drinking water—the groundwater that the base used as its water supply was contaminated. The residents were exposed via ingestion (i.e., by drinking the water), inhalation (i.e., from volatilization during shower/bathing or other household uses such as dishwashing and laundry), and dermal contact (during shower/bathing). Workers were also exposed by drinking contaminated water throughout the workday.

Table 2: Exposure Pathways

Past Completed Pathway

Media	Source	Exposure Point	Exposure Route	Notes
Groundwater	Water Treatment Plant supply wells	Drinking water; lesser for swimming and showering	Ingestion	Historical reconstruction estimates exposure occurred from Jan. 1952 to Feb 1985; exposure to low levels of benzene may have lasted until May 1996 at Hadnot Point.
		Showering and other household uses such as dishwashing and laundry; indoor swimming pools	Inhalation Dermal	Residents were exposed during showering and other household uses such as dishwashing and laundry from Jan. 1952 to Feb 1985.

Future Potential Pathway

Media	Source	Exposure Point	Exposure Route	Notes
Groundwater	Water Treatment Plant supply wells	Drinking water	Ingestion	Potential migration of contamination plumes to active supply wells. However, extensive monitoring efforts make this pathway unlikely.
		Showering and other household uses such as dishwashing and laundry; indoor swimming pools	Inhalation Dermal	Potential exposure during showering and other household uses such as dishwashing and laundry. However, extensive monitoring efforts make this pathway unlikely.

See ATSDR's Public Health Assessment Guidance Manual (ATSDR 2005) for additional information about the exposure pathway analysis.

Tables 3 and 4 summarize the specific assumptions used in our assessment of contaminant exposure through ingestion, dermal, and inhalation.

Table 3: Parameters Used for Exposure Assessment- Ingestion and Dermal Pathways

Age	ED (yrs)	EF (days/ yr)	LT[a] (yrs)	Ingestion Pathway						Dermal Pathway						ADAF
				Ingestion Rate[a] (L/day)				BW[a] (kg)		Skin surface area[a] (cm^2)		Lsc[b]	Kp	tau	t*	B	
				RME		CTE											
Child (age 0–1)	3	350	78	1.113	0.994	0.504	0.389	7.8	10.9	4,567	5,889	0.001	chemical-specific values[b]				10
Child (age 1–2)				0.893		0.308		11.4		6,100		0.001					10
Child (age 2–3)				0.912		0.356		13.6		7,000		0.001					3
Child (age 3–6)				0.977		0.382		17.4		9,500		0.001					3
Child (age 6–16)				1.690		0.574		44.3		17,700		0.001					3
Adult resident				3.092		1.227		80		24,265		0.001					1
Civilian worker	3-15	250	78	3.092		1.227		80		24,265		0.001					1
Marine-in-training*	3	350	78	4.334		4.334		80		24,265		0.001					1

[a] Values from U.S. EPA Exposure Factors Handbook (USEPA 2011d); Ingestion Rate-Table 3-1 (consumers-95th percentile); Body Weight- Table 8-1(50th percentile); Skin Surface Area- Table 7-1 (95th percentile)

[b] Values from U.S. EPA Dermal Risk Assessment Guidance (USEPA 2004)

ADAF = age dependent adjustment factor for chemicals that act by a mutagenic mode of action (kidney cancer for TCE) (USEPA 2005)

B = dimensionless ratio of the permeability coefficient of a compound through the stratum corneum relative to its permeability coefficient across the viable epidermis (unitless)

BW = body weight (kg)

CTE = central tendency exposure

ED = exposure duration (yrs)

IR = Ingestion rate (L/day)

K_p = permeability constant (cm/hr)

L_{sc} = apparent thickness of stratum corneum; used to calculate tau (cm)

LT= lifetime (yrs)

RME = reasonable maximum exposure

tau = lag time per event (hours/event)

t* = time to reach steady-state (hours)

*Marine-in-training: assumes water ingestion rate of 6 L/day for 3*x* per week and 3.1 L/day for 4*x* per week; developed by combining information gathered from former Marines at the community assistance panel meetings and recommended military fluid replacement guidelines (Kolka et al., 2003)

Table 4: Parameters Used for Exposure Assessment-Inhalation Pathway

Age	ED (yrs)	EF (days per yr)	LT (yrs)	Daily Inhalation Rate[a] (m^3/day)		Minute Inhalation Rate[a] (m^3/min)		T_s [a] (min/day)		k [b]	V_a [b] (L)	F_w [b] (L/ min)	ADAF
				RME	CTE	RME	CTE	RME	CTE				
Child (age 0–1)	3	350	78	9.2	5.4	0.011	0.008	70	20	0.6	10,000	8	10
Child (age 1–2)				12.8	8.0	0.016	0.012	70	15				10
Child (age 2–3)				13.7	8.9	0.016	0.012	70	20				3
Child (age 3–6)				13.8	10.1	0.014	0.011	65	20				3
Child (age 6–16)				19.25	13.6	0.016	0.012	70	20				3
Adult resident				22.4	16.0	0.016	0.012	60	20				1
Civilian worker	15	250	78	22.4	16.0	0.016	0.012	60	20				1
Marine-in-training	3	350	78	22.4	16.0	0.016	0.012	120	20		44,000	66	1

[a] Values from EPA Exposure Factors Handbook (USEPA 2011d); Inhalation Rates- Table 6-1 (95th percentile); Minute Inhalation Rates- Table 6-2 (Light intensity; 95th percentile); Showering Time- Table 16-32 (95th percentile for combined shower and post-shower duration)

[b] Equation from Andelman, 1990 $C_{air,max} = (k)\ (F_w)\ (T_s)\ (C_w)\ (CF) / V_a$

ADAF = age-dependent adjustment factor for chemicals that act by a mutagenic mode of action (kidney cancer for TCE) (USEPA 2005)

CTE = central tendency exposure

ED = exposure duration (yrs)

EF = exposure frequency (days per yr)

F_w = water flow rate (L/min)

K = Andelman volatilization factor (L/m^3)

k = volatilization coefficient from water to air

LT = lifetime (yrs)

RME = reasonable maximum exposure

T_s = total showering area time, including time before, during, and after showering (min/day)

V_a = bathroom air volume (L)

Additional Exposure Scenarios

ATSDR used information from the community assistance panel [13](CAP) and evaluated three additional exposure scenarios to estimate individual exposure to contaminants of concern and evaluated whether those exposures might have occurred at levels that could cause adverse health effects. The three exposure scenarios are

1. Swimming/training pools
2. Laundry facilities
3. Food preparation/dishwashing operations

ATSDR evaluated these three exposure scenarios separately from the toxicological and exposure assessment contained in this public health assessment. If some persons fell into an exposure category discussed in the body of this PHA and also engaged in one of the exposure categories discussed in Appendix E, they could expect to have the cumulative exposure from all the exposure categories that apply to their specific circumstance.

ATSDR used conservative, one-compartment models to estimate inhalation exposures from sources. The models tend to overpredict actual exposures and don't account for clean air ventilation. To estimate PCE, TCE, trans-1,2-DCE, VC, and benzene inhalation exposures to indoor swimming pool users, we employed equations obtained from the USEPA SWIMODEL. To estimate the inhalation exposures to laundry facility and mess hall workers, we employed the Andelman (1990) one-compartment model. Appendix E provides further details of how ATSDR evaluated these exposure scenarios and the modeling results.

Some CAP members were concerned about the exposure healthcare workers might experience because of numerous daily hand washings. Because absorption in water of volatile organic contaminants of concern across the skin surface requires an extended contact period (USEPA, 2004a), dermal exposure during hand washing activity is not considered a significant pathway. The onbase worker scenario, however, includes a daily onbase shower, which is a more significant inhalation exposure event than hand washing. Therefore, the worker scenario is likely to be inclusive of any exposures that could occur even to healthcare workers who wash their hands multiple times per day.

[13] ATSDR has created a community assistance panel (CAP) for the Camp Lejeune site. The purpose of the CAP is to voice the concerns of the affected community of Marines and their families and to provide input for health studies. Members of the CAP will provide individual input as well as represent the views of the community and groups to which they belong. The CAP consists of community members, one representative from the Department of Defense, independent scientific experts, and ATSDR staff. The CAP meets quarterly to discuss site activities.

Health Effects Evaluation

Exposure Dose Calculations

For this public health assessment, ATSDR developed estimates of exposure doses for the following groups who lived or worked at—or lived and worked at—MCB Camp Lejeune:

- Children who lived onbase with their families
- Adults who lived onbase (including pregnant women)
- Workers employed at the base, but who lived off-base[14]
- Marine[15] and naval personnel who trained and lived onbase[16]

We based the values selected for these exposure factors on several information sources, including ATSDR-conducted surveys during the health studies of persons who lived at MCB Camp Lejeune.

- The tour-of-duty data from base housing records show the mean tour of duty time as 21.3 months and the median time spent at the base as 18 months. ATSDR determined that 85% of the active duty Marines and their families lived onbase for 3 or fewer years (Bove 2013). The 95th percentile residency time was 4 years for active duty Marines and 4.8 years for Marine families. Using this information, a 3-year exposure duration is considered a conservative onbase-time estimate for most Marine personnel and their families.
- The Defense Manpower Data Center (DMDC) was used to estimate onbase civilian workers as having an average exposure duration of 15 years (Bove 2014).
- The "Marines who trained and lived onbase" group includes those service men and women who regularly engaged in field exercises. If a person lived onbase and either worked onbase or was the spouse of an active duty Marine but did not regularly engage in field exercises, then that person would be considered an "adult who resided onbase." A Marine or civilian who worked onbase but lived offbase would be considered part of the "workers who were employed at the base group."

Estimates of physical characteristics, (i.e., body weight, skin surface area, average lifespan, and water ingestion rates) were selected from the 2011 U.S. EPA Exposure Factor Handbook. These exposure factors help determine the amount of chemicals that enter a person's body (the dose) from contaminated water—either through ingestion, absorption through the skin, or inhalation of vapors during showering/bathing.

The exposure dose calculations also use estimates of the chemical concentrations in the water supply system at MCB Camp Lejeune at different times. We obtained the concentration used in these calculations by taking the 3-year running average of the concentrations provided by the historical reconstruction. A 3-year average was selected because, as mentioned above, 85% of the active duty personnel had a tour of duty at MCB Camp Lejeune of fewer than 3 years. We recognized that some Marines spent more time onbase than the usual < 3-year tour of duty. The intention was that the onbase worker scenario with a 15-year exposure duration would include those Marines. Figure 5 shows Hadnot Point's 3-year rolling average for each chemical during that period, whereas Figure 6 shows Tarawa

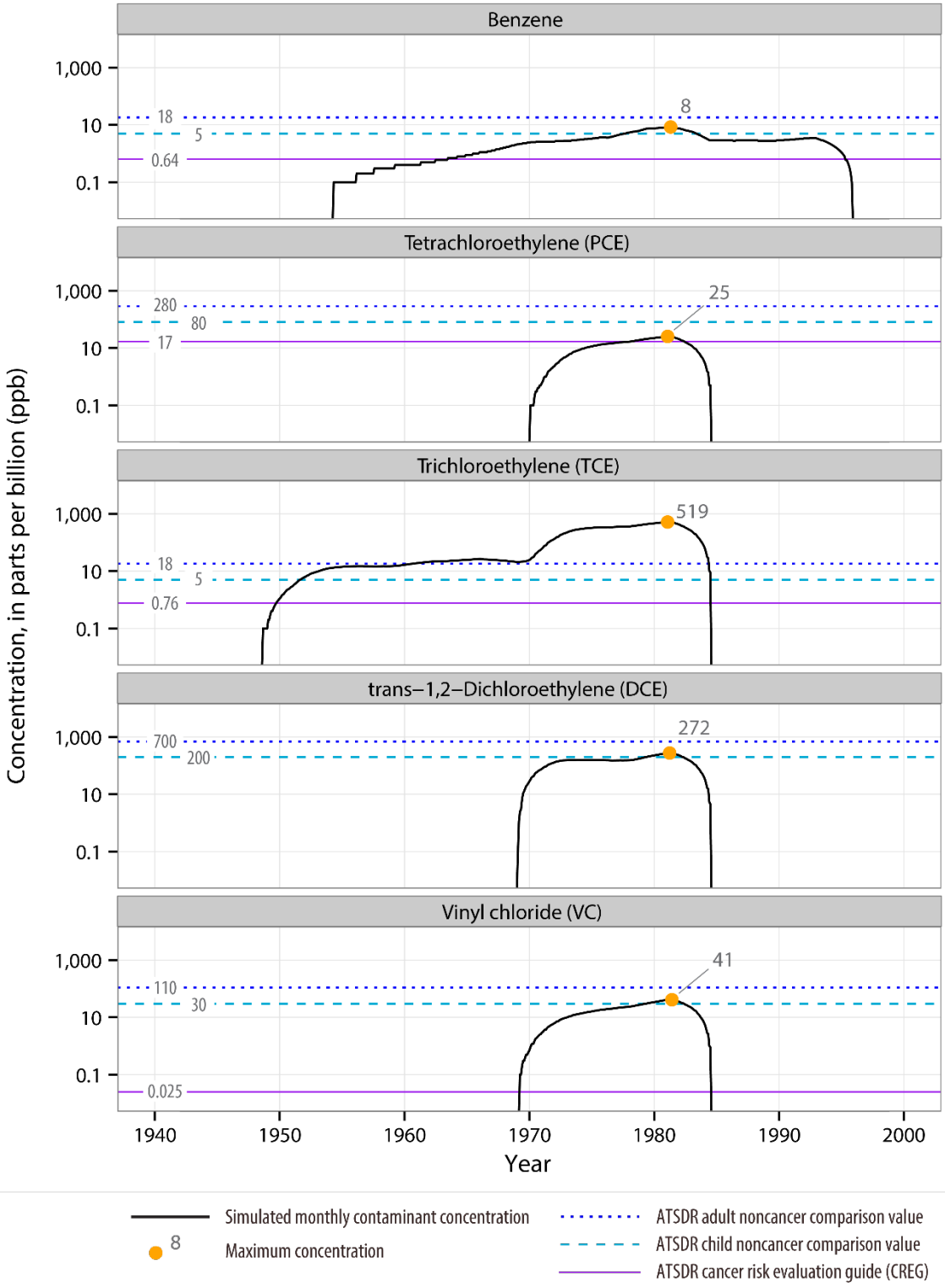
[14] Workers at the base includes several different categories of employment. The exposure scenario for typical workers would include drinking water ingestion and one shower on-base per day. The exposure for workers with more intensive daily water exposure (e.g., laundry, kitchen work) were assessed separately.

[15] The term Marines as used throughout this document includes naval personnel.

[16] The level of exposure of military personnel who trained at MCB Camp Lejeune, but lived offbase or in areas not served by contaminated water would have been somewhat less. We expect, however, that exposure of military personnel to contaminated water was mainly the result of intensive drinking water use during training activities and showering in water supplied by the Hadnot Point water system.

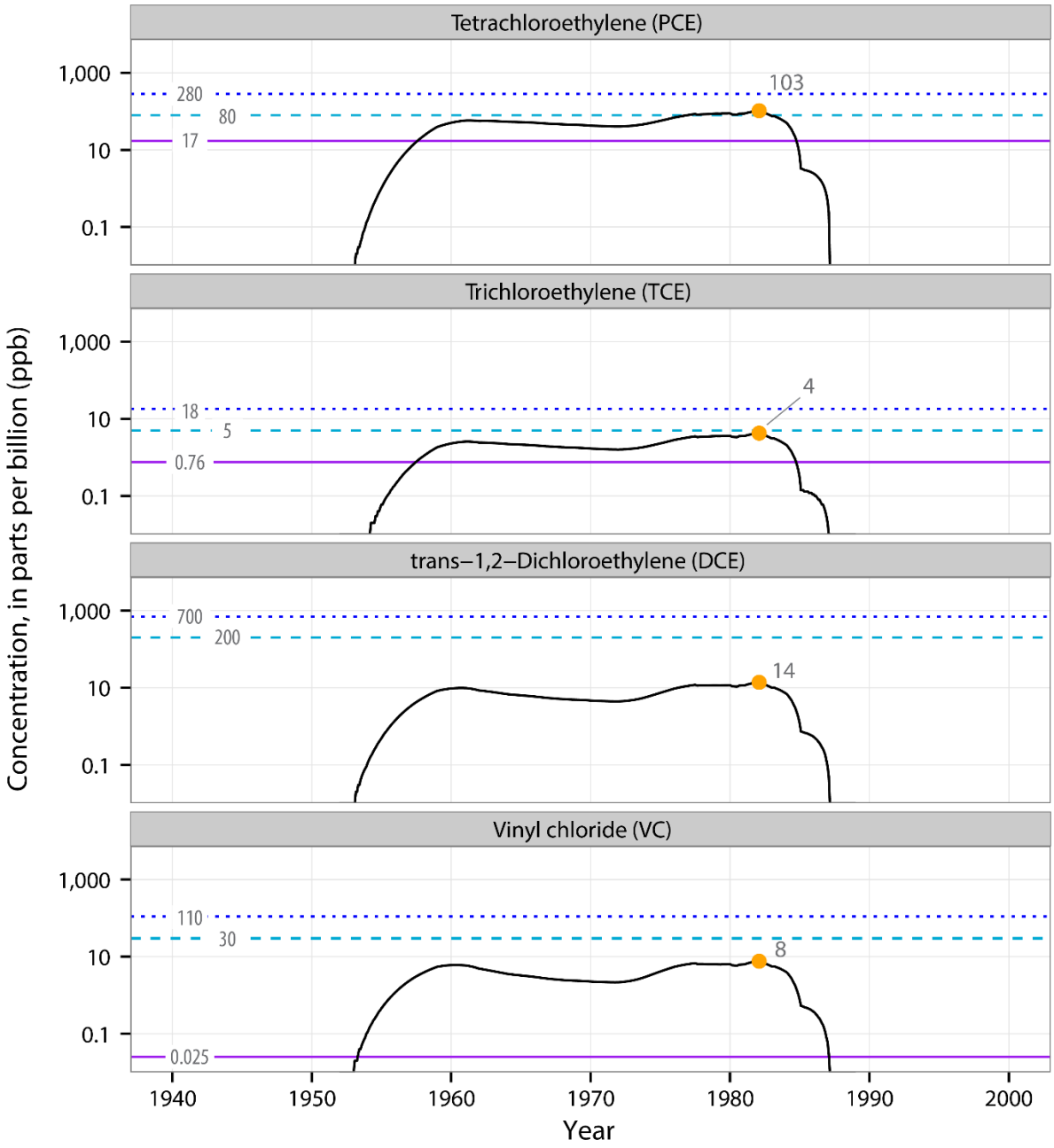
Terrace's 3-year rolling average. We chose the 3-year rolling arithmetic average for calculating exposure doses to reflect the average exposure levels during an onbase residency. But ATSDR did not use the 3-year average concentrations to evaluate exposures to pregnant women. We had concerns associated with fetal heart effects and other potential birth outcomes that might occur from TCE exposures during the first trimester of pregnancy. To evaluate pregnant women's exposure then, we used the historical reconstructed concentrations for each month.

Figure 5. Hadnot Point: Summary of the Rolling 3-year Average VOC Concentrations in Drinking Water (1942–1999), with ATSDR Comparison Values



Agency for Toxic Substances and Disease Registry (ATSDR) adult and child noncancer comparison values for benzene, tetrachloroethylene, and vinyl chloride are chronic environmental media evaluation guides (EMEGs). Noncancer comparison values for trichloroethylene and trans-1,2-dichloroethylene are reference dose media environmental guidelines (RMEGS).

Figure 6. Tarawa Terrace: Summary of the Rolling 3-year Average VOC Concentrations in Drinking Water (1952–1987), with ATSDR Comparison Values



Agency for Toxic Substances and Disease Registry (ATSDR) adult and child noncancer comparison values for tetrachloroethylene and vinyl chloride are chronic environmental media evaluation guides (EMEGs). Noncancer comparison values for trichloroethylene and trans-1,2-dichloroethylene are reference dose media environmental guidelines (RMEGS).

Estimating an exposure dose requires identifying how much, how often, and how long a person might contact a contaminant concentration in a specific medium (e.g., air, water, soil). Tables 3 and 4, and Appendix C show the equations and exposure assumptions used to estimate exposure doses from ingesting drinking water and from inhalation and dermal absorption of vapors while showering/bathing. Tables 3 and 4 summarize the specific values for those exposure parameters. Appendices A and C contain more detailed descriptions of how ATSDR conducts its screening and exposure dose calculations.

To determine the dose associated with specific contaminant concentrations in water at different times, this public health assessment used the Contaminated Media (Risk) calculator program at the Risk Assessment Information System (RAIS), available on the Oak Ridge National Laboratory site.[17] The program follows USEPA Risk Assessment guidance in the calculation of exposure doses for ingestion, dermal, and inhalation.

The exposure doses for the ingestion and dermal pathways were calculated for a given concentration of each chemical for each exposure group. For the inhalation pathway, an indoor air model (Andelman 1985, 1990) helped calculate the inhalation concentration for children and adults. The indoor-air model is a one-compartment model that predicts the average indoor air concentration resulting from a chemical volatilizing into the air during showering. The predicted indoor air concentration was assumed as a continuous 24-hour exposure that could occur in a residence throughout the day when contaminated water was used for showering/bathing. In addition, the Andelman model helped to estimate the daily exposure concentration using the peak bathroom concentration that would have occurred during showering/bathing.. Table 4 shows the exposure parameters used in those calculations.

Approach for Using Dose Estimates to Calculate Cancer and Noncancer Risk

For a given water concentration, the estimated exposure doses were combined for the ingestion and dermal pathways. Using the oral toxicity values in Tables 4 and 5 and the equations shown in the sections titled Calculation of Hazard Quotient/Hazard Index and the Calculation of Cancer Risk, we calculated the noncancer hazard quotient and cancer risk for each chemical at that given concentration. The exposure concentration for the inhalation pathway and the inhalation toxicity values was used to calculate the hazard quotients and cancer risks for that pathway. The pathway-specific hazard quotients (ingestion/dermal and inhalation) were added together to calculate the total Hazard Quotient. Likewise, the pathway-specific cancer risks were added together for each chemical to calculate the total cancer risk.

To calculate the noncancer hazard quotient and cancer risk for any water contaminant concentration, the ratio of the noncancer hazard quotient and estimated cancer risk for that given water concentration was then calculated for each chemical and each exposure group. To get the hazard quotient and cancer risk for the 3-year rolling average for a residency that began on a specific month, we multiplied the chemical-specific ratio by the estimated average water concentration for that month. The exception was for TCE exposure to women who may have been pregnant during their time at Camp Lejeune. Given concerns about potential developmental effects resulting from a short-term exposure to TCE, the individual monthly values were used directly for the hazard quotient calculation for children and adult residents, workers who live off-base, or Marines-in-training who live on base without averaging over time.

Calculation of the total Hazard Index and overall cancer risk involved summing the hazard quotients and cancer risks for all chemicals for each month. A sample of this procedure for summation of hazard and cancer risk, with water concentration is shown in Appendix B. Figures 7–10 show these results.

[17] http://rais.ornl.gov/cgi-bin/prg/RISK_search?select=chem

Discussion of Noncancer and Cancer Health Effects

Potential Health Effects from Exposure

This section will summarize the toxicological guidelines ATSDR used to evaluate whether the estimated levels of exposure could have resulted in health effects for residents, workers, and Marines in training (including naval personnel) at MCB Camp Lejeune. The toxicological guidelines include those developed by ATSDR and U.S. EPA. Those guidelines are defined as:

ATSDR Minimal Risk Levels (MRLs): An MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. These include MRLs based on oral and inhalation exposure, and specific durations: Acute (1–14 days); Intermediate (15 days–1 year); Chronic (longer than 1 year). Uncertainties are accounted for by applying "uncertainty factors" to the no observed adverse effect level (NOAEL), lowest observed adverse effect level (LOAEL), or Benchmark Dose (BMD) Benchmark Concentration (BMC) from which the MRL is derived.

U.S.EPA Reference Dose (RfD): An estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark dose, with uncertainty factors generally applied to reflect limitations of the data used.

U.S. EPA Reference Concentration (RfC): An estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark concentration, with uncertainty factors generally applied to reflect limitations of the data used.

U.S. EPA Cancer Slope Factor (CSF): An upper bound, approximating a 95% confidence limit, on the increased cancer risk from a lifetime exposure to an agent. This estimate, usually expressed in units of proportion (of a population) affected per mg/kg-day, is generally reserved for use in the low-dose region of the dose-response relationship, that is, for exposures corresponding to risks less than 1 in 100.

U.S. EPA Inhalation unit risk (IUR): The upper-bound excess lifetime cancer risk estimated to result from continuous exposure to an agent at a concentration of 1 ppb in water, or 1 $\mu g/m^3$ in air.

The development of MRLs, RfDs, and RfCs, specific uncertainty factors are applied to account for: animal to human extrapolation (up to 10X), variability in human populations (up to 10X), (dosimetric adjustments (up to 10X) and lack of sufficient data (up to 10X). The specific uncertainty factors used for the toxicity factors in this document are summarized in Appendix D. The following two tables list the values ATSDR used in its noncancer and cancer toxicological assessment. To see a detailed toxicological discussion of the guidelines development, please refer to Appendix D.

Table 5a: Noncancer Toxicity Values for Ingestion

Chemical	Effect	Point of Departure (mg/kg-day)	Uncertainty Factors	Toxicity Value (mg/kg-day)	Source
Benzene	Diminished immune function (human)	0.014 ($BMDL_{0.25sd}$)	30	5.0E-04	ATSDR Chronic Oral MRL
PCE	Neurologic - loss of color vision (human)	2.6 (LOAEL)	1,000	6.0E-03	USEPA RfD
	Neurologic - cognitive effects (human)	9.7 (LOAEL)	1,000		
TCE	Cardiac abnormalities	0.0051 (HED_{99})	10	5.0E-04	USEPA RfD/ ATSDR Chronic and Intermediate Oral MRL
	Altered immune system development - *in utero* (animal)	0.37 (LOAEL)	1000		
	Decreased thymus weight (adult animal)	0.048 (HED_{99})	100		
trans-1,2-DCE	Immune function (animal)	65 (BMDL)	3,000	2.0E-02	USEPA RfD
VC	Liver cell polymorphism	0.09 (NOAEL)	30	3.0E-03	USEPA RfD/ ATSDR Chronic Oral MRL

MRL – minimal risk level
RfD – reference dose
RfC – reference concentration
PCE – tetrachloroethylene
TCE – trichloroethylene
DCE – dichloroethylene
VC – vinyl chloride

mg/kg/day – milligram per kilogram per day
mg/m^3 – milligram per cubic meter
BMDL- benchmark dose lower bound
$BMDL_{0.25sd}$ – BMDL-based on 25% of the standard deviation below the control mean
HED_{99}- 99th percentile human equivalent dose
LOAEL- lowest observed adverse effect level
NOAEL- no observed adverse effect level

Table 5b: Noncancer Toxicity Values for Inhalation

Chemical	Effect	Point of Departure (mg/m^3)	Uncertainty Factors	Toxicity Value (mg/m^3)	Source
Benzene	Immune- decreased B cell count	0.33 ($BMCL_{0.25sd}$)	10	9.6E-03	ATSDR Chronic Inhalation MRL
PCE	Neurologic- loss of color vision (human)	15 (LOAEL)	300	4.0E-02	USEPA RfC/ATSDR Acute, Intermediate, Chronic Inhalation MRL
	Neurologic - cognitive effects (human)	9.7 (LOAEL)	1,000		
TCE	Developmental cardiac effect from ingestion study	0.02 (BMDL; HEC_{99})	10	2.0E-03	USEPA RfC/ATSDR Intermediate, Chronic Inhalation MRL
	Immune effects from ingestion study	0.18 (LOAEL; HEC_{99})	100		
trans-1,2-DCE	Lung, liver, cardiac	189 (LOAEL; HEC)	3,000	6.0E-02	USEPA Provisional RfC (archive)
VC	Liver toxicity	2.6 ($BMCL_{10}$)	30	7.7E-02	ATSDR Intermediate Inhalation MRL

MRL – minimal risk level
RfD – reference dose
RfC – reference concentration
PCE – tetrachloroethylene
TCE – trichloroethylene
DCE – dichloroethylene
VC – vinyl chloride
mg/kg/day – milligram per kilogram per day
mg/m^3 – milligram per cubic meter
BMCL- benchmark concentration lower bound
$BMDL_{0.25sd}$ – BMDL-based on 25% of the standard deviation below the control mean
HEC- human equivalent concentration
HEC_{99} - 99th percentile human equivalent concentration
LOAEL- lowest observed adverse effect level
NOAEL- no observed adverse effect level

Table 6: Cancer Toxicity Values for Ingestion and Inhalation

Chemical	Ingestion $(mg/kg\text{-}day)^{-1}$	Source	Inhalation $(mg/m^3)^{-1}$	Source
Benzene	5.5E-02	USEPA Oral Slope Factor	7.8E-06	USEPA Inhalation Unit Risk
PCE	2E-03		2.6E-07	
TCE	4.6E-02 (ADAFs apply for children)		4.1E-06 (ADAFs apply for children)	
trans-1,2-DCE	NA		NA	
VC	7.2E-01		4.4E-06	

PCE – tetrachloroethylene
TCE – trichloroethylene
DCE – dichloroethylene
VC – vinyl chloride
mg/kg/day – milligram per kilogram per day
mg/m^3 – milligram per cubic meter
NA – not available

Calculation of Hazard Quotient/Hazard Index

To evaluate the levels of exposure to the specific groups for noncancer and cancer effects, ATSDR compared the results of dose calculations described in the previous sections with the appropriate toxicity criteria. The noncancer evaluation for each chemical is summarized as a Hazard Quotient, which is calculated for each route of exposure: ingestion, dermal, and inhalation:

$$\text{HQ (ingestion)} = \frac{\text{Exposure Dose (ingestion)}}{\text{MRL or RfD}}$$

$$\text{HQ (dermal)}^{18} = \frac{\text{Exposure Dose (dermal)}}{\text{MRL or RfD}}$$

$$\text{HQ (inhalation)} = \frac{\text{Exposure Concentration (inhalation)}}{\text{MRL or RfC}}$$

$$\text{HQ (all pathways)} = \text{HQ (ingestion)} + \text{HQ (dermal)} + \text{HQ (inhalation)}$$

To integrate the HQ values for all chemicals, the individual HQs are summed to represent a total Hazard Index (HI).

$$\textbf{Hazard Index} = \mathbf{HQ_{chemical\ 1}} + \mathbf{HQ_{chemical\ 2}} + \mathbf{HQ_{chemical\ 3}} \ \cdots\cdots$$

The evaluation of the combined exposure to multiple chemicals followed the ATSDR Guidance Manual for the Assessment of Joint Toxic Action of Chemical Mixtures (ATSDR, 2004). The approach followed the overall summation of Hazard Index, followed by an assessment of exposure for chemicals to chemicals that affect the same target organ, followed by an integration of evidence for interaction based on the mechanism of action of those chemicals.

The interpretation of the Hazard Index assessment is that HI values less than or equal to 1 indicate no hazard from the combined exposure. HI values greater than 1 do not mean that health effects will occur, only the need to evaluate exposure levels further to determine the potential for the combined effect of the chemicals that may could be affecting the organ system in the body and by the same mechanism of action. This step involves calculating an HI value for each target organ that may be affected by the mixture of chemicals. Note too that the higher the HI value, the greater the potential for adverse health effects.

Hazard Index Results

Figures 7 and 8 show the noncancer Hazard Index values, which themselves represent the combined evaluation for all the chemicals present in water systems for the different age groups at Hadnot Point and Tarawa Terrace. For all age groups at both sites, the noncancer HI values were highest from 1970 to 1985. Consistent with the timing of increased concentrations in drinking water shown in Figures 3 and 4, the HI values peaked in 1984 then decreased with the 1985 resolution of drinking water system contamination at MCB Camp Lejeune. For both the Hadnot Point and Tarawa Terrace systems, the highest HIs were for the youngest children, long-time workers, and the Marines who trained on the base.

[18] Because of the absence of any dermal-specific MRLs or RfDs, ATSDR used the oral values to calculate HQs for the dermal pathway. That said, however, oral toxicity values are based on administered dose, whereas the dermal exposure dose is based on absorbed dose. For organic compounds, the default assumption is that 100% of the chemical is absorbed from the gastrointestinal tract into the blood. In these cases, no adjustment is needed. But for inorganic compounds with a lower gastrointestinal absorption, an adjustment of the MRL or RfD is needed. All of the chemicals evaluated in this section are organic compounds, thus no adjustment was applied.

These HIs are high for young children because of children's higher water ingestion rate relative to body weight. Finally, the HIs are high for Marines in training, given their higher intake of water during intense exercise and their exposure during more frequent showering/bathing than the typical resident.

The HI data indicate higher health risk at Hadnot Point than at Tarawa Terrace across all age groups. This indication is also consistent with the contaminant concentration profiles in Figures 3 and 4. At Hadnot Point, estimations of Hazard Index for children, workers, and Marines indicated that exposure to TCE accounted for a significant majority (about 98%) of the noncancer hazard. For Tarawa Terrace, the largest contributor to the total HI for children and Marines in training was PCE (about 60%) and TCE (about 35%). For workers who were presumed to have used water on-base supplied by the Hadnot Point Water Plant, TCE contributed to a majority of the noncancer hazard.

Target Organ-Specific Hazard Evaluations

To better define the specific targets for the effects of exposure to chemicals in the Camp Lejeune drinking water system, the next step in the assessment is to compare with target organ-specific toxicity criteria for each chemical. Based on the comparative noncancer toxicity of these chemicals, the following target organs were identified as being more sensitive: renal (kidney), liver, immune system, hematopoietic (blood forming), neurologic, and developmental effects. To derive these values, we reviewed the ATSDR Toxicological Profile and other toxicological data to identify a target-organ toxicity dose (TTD). The methodology for deriving a TTD value is described in the ATSDR Mixtures Guidance document (ATSDR, 2004). The method involves identifying a critical study for each endpoint, for a Point of Departure that represents a Human Equivalent Dose or Concentration), then applying appropriate uncertainty factors (according to ATSDR guidance) to derive the TTD. The ratio of the exposure dose to the TTD is expressed as the target organ-specific hazard quotient for that chemical. The sum of the target organ HQ values for all chemicals then represents the Hazard Index for that organ.

The results of the TTD analysis for the most sensitive or exposure populations (young children- ages birth to 3 yrs of age; and Marines-in-training) are presented in Appendix D (Tables D-1 to D-10). The summary of that analysis is as follows:

Hadnot Point: Based on the TTD analysis using the upper end level of exposure, the primary impact for young children living at Hadnot Point is the effect of TCE on the immune system (HI_{immune}= 130 for ingestion and 595 for inhalation). For Marines-in-training that used the Hadnot water system, the primary impacts were the developmental effects of TCE (i.e., immune and cardiac) during pregnancy ($HI_{developmental}$ = 96 for ingestion and 1085 for inhalation).

Tarawa Terrace: Based on the TTD analysis using the upper end level of exposure, the primary impact for young children living at Tarawa Terrace is the effect of inhalation of PCE on the liver (HI_{liver} = 3.5) and the effect of TCE and vinyl chloride inhalation on immune function (HI_{immune}= 9). For adult individuals using the Tarawa water system, the primary effect was the inhalation of PCE on the liver (HI_{liver} = 29) and inhalation of TCE and vinyl chloride on immune function (HI_{immune}= 15).

Figure 7. Hadnot Point: Hazard Index by Age Group over Time for All Chemical Contaminants Evaluated in Drinking Water from the Hadnot Point Treatment Plant (3-year averaging time)

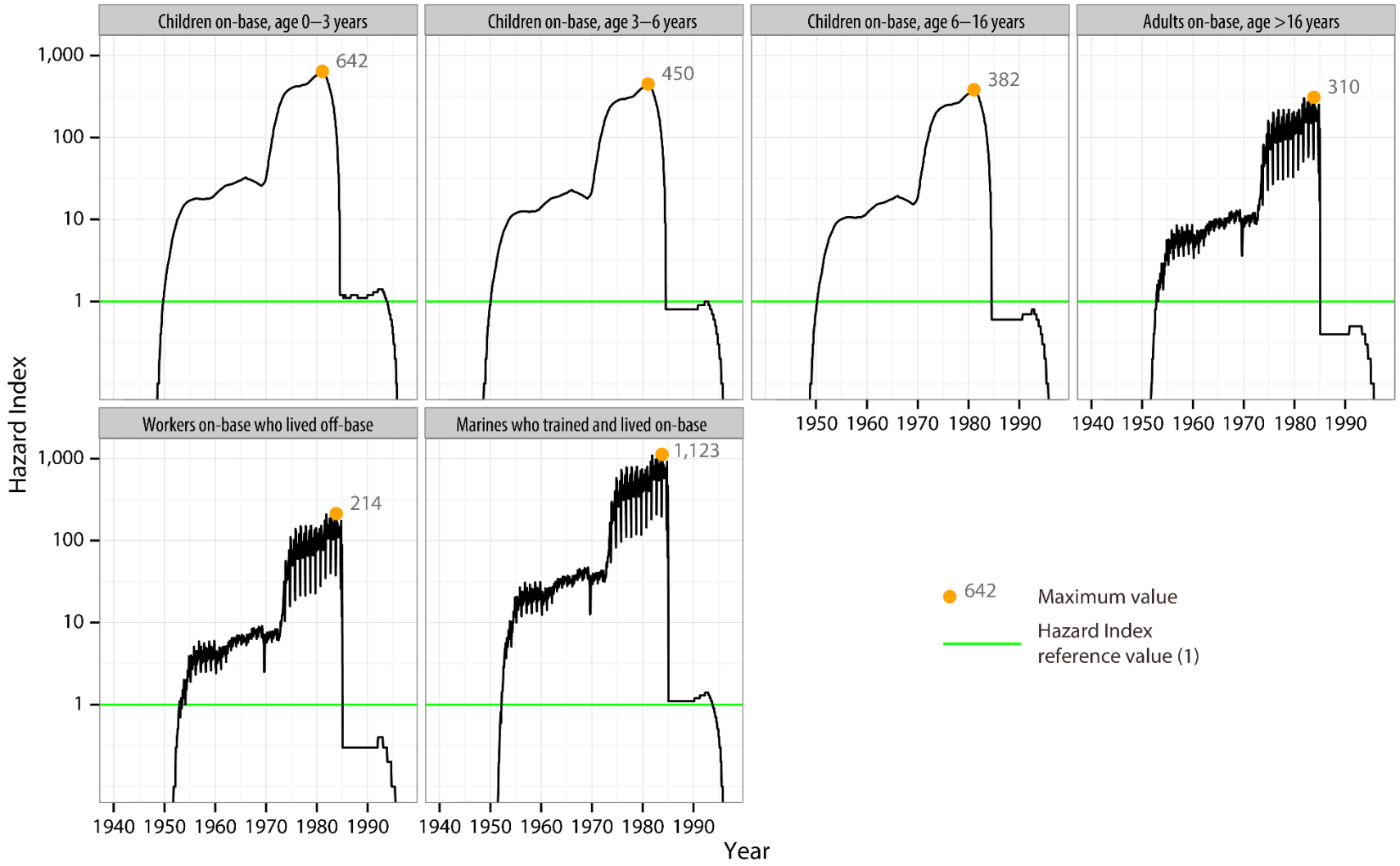
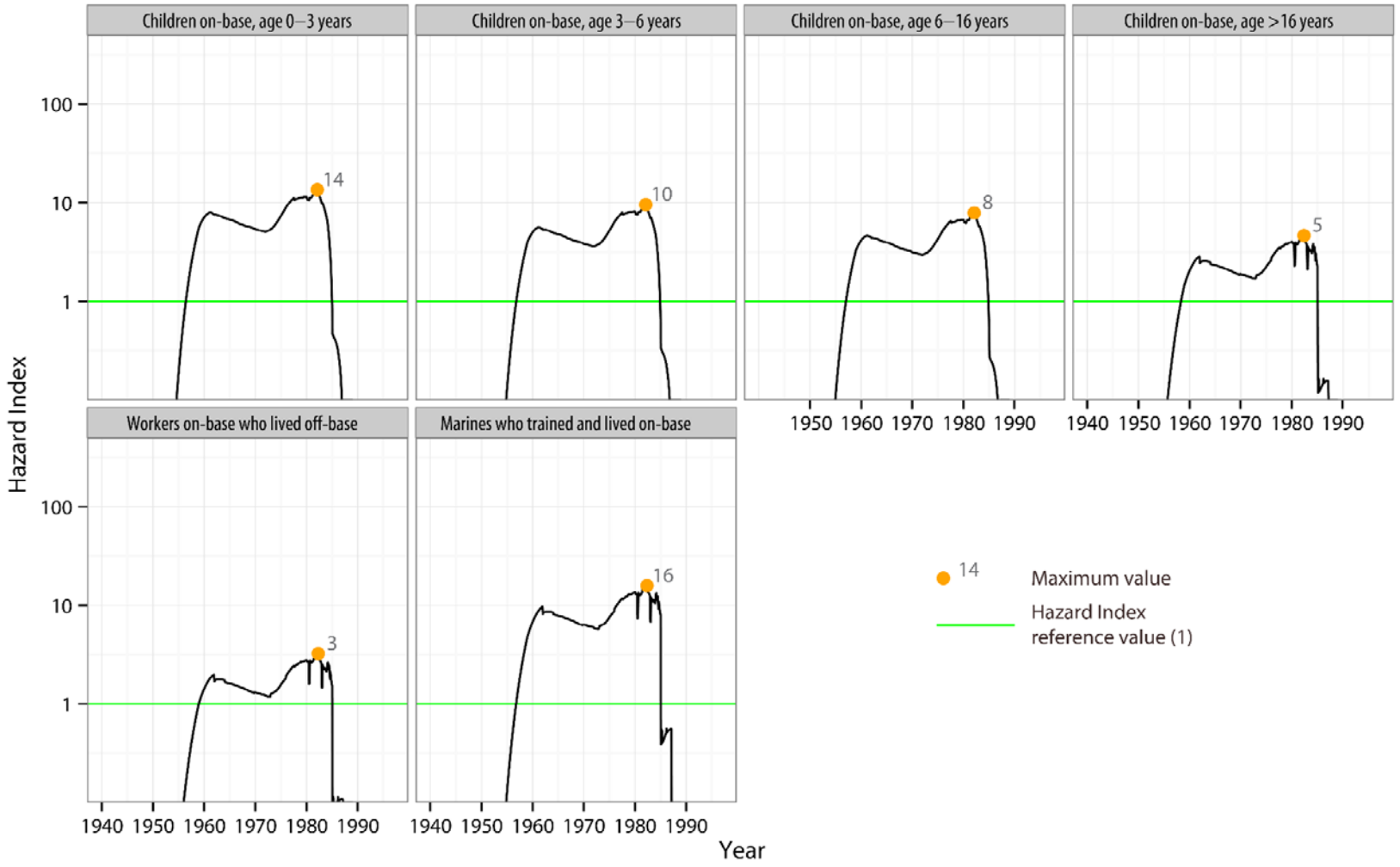


Figure 8. Tarawa Terrace: Hazard Index by Age Group over Time, Based on 3-Year Exposure for Residents, for Marines-In-Training, and for a 15-Year Exposure for Workers for All Chemical Contaminants Evaluated in Drinking Water at the Tarawa Terrace Water Treatment Plant



Calculation of Cancer Risk

To evaluate the levels of exposure to the specific groups for noncancer and cancer effects, ATSDR compared the results of dose calculations described in the previous sections with the appropriate toxicity criteria. We calculated the cancer risk estimation for each chemical and for each route of exposure: ingestion, dermal[19], and inhalation:

$$\text{Estimated Cancer Risk (ingestion)} = \text{Exposure Dose (ingestion) x Oral Slope Factor}$$

$$\text{Estimated Cancer Risk (dermal)} = \text{Exposure Dose (dermal) x Oral Slope Factor}$$

$$\text{Estimated Cancer Risk (inhalation)} = \text{Exposure Concentration (inhalation) x Inhalation Unit Risk}$$

To apply the best available science to the assessment, the calculation of cancer risks for TCE and vinyl chloride have additional components. TCE exposure is associated with kidney cancer, liver cancer, and lymphoma. However, the experimental evidence indicates that the mutagenic mode of action only applies to the kidney (USEPA, 2011b). Therefore, the Age-Dependent Adjustment Factor (ADAF) to the kidney component of the TCE cancer slope factor and to the inhalation-unit risk equation for exposures during childhood (USEPA 2005). The application of this factor is to account for the increased sensitivity of young persons to the effects of exposure to carcinogens that act through a DNA-damaging action mode. For the calculation of cancer risks from birth up to 2 years of age, an ADAF of 10 is applied. For ages 2–16 years, an ADAF of 3 is applied. An EPA spreadsheet provides that basis for these calculations.[20]

For vinyl chloride, exposure during early life is possibly associated with a cancer risk that is not limited by exposure duration (USEPA, 2000). Therefore, compared with exposures that occur later in life, persons exposed at birth possibly have a significantly higher cancer risk. To account for this additional sensitivity, a different cancer slope factor and an additional exposure term are applied to the youngest age groups (birth to six years of age) to calculate vinyl chloride-exposure cancer risk. Appendix C shows the detailed exposure dose equations for calculating ingestion, dermal, and inhalation exposure to vinyl chloride.

$$\text{Estimated Chemical} - \text{specific Cancer Risk (all pathways)} = \text{CR (ingestion)} + \text{CR (dermal)} + \text{CR (inhalation)}$$

To integrate the cancer risk for all chemicals, the individual chemical-specific cancer risk estimates are summed to represent a total Cancer Risk for each exposure group.

$$\text{Total Estimated Cancer Risk} = \text{CR}_{\text{chemical 1}} + \text{CR}_{\text{chemical 2}} + \text{CR}_{\text{chemical 3}} \ldots\ldots$$

Excess cancer risk is the estimated number of increased cases of cancer in a population above background that might result from exposure to a particular contaminant under the assumed exposure conditions from site-related contamination. For example, a lifetime estimated cancer risk of 1×10^{-6} represents a possible one excess cancer case in a population of 1 million persons exposed for a lifetime. Because of the

[19] Because of the absence of any dermal-specific cancer slope factors for the chemicals of concern, ATSDR used the oral values to calculate HQs for the dermal pathway. That said, however, oral toxicity values are based on administered dose, whereas the dermal exposure dose is based on absorbed dose. For organic compounds, the default assumption is that the 100% of the chemical is absorbed from the gastrointestinal tract into the blood. In these cases, no adjustment is needed. But for inorganic compounds with a lower gastrointestinal absorption, an adjustment of the MRL or RfD is needed. All of the chemicals evaluated in this section are organic compounds, thus no adjustment was applied.

[20] http://www.epa.gov/reg3hwmd/risk/human/rb-concentration_table/faq.htm#FAQ19

uncertainties and conservative assumptions inherent in deriving the cancer slope factors, this is only an estimate of risk; the true risk is unknown, and might be as low as zero (ATSDR 2005).

The following two plots (Figures 9 and 10) present the total, upper-bound cancer risk estimates for Hadnot Point and Tarawa Terrace. The plots also display the target cancer-risk range (10^{-4} to 10^{-6}) that U.S. EPA uses for making risk management decisions about site remediation (USEPA, 1991). A summary of the potential health effects (i.e., cancer and noncancer) from drinking water at Camp Lejeune is provided following the plots.

The chemicals that contribute to estimated cancer risk differ between exposure groups. For children (0–3 years of age) at Hadnot Point, about 92% of the cancer risk is associated with vinyl chloride exposure. The determination that people are at greater risk for the development of liver cancer if their exposure occurs during childhood compared with exposures during adulthood supports this estimated risk. For workers and Marines in training, most of the cancer risk (77–85%) is associated with TCE exposure; the remainder is associated with vinyl chloride.

At Tarawa Terrace, vinyl chloride exposure for children (0–3 years of age) contributes to 99% of the estimated cancer risk. For workers and Marines in training, 65% of the cancer risk is associated with vinyl chloride, with a lesser contribution (20–24%) from PCE.

Evaluation of Combined Cancer and Noncancer Effects of Exposure to Chemical Mixtures

The effect of exposure to a mixture of chemicals could be different from the effect of exposure to each chemical individually. The application of the Hazard Index methodology is an additive approach to evaluate the impact of exposure on the same target organ. This approach is generally considered to be conservative (health-protective) in estimating the effect of exposure to chemical mixtures. Ideally, it would be useful to study the actual mixture to which a population has been exposed to measure the true impact of that mixture. Of the chemicals detected in the Camp Lejeune water systems, several combinations have been evaluated in toxicologic experiments. ATSDR published an Interaction Toxicological Profile to summarize studies where various combinations have been evaluated (ATSDR, 2004).

PCE-TCE Interaction: Several studies have examined the effect of combined exposure to TCE and PCE, through inhalation or ingestion. The endpoints in most of those studies were adverse effects on the liver and kidney, which are thought to be largely the result of the interaction of TCE and PCE metabolites on molecular targets in those tissues. TCE is generally metabolized at a higher rate than PCE. As a result, TCE is primarily eliminated from the body in the urine, whereas PCE is eliminated primarily by exhalation. Evidence in animal studies suggests that PCE will inhibit the metabolism of TCE. However, that effect may only occur at exposure doses that are much higher than would have been experienced by individuals contacting water from the Camp Lejeune systems. There does not appear to be evidence synergistic effects (i.e., greater than additive) resulting from combined exposures to PCE and TCE. The results of the Binary Weight of Evidence (BINWOE) analysis from the Interaction Toxicological Profile (ATSDR, 2004; shown in Appendix D) shows that the effects of TCE on PCE are considered to be additive and the effect of PCE on TCE toxicity are additive for neurologic effects and slightly inhibitory for effects on the liver and kidney (likely due to the effects on TCE metabolism) (ATSDR, 2004). In summary, given the limited information about the combined effect of these chemicals at the levels at Camp Lejeune, the additive approach used for Cancer Risk and Hazard Index provides a conservative (health-protective) evaluation of exposure and has been incorporated into this assessment.

TCE-Vinyl Chloride Interaction: The estimated interaction between TCE and VC is based on pharmacokinetic modeling. Because both chemicals are metabolized by the same cytochrome P450 enzyme (CYP2E1) each chemical has the potential to inhibit the metabolism of the other and likely reduce their toxic effects on the liver. However, the threshold for this inhibitory (less than additive) effect

based on modeling of inhalation exposure is 30 ppm in air. Below this level of exposure, the inhibitory effect would be unexpected (ATSDR, 2004). The results of this interaction analysis are presented in Appendix D. Therefore, the additive approach used for Cancer Risk and Hazard Index is a health–protective evaluation of exposure and has been incorporated into this assessment.

Figure 9 Hadnot Point: Estimated Lifetime Cancer Risk by Age Group over Time Based on 3-Year Exposure for Residents and Marines-In-Training, and 15-Year Exposure for Workers to All Chemical Contaminants Evaluated in Drinking Water from the Treatment Plant.

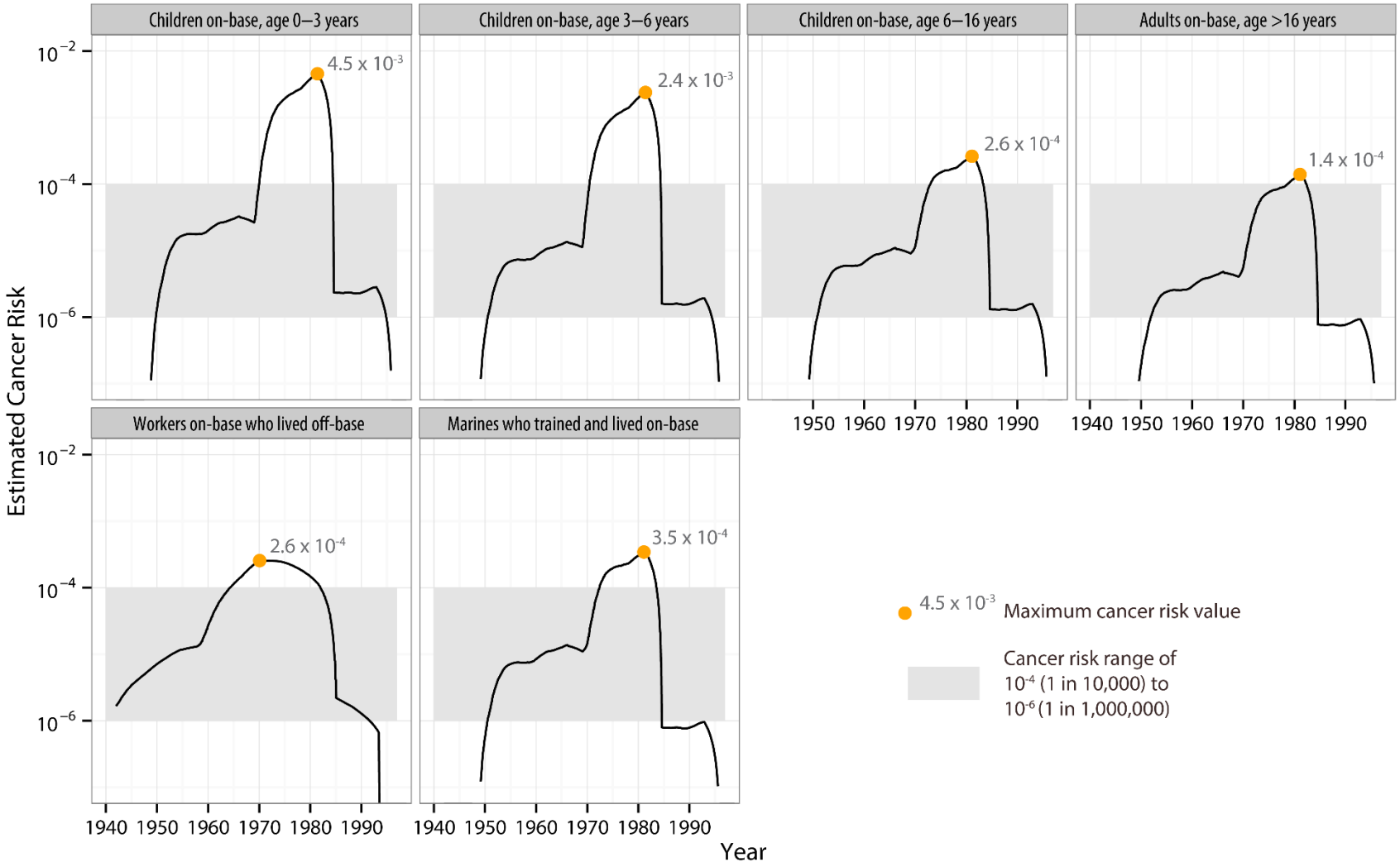
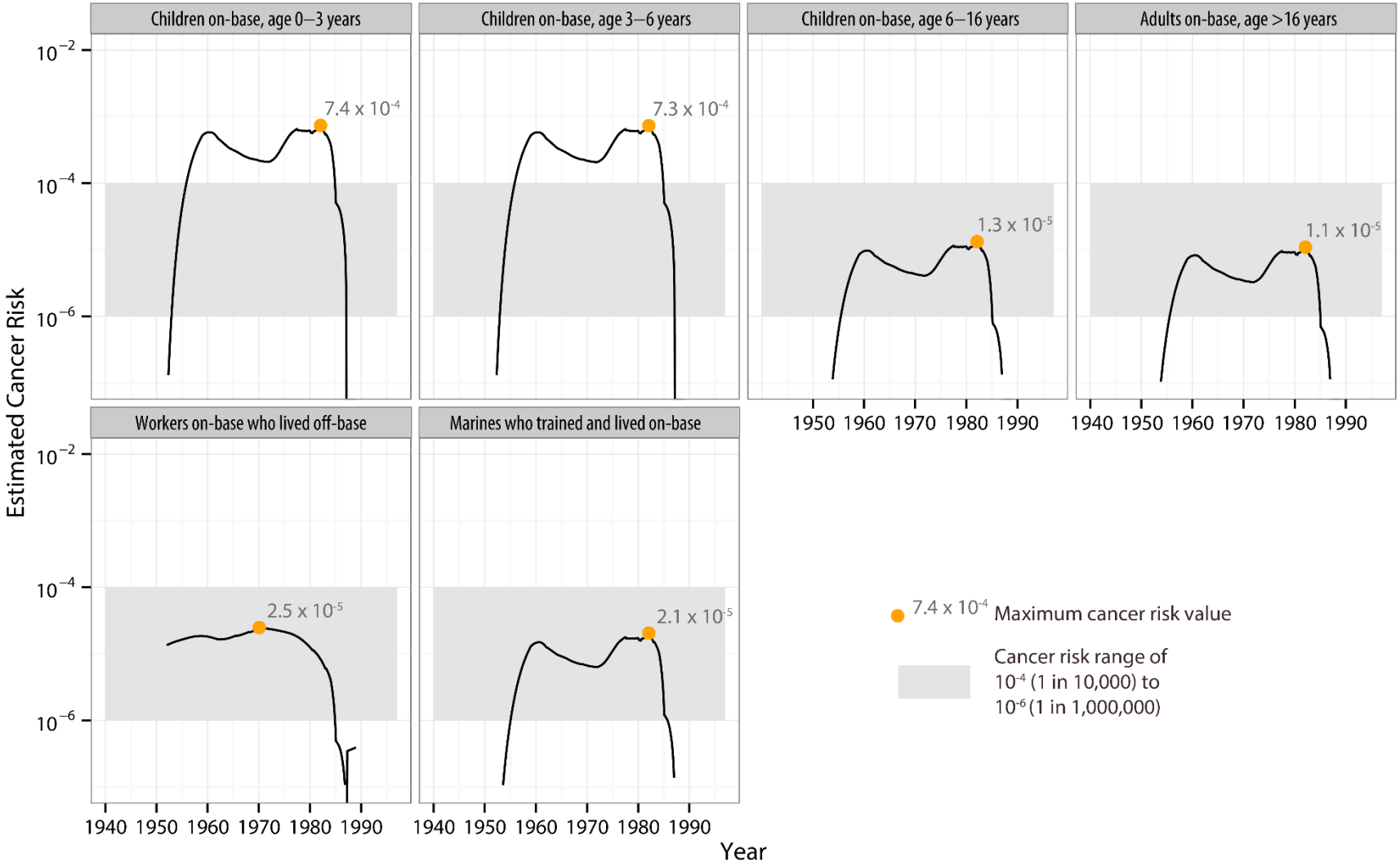


Figure 10. Tarawa Terrace: Estimated Lifetime Cancer Risk by Age Group over Time Based on 3-Year Exposure for Residents and Marines-In-Training, and 15-Year Exposure for Workers Exposed to All Chemical Contaminants Evaluated in Drinking Water from the Treatment Plant



Summary of Potential Health Effects from Contaminated Water Supplies

For residents and workers who used the Hadnot Point Water Supply System, TCE and VC levels significantly exceeded the current drinking water standards and health-based screening levels. A particular concern is for potential health effects from exposures from about 1970 until the contaminated wells closed in 1985. And for several years, PCE levels in the Tarawa Terrace water supply system also exceeded current drinking water standards and health-based screening levels.

The key question is whether those people who lived or worked at MCB Camp Lejeune were harmed when they were exposed to contaminated Hadnot Point and Tarawa Terrace drinking water. To determine whether the levels of chemical exposure could have caused harm to people's health, ATSDR uses what is referred to as a weight-of-evidence approach (ATSDR, 2005). To reach a conclusion about possible harmful effects, ATSDR considers all available information about chemical exposures and health effects from both animal and human studies.

One of the evidentiary lines in a public health assessment is the epidemiological evaluation of birth outcomes of children born at Camp Lejeune.

- Previous ATSDR studies of women exposed to TCE-contaminated drinking water have shown an association between infants with low birth weight and small for gestational age status (Ruckart 2014).
- ATSDR conducted a study of children born to mothers exposed to contaminated drinking water at Camp Lejeune from 1968 to 1985. The findings indicated a possible association between maternal exposure to chemical contaminants in drinking water and neural tube defects (e.g., spina bifida and anencephaly) in the children. A weaker association, with lower odds ratios, was found with childhood hematopoietic cancer (Ruckart et al., 2013).
- Another ATSDR study of pregnant women exposed to contaminated drinking water at MCB Camp Lejeune found suggested associations between exposure to contaminants in the water supply from 1968 to 1985 and several adverse birth outcomes, including low birth weight, small for gestational age, and preterm birth (Ruckart et al., 2014).

A mortality study of MCB Camp Lejeune personnel showed that, compared with personnel from Camp Pendleton, California (a similar training facility, with the only difference being the lack of drinking water contamination; ATSDR, 2008), Camp Lejeune personnel showed elevated hazard ratios for several causes of death, including multiple myeloma, Hodgkin lymphoma, and cancers of the kidney, liver, esophagus, and cervix (Bove et al., 2014).

The figures that serve as a resource for this discussion of health effects from chemical exposure are presented in logarithmic scale (Figures 11-13). A logarithmic scale is a useful way to represent information when there are exponential changes in the magnitude of the numbers. Please note that the y-axis marks represent changes by orders of magnitude or the value multiplied or divided by ten, one hundred, one thousand, etc.

Hadnot Point Water Supply Users

Pregnant women exposed to TCE both through ingesting drinking water and inhaling airborne TCE released during household water use (e.g., showering/bathing) during 1970–1985 could also have resulted in an increased risk of their children having abnormal heart development. Several animal studies substantiate this risk estimation; these studies show defects in the hearts of young animals exposed to TCE during embryonic development (Johnson et al., 1993). Birth defects include structural defects in the heart wall and in the heart valves. An Endicott, NY study of birth defects analyzed outcomes among women who lived in areas where groundwater was contaminated with either TCE alone, PCE alone, or both TCE and PCE. The expected exposure pathway was through inhaling chemical vapors migrating into the indoor air from contaminated groundwater and subsurface soil. The results of the Endicott study

indicated that the rates of cardiac defects, low birth weights, and fetal growth restriction were elevated above statistical significance in infants born to women who lived in the TCE area during their pregnancies (Forand et al., 2012). Although the air sampling data are insufficient to verify the levels of exposure to correlate those levels with these adverse health effects, the findings are generally consistent with those of other epidemiological and animal studies (Bove et al., 1995, 2002; Goldberg et al., 1990). The highest monthly level of exposure to residents and Marines at Hadnot Point exceeded the human equivalent doses for water ingestion that resulted in the cardiac effects in animals (Figure 11). The estimated levels of TCE in the indoor air generated through showering in Hadnot Point residences also exceeded the human equivalent concentration for these effects in animals (Figure 11).

From 1970 to 1985, pregnant women at MCB Camp Lejeune were exposed to TCE above the level of exposure associated with an alteration in the immune system—a level that, based on an animal study, could result in an increased risk for autoimmune disease for the child (Peden-Adams 2006). Children and adults (e.g., Marines, workers, residents) exposed to TCE during this same period could have also been at greater risk for the development of an increase in the delayed hypersensitivity response (Keil 2009). The highest predicted risk for the immune effects was for children less than 1 year of age. Assessment of adult exposure from studies of occupational exposure to TCE through inhalation have found associations with specific immune system abnormalities, including systemic autoimmune diseases and altered cytokine levels (as reviewed in Cooper, 2009). However, the exposure levels in those studies were either unknown or at much higher concentrations than would be expected from exposure to drinking water at Camp Lejeune.

The cancer risk estimated for residents, workers, and Marines who used Hadnot Point's water system exceeded the upper end of U.S. EPA's cancer target risk range for risk management decisions (1 additional cancer case among 10,000 exposed persons over a lifetime = 1×10^{-4} cancer risk). All of the exposure groups exceeded this level, with the highest estimated risk for young children (Figure 9). The maximum cancer risk was 4.6×10^{-3} cancer risk for a 3-year exposure period, which corresponds to an estimated five additional cancer cases among 1,000 exposed persons. Children less than 1 year of age had the highest estimated cancer risk, accounting for 50% of the risk for the 0–3 year age group. This cancer risk is associated mainly with VC exposure (Figure 13) and, to a lesser extent, TCE (Figure 11). These cancer risk estimates are based on dose-response experiments in animals, which have shown that exposure to VC and TCE are associated with liver cancer, kidney cancer, and non-Hodgkin lymphoma. Human epidemiological studies of populations exposed to TCE exposure have also shown an association with liver cancer, kidney cancer, and non-Hodgkin lymphoma (reviewed in EPA, 2011d). Although the MCB Camp Lejeune VC exposure doses were below those where tumors were observed in animal studies (Figure 13), it should be noted that the doses used in these animal studies are generally designed to be high enough to induce tumors and are not considered to be threshold level of cancer effects. Adults, particularly Marines-in-training also had an increased cancer risk, with the highest estimated risk of up to four additional cancer cases among 10,000 exposed individuals.

Tarawa Terrace Water Supply Users

The noncancer hazard and cancer risk levels for Tarawa Terrace residents are generally lower than those for Hadnot Point. The peak levels of TCE in the Tarawa Terrace water supply were only slightly above the current drinking water standard and ATSDR guidelines. Still, the estimated levels of ingestion and inhalation exposure for persons who had frequent and prolonged exposure to water from Hadnot point during 1956–1985, particularly Marines in training, were at levels that would have been a health concern for fetal developmental effects. And at peak estimated TCE levels, a potential existed for adverse immune system effects. Young children could have also experienced an increased risk for adverse immune system effects if they were exposed to the peak estimated TCE levels. The ATSDR epidemiologic study did identify a suggested association between first trimester exposure to TCE and neural tube defects at birth (Ruckart et al., 2013).

The maximum estimated exposures through ingestion and inhalation doses of PCE for all Tarawa Terrace exposure groups were only slightly above the ATSDR and U.S. EPA health guidelines (Figure 12). Based on our current understanding, noncancer and cancer health effects from exposure were unlikely for Tarawa Terrace residents, workers, or Marines, even for exposures to peak concentrations of PCE usually associated with adverse health effects.

The maximum estimated ingestion exposure doses of trans-1,2-DCE and VC at Tarawa Terrace were below current U.S. EPA and ATSDR health guidelines. The maximum estimated inhalation concentrations for trans-1,2-DCE and VC at Tarawa Terrace are also below the ATSDR health guidelines. Past exposure to even the highest concentrations of trans-1,2-DCE and VC in the drinking water is unlikely to be associated with noncancer health effects to the residents, workers, or Marines at Tarawa Terrace.

Of those who used the Tarawa Terrace water system, the estimated cancer risk for children younger than age 6 did exceeed the U.S. EPA target risk range (Figure 10). For instance, during early 1982, exposures to contaminants by children 0–3 years of age is expected to produce five excess cancer cases per 1,000 exposed persons. Therefore, children would have a moderate to high increased cancer risk, whereas adults would have a low increased cancer risk. The increased cancer risk for Tarawa Terrace was associated almost completely with exposure to VC.

Holcomb Boulevard Water Supply Users

Exposure to TCE above health guidelines in the Holcomb Boulevard water system only occurred during relatively brief periods from May 1978 to Feb 1985, when the water was blended with water from the contaminated Hadnot Point well. The exposure during those times would not be expected to have resulted in health effects for children, men, or nonpregnant women. Women who were pregnant during these periods could have been exposed to TCE levels that might have carried an increased risk for fetal cardiac effects, if the women were exposed during their first trimester. The risk is uncertain for other possible adverse birth outcomes as a result of short-term exposure for Holcomb Boulevard residents.

Figure 11. Health Effects Associated with Exposure Doses for TCE – Ingestion & Inhalation

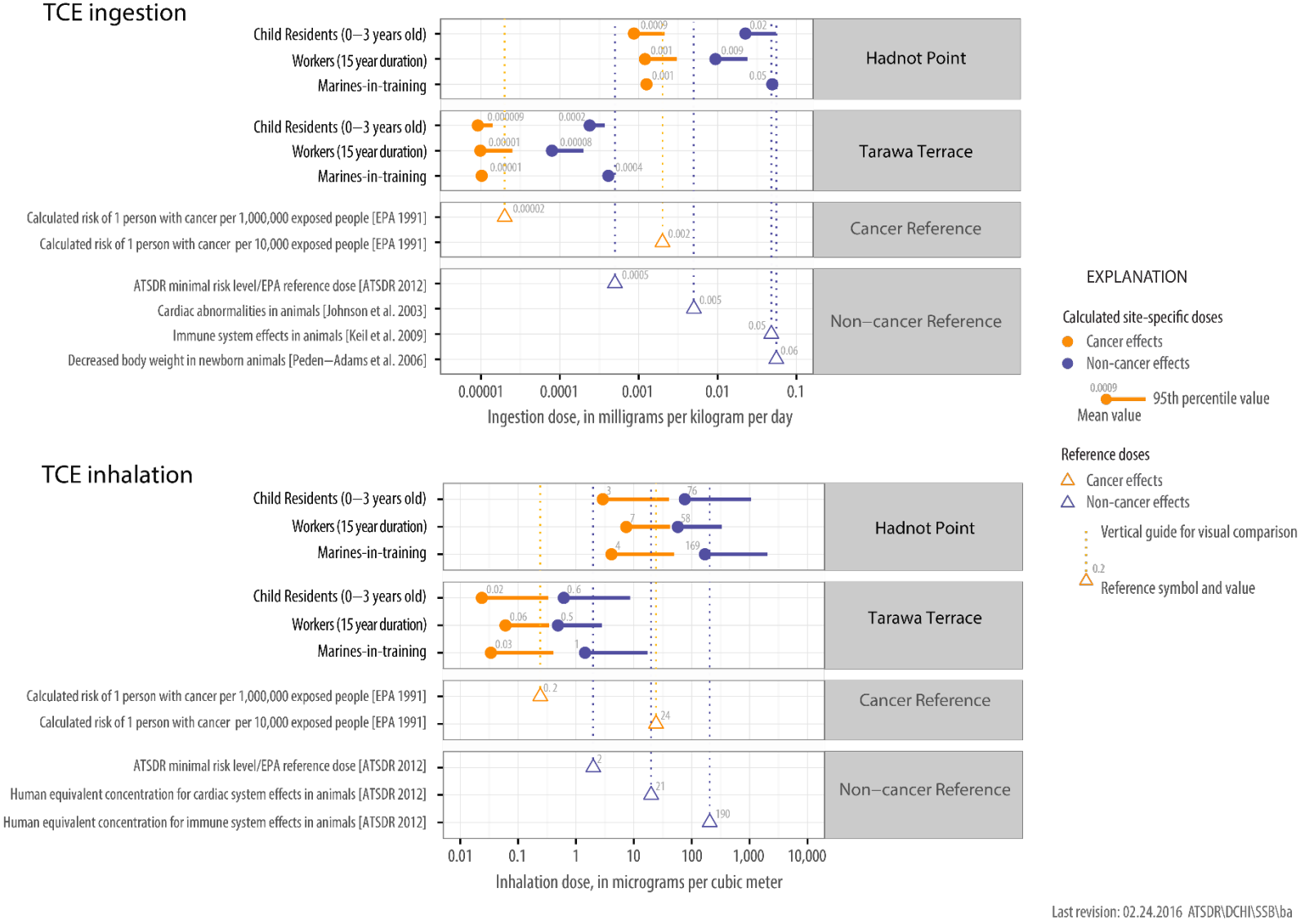


Figure 12. Health Effects Associated with Exposure Doses for PCE – Ingestion & Inhalation

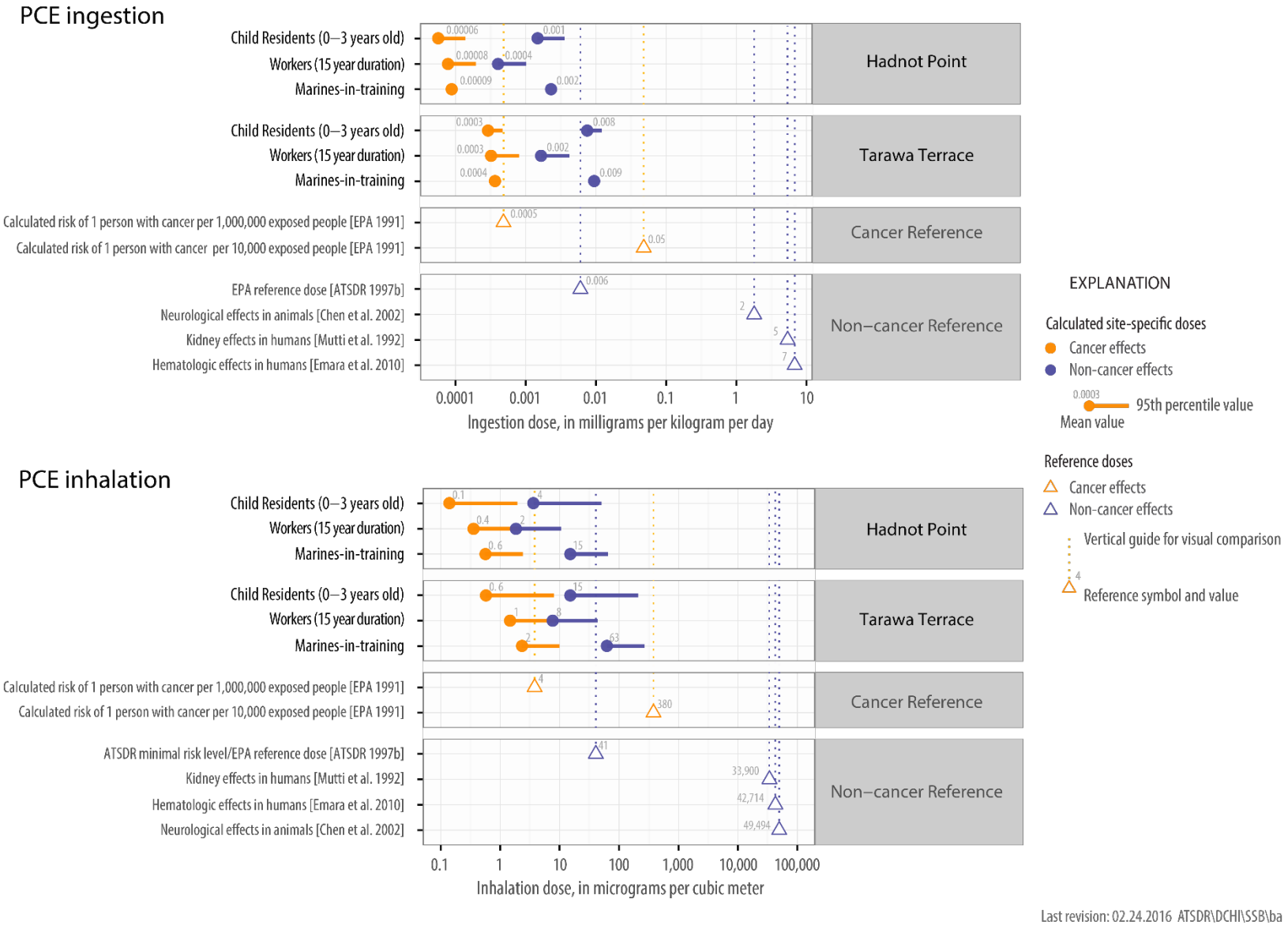
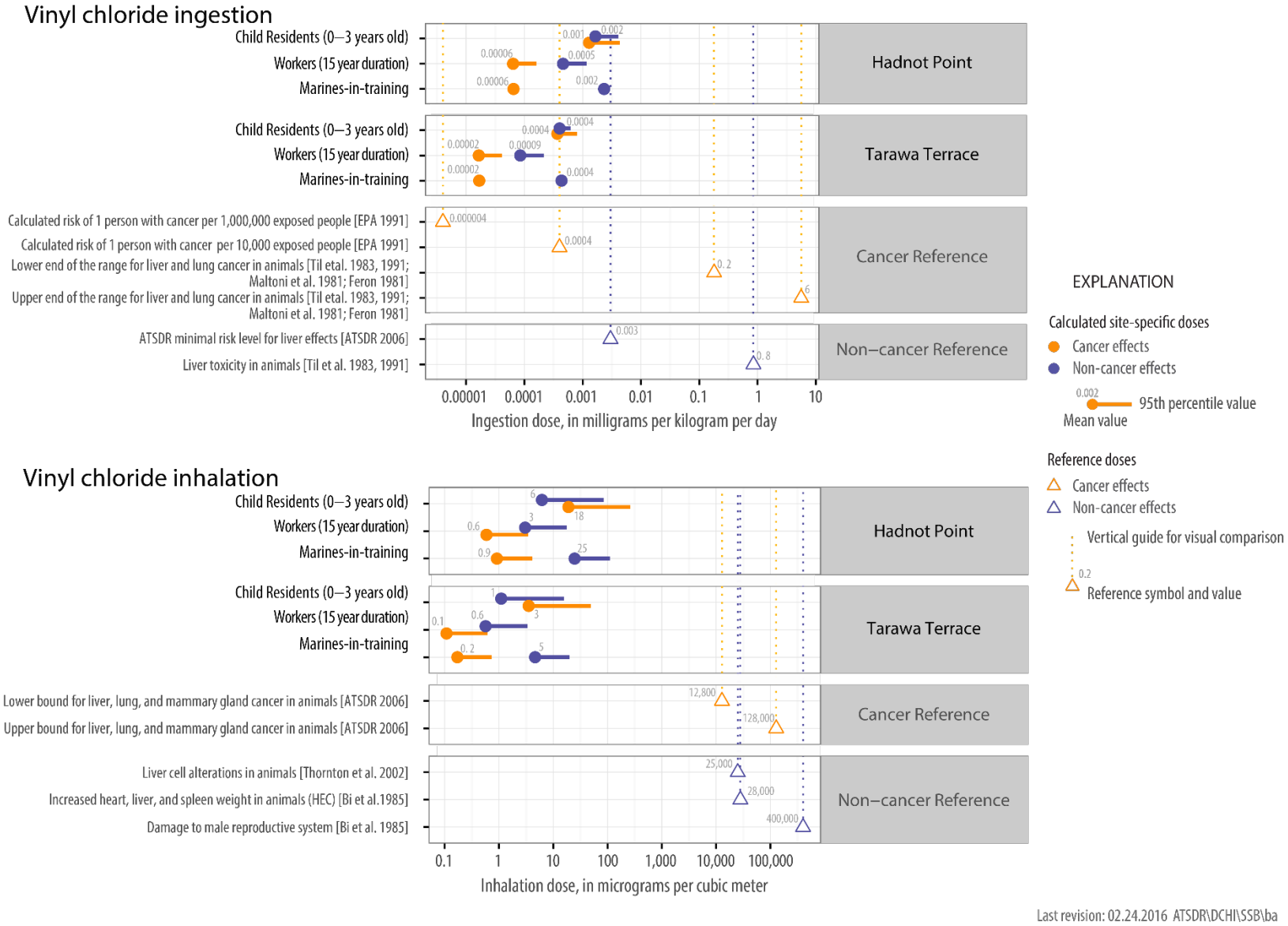


Figure 13. Health Effects Associated with Exposure Doses for VC – Ingestion & Inhalation



Data Limitations for VOCs

ATSDR attempted to assess accurately the potential health effects that contamination had on the MCB Camp Lejeune community. But limitations exist in the environmental data used to make that assessment. When such data limitations appeared, ATSDR chose conservative (health-protective) data-interpretation options that were estimates of exposure in the upper end of the range of recommended values.

1. ATSDR attempted to identify accurate exposure concentrations for this assessment. However, a major data limitation was the small number of drinking water contaminant results from actual samples taken at the water treatment plant or at the point of exposure. As previously discussed, the concentrations used in the dose calculations are simulated values with the uncertainty inherent in such simulations. But the actual concentrations could have been higher or lower than the values generated by the historical reconstruction process. The approach used in this assessment was to assume the historical reconstruction concentrations were the point of exposure concentrations, which is consistent with the approach used in the ATSDR health studies,
2. Additionally, a person's exact exposure duration to contaminated groundwater at MCB Camp Lejeune is unknown. To construct models, a great amount of data collection and research went into contaminant fate and transport and site-specific geology. But the actual exposure duration could have begun even before or after January 1952. Also, it's difficult to ascertain how long active duty personnel and dependent women and families were stationed at Camp Lejeune. This public health assessment uses the ATSDR mortality health study dataset to determine base residency periods. From this dataset ATSDR estimated a conservative 85th percentile residency time of 3 years. Three years was also the exposure-duration estimate used in the dose calculations.
3. Of note is the absence of site-specific data for water consumption, showering/bathing water flow rates, the base population's showering/bathing frequency, breathing rates, and body weights. To ensure that the assessment was conservative (health-protective), ATSDR used values for these parameters that generally reflected the upper end of exposure (USEPA 2011d; Kolka 2003; ATSDR 2005; CDC 2004; Maslia et. al, 1996).
4. Without indoor air samples for the additional exposure scenarios (e.g., swimming/training pools, laundry facilities, and food preparation/dishwashing operations), ATSDR's conservative (health-protective) approach estimated the concentrations to which persons were exposed by using one-compartment air models. One-compartment models, however, tend to overpredict actual exposures and do not take into account clean air ventilation.

ATSDR notes that a limitation inherent in the public health assessment process is that scientists do not have a complete understanding of how simultaneous exposures to several environmental contaminants may cause health effects. This is a limitation of the evolving field of mixtures assessments. Data limitations for the lead evaluation are discussed in the Data Limitations for Lead section.

Conclusions

For those exposed to VOC-contaminated drinking water at MCB Camp Lejeune, ATSDR concludes the following. These conclusions are based on exposure to the historical reconstruction concentrations.

The lead evaluation conclusion can be found after the lead discussion.

Conclusion 1- Hadnot Point

Residents, workers, Marine and naval personnel, and Marines-in-training at MCB Camp Lejeune were in the past exposed to contaminants in drinking water supplied by the **Hadnot Point** WTP. And, using the estimates described in our report, this contaminant exposure was at levels that could have harmed their health. **The estimated levels to which all the above-mentioned groups of people were exposed would have resulted in an increased cancer risk and increased potential of experiencing adverse, noncancer health effects.**

TCE and vinyl chloride were the chemicals that contributed most to the increased cancer risk. The magnitude of the cancer risk estimated in this public health assessment depends on the period during which people were on the base and their ages while there. Using a 3-year exposure duration, the increased, upper-bound cancer risk exceeds the USEPA's Superfund target cancer-risk range (1 excess case for every 10,000 exposed persons to 1 excess case for every 1,000,000 exposed) during the years 1964–1985 (Figure 9). Specifically,

- Children living on-base from the early 1970s to the mid-1980s had an estimated, upper-bound cancer risk up to about 50 excess cases of cancer for every 10,000 exposed persons. This exceeds the USEPA's Superfund target cancer-risk range by about 50 times.
- Workers from the mid-1960s to the early-1980s had an estimated, upper-bound cancer risk of about three excess cases of cancer for every 10,000 exposed persons.
- Marines-in-training from the mid-1960s to the early-1980s had an estimated, upper-bound cancer risk of about four excess cases of cancer for every 10,000 exposed persons.
- Other adults living on-base from the late 1970s to the early-1980s had an estimated, upper-bound cancer risk of about one excess case of cancer for every 10,000 exposed individuals. This is within EPA's Superfund target cancer-risk range.

TCE was the main contributor to potential noncancer health effects. All exposure groups evaluated had exposures in the range of those that caused health effects in animal studies, increasing the risk of experiencing adverse noncancer health effects. Specifically,

- Pregnant women using Hadnot Point drinking water from 1972 to 1985 would have been exposed to TCE levels that could have resulted in effects to a developing fetus. Women in the first trimester of pregnancy are one of the most sensitive populations for exposure to TCE, primarily because of concerns associated with fetal heart malformations that could occur from exposure during that critical period of development.

- Children and all adults exposed to TCE during the years 1972–1985 were at an increased risk for immune system effects.

Conclusion Basis

TCE exposure is associated with an increased risk for kidney cancer, liver cancer, and non-Hodgkin lymphoma. Vinyl chloride exposure is associated with angiosarcoma of the liver and variable associations with lung and brain cancer. TCE and vinyl chloride are both considered known human carcinogens by the National Toxicology Program (NTP). The ATSDR mortality study of military personnel stationed at MCB Camp Lejeune found elevated hazard ratios for several cancers, including kidney cancer, liver cancer, esophageal cancer, cervical cancer, multiple myeloma, and Hodgkin lymphoma.

Exposure to vinyl chloride is mainly associated with increased risk of liver cancer.

For noncancer health effects, Hadnot Point area TCE exposure estimates of the dose for residents and workers not only exceeded the EPA Reference Dose (RfD) and ATSDR Oral Minimal Risk Level (MRL), but were in the same range as the human equivalent doses in laboratory animal studies that found associations with developmental and immune effects. These developmental health effects could include cardiac malformations and altered function of immune systems that could occur in children whose mothers were exposed during pregnancy. In addition, children and adults exposed to estimated TCE levels during the years in question might have resulted in increased risk for autoimmune disease and an increase in the delayed hypersensitivity response of the immune system.

Next Steps

ATSDR will conduct a cancer incidence study and continue to provide health education and followup materials to persons concerned about the potential magnitude of the increased risk of developing cancer or of the likelihood of noncancer health effects. ATSDR will work with the Community Assistance Panel[21], and the U.S. Department of Veterans Affairs to communicate health information to military personnel, workers, and families who were located at Camp Lejeune. This will include providing educational materials on the ATSDR Camp Lejeune Web site at http://www.atsdr.cdc.gov/sites/lejeune/index.html. Concerned persons can discuss any health concerns with their own healthcare providers, who may refer them to an Association of Occupational and Environmental Clinic (AOEC), which has doctors who specialize in occupational and environmental medicine. A list of AOEC locations is available at http://www.aoec.org/.

Conclusion 2- Tarawa Terrace-

Past exposure to contaminants of concern in drinking water supplied by the **Tarawa Terrace** WTP might have harmed the health of young children and Marines in training. **The estimated levels to which young children were**

[21] ATSDR created a community assistance panel (CAP) for the Camp Lejeune site for the purpose of having a forum to voice the concerns of the affected community of Marines and their families and to provide input for health studies. The CAP consists of community members, one representative from the Department of Defense (DoD), independent scientific experts, and ATSDR staff.

exposed would have resulted in an increased cancer risk and increased potential of adverse, noncancer health effects.

Vinyl chloride contributed most to any increased cancer risk for those using the Tarawa Terrace water supply. The estimated magnitude of that risk as measured in this public health assessment depended on the time persons occupied the base and their ages while there. During 1956–1984, for those who used Tarawa Terrace water system drinking water, the cancer risk for children below age 6 did exceed the USEPA target risk range (Figure 10). Specifically,

- Children who lived on-base during 1956–1984 had an estimated, upper-bound cancer risk of up to about seven excess cases of cancer for every 10,000 exposed persons.
- For adults, workers, and Marines-in-training who were only exposed to water from Tarawa Terrace, the estimated, upper-bound cancer risk was within the EPA Superfund target risk range. However, Marines who were exposed to water from the Hadnot Point system during training may have had cancer risks similar to Marines who lived in Hadnot Point housing, which is described in Conclusion 1.

Regarding potential noncancer health effects associated with TCE exposure,

- Young children and Marines-in-training who lived on-base during the years 1956–1984 may have had an increased risk for adverse immune system effects.
- Children born to women who were pregnant when they lived at Tarawa Terrace and exposed to water from Hadnot Point system during training during the years 1956–1984 may have been at a greater risk for developmental and immune system effects resulting from exposures to peak concentrations.

Conclusion Basis

Vinyl chloride exposure has been associated with an increased liver cancer risk. The mortality study of military personnel stationed at MCB Camp Lejeune found elevated hazard ratios for several cancers, including liver cancer. For instance, during early 1982, hazard ratios for children 0–3 years of age exposed to drinking water contaminants were estimated to result in up to seven excess cancer cases per 10,000 persons. Children would have an increased cancer risk, while adults would have a low increased cancer risk. The cancer risk for Tarawa Terrace was almost completely associated with vinyl chloride exposure.

Regarding potential noncancer health effects, at Tarawa Terrace the maximum estimated ingestion of PCE and TCE exposure doses and inhalation concentrations were only slightly above the ATSDR and USEPA health guidelines (Figures 4 and 6). The estimated level of TCE exposure for women who had contact with Tarawa Terrace drinking water during the early stages of pregnancy, particularly those in training, could have resulted in adverse effects on fetal cardiac development, based on the results from an animal study.

Based on our current understanding from animal studies, noncancer and cancer health effects from exposure to even the peak PCE concentrations would not be expected to be associated with adverse health effects to residents, workers, or Marines at Tarawa Terrace. However, that conclusion is limited by the available dose-response information about all possible health outcomes. An ATSDR

	epidemiologic study found a suggested association between PCE exposure at the highest concentrations in the water supply and preterm birth (Ruckart et al., 2014). Although there are limitations in using this type of study to attribute such an effect to a specific chemical and exposure level, we acknowledge that there is uncertainty in the conclusion of no expected adverse effects. The maximum estimated ingestion exposure doses and inhalation concentrations of trans-1,2-dichloroethylene (trans-1,2-DCE) and vinyl chloride at Tarawa Terrace were below the ATSDR and USEPA health guidelines. Exposure to even the highest trans-1,2-DCE and vinyl chloride concentrations in the drinking water would unlikely be associated with health effects to the residents, workers, or Marines living at Tarawa Terrace.
Next Steps	ATSDR will continue to provide health education and followup materials to persons concerned about the potential magnitude of the increased cancer risk by working with the Community Assistance Panel, U.S. Department of Veterans Affairs, and by providing educational materials on the ATSDR Camp Lejeune Web site at http://www.atsdr.cdc.gov/sites/lejeune/index.html. Concerned persons can discuss any health concerns with their own healthcare providers, who may refer them to an AOEC, which has doctors who specialize in occupational and environmental medicine. A list of AOEC locations is available at http://www.aoec.org/.
Conclusion 3– Holcomb Boulevard	During brief periods (in June, 1978 and from January 28 to February 4, 1985), women in their first trimester of pregnancy exposed to TCE in drinking water from the **Holcomb Boulevard** water supply area could have had an increased risk for fetal cardiac effects and other adverse birth outcomes. At other periods, the levels of contaminants of concern in the water supply serving the Holcomb Boulevard housing areas were highly variable. **Still, the average levels of contaminants of concern over a 3-year residency are not considered to have been a health concern for children, men, or nonpregnant women.**
Conclusion Basis	For Holcomb Boulevard area drinking water, TCE was the only contaminant of concern whose historically reconstructed, estimated concentrations exceeded health-based screening values. The average levels over a 3-year residency did not result in exposures considered capable of adverse health effects. Still, during two periods the Holcomb Boulevard water system used exclusively contaminated Hadnot Point drinking water. For several weeks, this exclusive use resulted in drinking water TCE levels over 50 ppb. Developmental toxicology studies in animals indicate that TCE exposure is associated with an increased occurrence of fetal cardiac effects. Exposure of Holcomb Boulevard residents to TCE from water ingestion and inhalation of vapors during showering/bathing were estimated at levels similar to those associated with fetal cardiac effects in animal studies. Women exposed during the period when TCE concentrations exceeded 50 ppb and who were in their first trimester of pregnancy (i.e., when the fetal cardiac system is developing) could have had an increased risk for fetal cardiac effects.
Next Steps	Any Holcomb Boulevard resident concerned about drinking-water related exposures should visit the ATSDR Camp Lejeune Web site at http://www.atsdr.cdc.gov/sites/lejeune/index.html. Concerned persons can

	discuss any health concerns with their own healthcare providers, who may refer them to an Association of Occupational and Environmental Clinic (AOEC), which has doctors who specialize in occupational and environmental medicine. A list of AOEC locations is available at http://www.aoec.org/.
Conclusion 4- Other Exposures	**Persons working in laundry facilities or dining operations and persons who used Hadnot Point area indoor training pools from the early 1950s to February 1985 were exposed to contaminants of concern at levels that might have harmed their health.**
Conclusion Basis	ATSDR developed conservative (health-protective) models to estimate exposure for three different scenarios presented by the Community Assistance Panel. Model results produced concentrations that exceeded comparison values of concern. The three exposure scenarios were 1) Marines and civilians training and recreating at indoor swimming pools, 2) civilians working at laundry facilities, and 3) Marines and civilians working in dining halls. In all three scenarios, TCE and benzene exceeded their ATSDR intermediate and chronic minimal risk level (MRLs), and PCE exceeded its acute, intermediate, and chronic MRL. According to the applicable air studies in ATSDR's TCE toxicological profile, estimated TCE exposures also exceeded study effect levels.
Next Steps	ATSDR will conduct a cancer incidence study and continue to provide health education and followup materials to exposed persons by working with the Community Assistance Panel, U.S. Department of Veterans Affairs, and by providing educational materials on the ATSDR Camp Lejeune Web site at http://www.atsdr.cdc.gov/sites/lejeune/index.html. Concerned persons can discuss any health concerns with their own healthcare providers, who may refer them to an AOEC, which has doctors who specialize in occupational and environmental medicine. A list of AOEC locations is available at http://www.aoec.org/.

Lead in Drinking Water

In its 1997 public health assessment, ATSDR determined that lead exposure in drinking water at MCB Camp Lejeune was an immediate health concern (ATSDR 1997). As a result, Camp Lejeune took action to reduce exposure by educating residents and workers, restricting use in certain sinks, installing filtration systems, and replacing lead laden piping in certain residences (ATSDR 1997).

In this public health assessment, ATSDR updates its 1997 assessment by evaluating the public health significance of more recent exposure to lead in drinking water, based on lead sampling data collected at MCB Camp Lejeune from 2005 through 2013.

Sources of Lead in the Environment

Lead is a naturally occurring bluish-gray metal found in the earth's crust. Industry uses lead to produce batteries, ammunition, metal products (solder and pipes), and devices to shield X-rays. Because of health concerns, in recent years, industry has dramatically reduced lead from paints and ceramic products, caulking, and pipe solder. Lead-based paint (containing up to 50% lead) was in widespread use through the 1940s (CDC 1991). In 1978, the lead concentration in new paints was reduced to less than 0.06% lead in paint and further reduced to 0.009% in 2008 (CPSC 2011). Using lead as an additive to gasoline was banned in 1996 in the United States (USEPA 1996).

Lead-based paint and contaminated dust are the most widespread and dangerous sources of lead exposure for young children in the United States (CDC 2015b). Lead occurs in drinking water through leaching from lead in pipes, faucets, and solder found in plumbing of older buildings (ATSDR 2007a, 2007d). Lead can also be released from many other indoor and outdoor sources (CDC 2015b; NYDOH 2010). Table 12, in Appendix I, provides additional information about these sources.

Today, because of human activities such as burning fossil fuels, mining, manufacturing, and past uses, lead is in all parts of the environment (i.e., the land, air, and water) (ATSDR 2007c, 2007d). In the past three decades, however, because of the regulation of lead in gasoline, paint, and plumbing materials, blood lead levels (BLLs) in the public generally have decreased by 78% (ACCLPP 2007).

Lead Exposure Risk Factors

In addition to contact with lead-contaminated soil, water, and air, multiple factors have been associated with increased risk for higher BLLs (Bernard and McGeehin 2003; CDC 2005, 2013a, 2013b; Dixon et al., 2009; Holstege et al., 2013; Jones et al., 2009; Lee et al., 2005; Mielke et al., 2010; Shannon et al., 2005; US Census Bureau 2010; USEPA 2013a). These factors include

- Children[22] less than 6 years of age
- Blacks and Hispanics
- People who live in homes built before 1978
- People who live in rental properties
- People who live in poverty
- New immigrant and refugee populations
- People born in Mexico
- People who live in an urban area
- People who live in specific regions of the U.S. (i.e., Northeast > Midwest > South> West)

[22] Lead can also harm a developing fetus; pregnant women or women likely to become pregnant should be especially careful in avoiding lead exposure (CDC 2013c; Mayo Clinic 2015).

Lead in the Body

As reported in ATSDR's Toxicological Profile for Lead (ATSDR 2007d):

> Lead has no known physiological value. If it gets into the body, lead can affect various organ systems and accumulate in the bones. Lead not stored in bones leaves the body as waste. About 99% of the amount of lead taken into an adult's body is excreted as waste within a couple of weeks; about 30% of the lead taken into the child's body leaves as waste during a similar period. Most of the remaining lead—especially in children's bodies—moves into bones and teeth. Although lead can stay in bones for decades, under certain circumstances some lead can leave bones and reenter the blood and organs. Some examples include during pregnancy, after a bone is broken, and during advancing age.

Nutrients such as calcium and iron, as they occur in meals or with intermittent eating, influence lead uptake, especially from the gastrointestinal tract (CDC 1991; Mahaffey 1981; Mahaffey and Michaelson 1980; Rabinowitz et al., 1980). Lead uptake generally increases as dietary levels of these nutrients decrease. Figure 17, Appendix I, provides ways people can reduce lead uptake, such as eating healthy foods.

Blood Lead Levels and Health Effects

Although lead can affect almost every organ and system in the body, the nervous system is the main target for lead toxicity. In general, the lead level in a person's blood gives a good indication of recent exposure to lead and correlates well with harmful health effects (ATSDR 2007c, 2007d).

In May 2012, the Centers for Disease Control and Prevention (CDC) updated its recommendations on children's blood lead levels. By shifting the focus to primary prevention of lead exposure, CDC wants to reduce or eliminate dangerous lead sources in children's environments before children are exposed.

- *Blood Lead Reference Level now 5 µg/dL* – Until 2012, children were identified by CDC as having a blood lead level of concern if the test result was 10 or more micrograms per deciliter (µg/dL) of lead in blood. Experts now use a reference value of 5 µg/dL[23] based on the U.S. population of children 1 to 5 years of age in National Health and Nutrition Examination Survey (NHANES) (ACCLPP 2012; CDC 2012b). The current (2011–2012) geometric mean BLL for that age group is 0.97 µg/dL (CDC 2015a).
- *No Change in Blood Lead Levels Requiring Medical Treatment* – The recommendation for when to use medical treatment for children has not changed. Experts recommend chelation therapy when a child's test results are equal to and greater than 45 µg/dL (CDC 2014a). Note chelation should be used with caution. Primary care providers should consult with an expert in the management of lead chemotherapy before using chelation agents. If unaware of a center with such expertise, primary care providers should contact their local or state lead poisoning prevention program, local poison control center, or CDC (CDC 2002).
- *Health Effects in Children with Measurable Blood Lead Levels less than 5 µg/dL and 10 µg/dL* – No clear threshold exists for some of the more sensitive health effects associated with lead exposures. In children, the National Toxicology Program reports conclusions on health effect

[23] In 2012, the upper value of the reference range (established as the 97.5 percentile) was 5 µg/dL.

studies of low-level lead exposure for both <5 µg/dL and <10 µg/dL where sufficient evidence[24] exists of (NTP 2012)

- Decreased academic achievement (<5 µg/dL),
- Decreased intelligence quotient (IQ) (<5 µg/dL and <10 µg/dL) [25],
- Decreased specific cognitive measures (<5 µg/dL),
- Increased incidence of attention-related and problem behavior (<5 µg/dL),
- Decreased hearing (<10 µg/dL),
- Reduced postnatal growth (<10 µg/dL), and
- Delays in puberty (<10 µg/dL).

- *Health Effects of Lead on Developing Fetuses* – Lead crosses the placenta; consequently, it can pass from a pregnant woman to her developing fetus. To prevent exposure to the developing fetus and newborn, followup testing, increased patient education, and environmental, nutritional, and behavioral interventions are indicated for all pregnant women with BLLs greater than or equal to 5 µg/dL (CDC 2013c). Too much lead in a pregnant women's body can

  - Put her at risk for miscarriage,
  - Cause the baby to be born too early or too small,
  - Hurt the baby's brain, kidneys, and nervous system, and
  - Cause the child to have learning or behavior problems (CDC 2013c).

- *Health Effects for Adults* – Adults exposed to lead over many years could develop kidney problems, high blood pressure, cardiovascular disease, and cognitive dysfunction (Kosnett et al., 2007).

ATSDR notes that no clear threshold exists for some of the more sensitive health effects associated with lead exposures. CDC and ATSDR recommend reducing lead exposure wherever possible.

Source of Lead in Drinking Water at Camp Lejeune

MCB Camp Lejeune personnel found no buildings with lead plumbing. However, for all the drinking water systems, they did find buildings with copper pipes and lead-based solder (ATSDR 1997). Lead enters tap water through corrosion of plumbing materials. Homes built before 1986 are more likely to have lead pipes, fixtures, and lead-based solder (ATSDR 2007a, 2007d). Still, new homes might also contain lead-based plumbing components. Section 1417(d) of the Safe Drinking Water Act states that "lead-free" plumbing may contain up to 8% lead in piping and 0.2% in solder (USEPA 2012b). The most common lead problem in plumbing is with brass or chrome-plated brass faucets and fixtures that can leach significant amounts of lead into water—especially into hot water, given that lead dissolves more quickly in hot water. For example, in January 2003, MCB Camp Lejeune tested a school's drinking water. Lead was undetected in the samples except for the water from one kitchen sink that detected lead at 125 ppb. That sink faucet was replaced immediately.

Review of Annual Water Quality Reports

ATSDR reviewed 2000–2012 Annual Water Quality reports associated with five of MCB Camp Lejeune's water treatment plant service areas that are available on the North Carolina's Drinking Water

[24] NTP defines sufficient evidence: "An association is observed between the exposure and health outcome in studies in which chance, bias, and confounding could be ruled out with reasonable confidence." Although this public health assessment does not discuss the general strengths and limitations of each study, the NTP report does (see http://ntp.niehs.nih.gov/ntp/ohat/lead/final/monographhealtheffectslowlevellead_newissn_508.pdf).

[25] For decreased IQ, separate studies with suffient evidence of an association exist for both <5 µg/dL and <10 µg/dL BLLs in children.

Watch website at https://www.pwss.enr.state.nc.us/NCDWW2/. These service areas are: (1) Courthouse Bay, (2) Holcomb Boulevard, (3) Hadnot Point, (4) Rifle Range, and (5) MCAS New River. Multiple lead measurements from 1993 through 2011 were collected under the USEPA Lead and Copper Rule (LCR), which sets an action level[26] of 15 ppb for lead. MCB Camp Lejeune has had two violations of USEPA's LCR since 1993. These violations were for failure to submit optimal corrosion control treatment recommendations for the Holcomb Boulevard and Rifle Range systems. A fact sheet summarizing the requirements of USEPA's LCR law is included in Appendix H. Note that for this public health assessment, ATSDR did not evaluate the summary lead data provided in the annual reports but instead evaluated individual lead sampling results (see next section).

Lead Levels in Camp Lejeune's Drinking Water

MCB Camp Lejeune tests onbase tap water for lead. Samples are taken from locations where people can be exposed. For example, when MCB Camp Lejeune samples onbase residences, it takes the samples from the kitchen sink (MCB Camp Lejeune 2013). ATSDR reviewed the lead concentrations in these water samples and found:

- MCB Camp Lejeune took tap water samples from family housing units, barracks, and other buildings. The Hadnot Point, Holcomb Boulevard, Rifle Range, and MCAS New River service areas provide drinking water to these buildings.
- From 2005–2013 (data before 2005 were not included on the North Carolina Public Works Web site), 382 samples were taken and analyzed for lead; 284 of the 382 samples (about 75%) reported lead below the minimum detection level (3 ppb); 14 of 382 samples (about 4%) exceeded the 15 ppb lead action level; and the detected lead concentrations ranged from 3–1,750 ppb.
- The highest lead concentrations were at buildings serviced by Holcomb Boulevard and MCAS New River (1,750 ppb and 1,440 ppb, respectively). The next highest lead concentration was 82 ppb found at a building serviced by Holcomb Boulevard. Followup sampling about 1 year later at the two Holcomb Boulevard locations (assumed to be houses where the 1,750 ppb and 82 ppb were detected previously) showed lead levels below the 15 ppb action level. Followup sampling did not detect lead about 3 years later at the MCAS New River location (a transmitter building where 1,440 ppb had been detected previously).
- With the exception of MCAS New River location 458 AS 4025, followup samples taken at building locations where there were exceedances above the 15 ppb lead action level produced results that were all below 15 ppb lead. Followup samples were collected from one month to over one year later. Table 7 provides information about the locations where lead samples exceeded lead's 15 ppb action level.

ATSDR contacted MCB Camp Lejeune to gather additional information about the 14 locations where lead exceeded the 15 ppb action level. MCB Camp Lejeune reviewed the maintenance project database for records of major renovations and/or smaller projects for these 14 locations. Three of the locations had repairs/renovations. MCB Camp Lejeune reported no records of repairs at the other 11 locations.

The database indicated that major repairs were completed in 2007 at MCAS New River location 545 G 521 (a small building at Camp Geiger), and Table 7 shows the lead level decreased to below the USEPA

[26] The MCLG, a non-regulatory toxicity value, for lead is zero. USEPA set this level based on the best available science. No MCL has been established for lead. Instead, USEPA's regulation to control lead in drinking water is known as the Lead and Copper Rule (also referred to as the LCR or 1991 Rule). If lead concentrations exceed the 15-ppb action level in more than 10% of customer taps sampled, the system 1) must undertake a number of additional actions to control corrosion, 2) must inform the public about steps they should take to protect their health, and 3) might have to replace lead service lines under their control.

action level upon further sampling (i.e., lead was not detected). Partial renovations were completed in 2014 at MCAS New River location 541 G 560 (a recreation center at Camp Geiger), but Table 7 shows the lead tap water level had dropped to be below the USEPA action level before the renovation. Interior and exterior repairs were completed in 2011 at MCAS New River location 458 AS 4025 (barracks). ATSDR notes that sampling of tap water at these barracks showed lead was undetected in June 2007 and June 2010, which was before repairs were completed in 2011. However, in September 2013, at this same location, lead was detected above the 15 ppb action level. ATSDR recommends this tap water location be retested. For the remaining 11 locations where no repairs/renovations took place, the lead levels decreased to be below the USEPA action level upon further sampling, but in some instances the levels fluctuated. The reason for the fluctuations is unknown.

Table 7: 2005-2013 Tap Water Sampling Data for Locations with a Lead Level in Drinking Water Exceeding 15 ppb

Service Area*	Sample Location (use)†	Lead Level in ppb (date)				
		1st Sample	2nd Sample	3rd Sample	4th Sample	5th Sample
Holcomb Boulevard	835 PP 3212 (assumed to be a house)	**1,750‡** (8/11/2005)	10 (7/2/2006)	ND (6/25/2007)	ND (6/7/2010)	ND (7/10/2013)
	833 PP 3210 (assumed to be a house)	ND (8/11/2005)	82 (7/2/2006)	5 (6/8/2007)	ND (6/7/2010)	
	962 PP 3204 (unoccupied house)	13 (7/2/2006)	65 (6/25/2007)	ND (6/10/2010)	ND (7/9/2013)	
	961 PP 3203 (assumed to be a house)	38 (8/11/2005)	7 (7/2/2006)	4 (6/25/2007)	ND (6/16/2010)	ND (7/9/2013)
	834 PP 3211 (assumed to be a house)	32 (7/2/2006)	ND (7/13/2007)	ND (6/7/2010)	ND (7/10/2013)	
	950 PP 3232 (assumed to be a house)	18 (8/3/2005)	13 (6/29/2006)	ND (6/25/2007)	14 (6/10/2010)	ND (7/9/2013)
	954 PP 3215 (assumed to be a house)	ND (8/11/2005)	16 (6/28/2006)	ND (6/26/2007)	ND (6/10/2010)	
Rifle Range	712 RR49 (rifle range building)	28 (8/3/2006)	5 (6/11/2007)	10 (6/2/2010)		
MCAS New River	454 AS 903 (transmitter building)	1,440 (6/28/2007)	ND (6/4/2010)			
	545 G 521 (small building at Camp Geiger)	29 (6/14/2007)	ND (6/11/2010)			
	541 G 560 (recreation center at Camp Geiger)	23 (6/8/2010)	10 (8/28/2013)			
	445 AS 201 (administrative building)	ND (6/27/2007)	23 (8/28/2013)	5 (9/23/2013)		
	458 AS 4025 (barracks)	ND (6/21/2007)	ND (6/3/2010)	17 (8/28/2013)		
Hadnot Point	177 H 27 (unoccupied house)	ND (7/13/2007)	23 (8/5/2010)	4 (7/12/2011)		

* Tap water samples were collected from these service areas. These data do not represent samples collected from the distribution facility, but from the exposure point (like a kitchen sink).
† MCB Camp Lejeune reported the building usages provided in this table.
‡ **Bolded values** exceeded the 15 ppb action level.
ND not detected
ppb parts per billion

Health Effect Evaluation for Lead

Neither ATSDR nor USEPA has developed a MRL or RfD for lead. Therefore, ATSDR cannot follow the usual method of estimating human exposure to an environmental contaminant then comparing that dose to a health-based comparison value (such as an MRL of RfD). Instead, we had to evaluate lead using a biological model that estimates blood lead concentrations that could result from human exposure to environmental lead contamination. Specifically, for this public health assessment, ATSDR evaluated exposure to lead by using USEPA's Integrated Exposure Uptake Biokinetic (IEUBK) model for lead in children.

Whereas the other chemicals in this assessment were evaluated separately by each exposure pathway, ATSDR notes the IEUBK model calculates combined exposures from lead in air, water, soil, dust, diet, and other sources. The model then predicts the risk for elevated blood lead levels in children 6 months to 7 years of age. Researchers can also use the model to predict risk for specific age groups up to age 7. To predict blood lead concentrations for children 7 years of age and older, no generally accepted model is currently available. The IEUBK model integrates exposure with pharmacokinetic modeling to predict blood lead concentrations. The four main components of the current IEUBK model are (USEPA 1994):

1. An exposure model that relates environmental lead concentrations to age-dependent intake of lead into the gastrointestinal tract,
2. An absorption model that relates lead intake into the gastrointestinal tract and lead uptake into the blood,
3. A biokinetic model that relates lead uptake in the blood to the concentrations of lead in several organ and tissue compartments, and
4. A model for uncertainty in exposure and for population variability in absorption and biokinetics.

The IEUBK model results can be viewed as a tool for estimating changes in blood lead concentrations as environmental lead exposures are modified (USEPA 1994). The IEUBK model provides choices a user may make in estimating a child's blood lead concentration. These choices are referred to as "user-specified" parameters or decisions. But the reliability of the results obtained using the model is very dependent on the proper selection of site-specific coefficients and default values. USEPA notes that the IEUBK predicts a BLL value of 1.15 µg/dL even when all input values are set to zero; this is because in batch mode the contribution from other dietary sources is always present (USEPA 2015).

ATSDR ran the IEUBK model (IEUBKwin Model 1.1 Build 11) using default parameters for all inputs except the 1) drinking water lead levels, which were set to site-specific levels 2) soil level, which was set to 100 parts per million (ppm)[27] and 3) BLL reference level for risk estimation[28], which was set to 5 µg/dL. Note the first drinking water level was set to 0 ppb. The next drinking water levels was set to 3 ppb. About 75% of the site-specific samples showed lead was undetected in drinking water at the detection limit of 3 ppb. The next level was set to 15 ppb, which is the USEPA lead action level for drinking water. The remaining drinking water levels used in the IEUBK model correspond to the site-specific lead levels detected at MCB Camp Lejeune above the 15 ppb action level. In Table 8, ATSDR provides the IEUBK estimated probability of exceeding a BLL of 5 µg/dL and the geometric mean BLLs for these drinking water lead levels.

[27] ATSDR set the value of lead in soil to 100 ppm, which is greater than the lead levels found at Camp Lejeune in a wide range of soil types from both developed and undeveloped locations (CH2M HILL 2011). Overall, the report found that background soil levels at the base ranged from 0.45–54.6 ppm (CH2M HILL 2011). ATSDR notes also that USEPA recommends < 100 ppm lead in soil for gardens (USEPA 2014).

[28] ATSDR notes the default BLL level for risk estimation the model uses is 10 µg/dL.

Table 8: IEUBK* Estimated Probabilities and Estimated Geometric Mean BLLs for Several Drinking Water Lead Levels

Drinking Water Lead Concentration (ppb)	Estimated Probability (%) of exceeding a BLL of 5 µg/dL	Estimated Geometric Mean BLL (µg/dL)
0	0.49	1.5
3	1.2	1.7
15	8.9	2.7
16	9.9	2.7
17	11	2.8
18	12	2.9
23‡	18	3.3
28	25	3.6
29	26	3.7
32	30	3.9
38	38	4.3
65	67	6.2
82	79	7.3
1,440	NA†	NA†
1,750	NA†	NA†

* The IEUBK predicts the risk for elevated blood lead levels in children 6 months to 7 years of age.

† At elevated lead concentrations, the IEUBK model provides a warning that the predicted blood lead levels (> 30 µg/dL) are above the range of values used in the calibration and empirical validation of the model (USEPA 2002a). Therefore, USEPA cautions not to rely on the model to predict BLLs above 30 µg/dL (USEPA 2002a, 2002b).

‡ The lead level of 23 ppb was detected at three different locations.

BLL blood lead level
IEUBK Integrated Exposure Uptake Biokinetic Model for Lead in Children
µg/dL micrograms per deciliter
NA not applicable
ppb parts per billion

As stated previously, for the US, the BLL reference level for children 1 to 5 years of age is now 5 µg/dL, whereas the current (2011–2012) geometric mean BLL for that age group is 0.97 µg/dL (CDC 2015a). At the 15 ppb lead action level in drinking water, Table 8 shows that the IEUBK model estimates 8.9% of children could have BLLs exceeding 5 µg/dL, with a predicted geometric mean of 2.7 µg/dL. Overall, the site-specific lead data show that in the past, 14 of 382 drinking water samples exceeded 15 ppb lead and with increasing drinking water lead levels, the model estimated increasing probabilities of children exceeding 5 µg/dL. ATSDR finds a past potential for elevated BLLs in children who drank water from the tap at these 14 locations. In addition, tap water from these 14 locations indicated a past potential for elevating BLLs in the developing fetuses of pregnant women. The length of time 9 of the 14 locations had elevated lead levels is unclear. At 8 of the 14 locations, tap water sampling data were unavailable before a lead level was elevated. At the Marine Corps Air Station (MCAS) New River location 458 AS 4025, a follow up sample had not been collected as of 21 March 2016.Therefore, ATSDR finds the potential for elevated BLLs in children who drank or who drink MCB Camp Lejeune water.

Camp Lejeune Area Pediatric Blood Lead Levels, 2004-2015

In October 2015, the Navy and Marine Corps Public Health Center (NMCPHC), Environmental and Occupational Health Division, EpiData Center Department reviewed BLL tests ordered at medical treatment facilities in the Camp Lejeune area (Camp Lejeune and Cherry Point) for Department of the

Navy (DON) beneficiary children (NMCPHC 2015). Records were obtained from the Health Level 7 chemistry database through the Composite Health Care System. Records with a test collection date from March 30, 2004 through October 1, 2015 were evaluated by age group (<1 year, ≥1 to <6 years, ≥6 to ≤18 years), and BLL (NMCPHC 2015).

For its evaluation, NMCPHC used the BLL reference value of 10 µg/dL for the years 2004 through 2013 to determine elevated BLLs. For years 2014 through 2015, the current BLL reference value of 5 µg/dL was used to determine elevated BLLs (NMCPHC 2015).

The results of the evaluation found (NMCPHC 2015):

- **March 30, 2014 through December 31, 2013.** Records were analyzed for 3,484 children tested in the Camp Lejeune area, with two children showing BLLs above 10 µg/dL. One of the elevated results was from a child within the ≥1 to <6 years old age range with a BLL of ≥20 µg/dL in 2004. The other elevated result was from a child within the ≥6 to ≤18 years old age range with a BLL in the 10–19 µg/dL range in 2005. The report notes that before 2014, most BLL test results that did not exceed the reference value were reported as <10µg/dL. Therefore, it is unknown how many children would have had elevated lead levels by the current standard (5 µg/dL).
- **January 1, 2014 through October 1, 2015.** Records were analyzed for 870 children tested in the Camp Lejeune area, with three children showing BLLs above 5 µg/dL. One child in 2014 and two children in 2015 showed elevated results. The three children were in the ≥1 to <6 years old age range with BLLs in the 5–9 µg/dL range.

Limitations in the evaluation were noted such as (NMCPHC 2015):

- Although the Pediatric Lead Poisoning Prevention Program states that all Military Treatment Facilities must operate a formal pediatric lead screening program, universal BLL screening is not required. Lead poisoning surveillance is focused on children aged 6 months to 6 years because of their increased susceptibility to high BLLs. Therefore, the number of children with high BLLs may not be a true representation of the BLLs in the Camp Lejeune population because lead testing is based on the discretion of healthcare practitioners.
- The data reviewed for the evaluation do not include records from all sources, like purchased care providers.
- Based on the way the tests are classified in the database, some results may not have been captured in the search terms used to query the data. Some test results were possibly misclassified, though validation steps were included to reduce error.

Although the evaluation has limitations, only a few elevated BLLs[29] in children (i.e., 5 of 4,354 children tested) were found between March 2004 and October 2015. These data may not necessarily be representative of all children in the site area because 1) the BLL program endeavors to test children with the highest risk for elevated blood lead levels and not all children, and 2) the evaluation did not include data from all sources like purchased care providers.

[29] Elevated BLL is based on the reference level in place at the time of testing.

Lead Followup

ATSDR notes that if water sits in pipes for a long period, such as overnight, this water may have higher levels of lead; lead will leach out of the plumbing fixtures and pipes into the water (ATSDR 2007a, 2007d; CDC 2014b). Hot water is more likely to contain lead (CDC 2014b). Drinking water from buildings with copper piping and lead-containing solder could potentially result in exposures to elevated lead levels (ATSDR 2007a, 2007d). ATSDR recommends people use only cold water from the tap for drinking, cooking, and for making baby formula, and that people run the cold water 1–2 minutes before using it. Following these measures will lower the risk for exposure to lead in drinking water.

Since 2013, MCB Camp Lejeune has followed its Environmental Standard Operating Procedure, which requires increased monitoring frequency and an immediate followup sample to be collected following any detection of an inorganic contaminant, including lead (MCB Camp Lejeune 2013). This is a voluntary action undertaken by the base—an action that goes beyond regulatory requirements. In 2014, as its school and daycare sampling strategy, MCB Camp Lejeune began to follow the USEPA 3T guidance[30] (MCB Camp Lejeune 2014). The USEPA 3T guidance provides for identifying potential sources of lead in schools, monitoring schools drinking water for elevated lead levels, resolving problems if elevated lead levels are found, and communicating about the lead control program. Appendix J includes a fact sheet summarizing USEPA's 3T guidance. MCB Camp Lejeune has a Web site that contains information on their priority areas sampling program, which includes daycare facilities and schools (http://www.lejeune.marines.mil/OfficesStaff/EnvironmentalMgmt/LeadinPriorityAreas.aspx). This Web site contains drinking water samples that are collected in accordance with the USEPA 3T guidance. Because ATSDR recognizes that even low levels of lead in blood have been shown to have harmful effects, the agency supports the base's additional efforts.

Yet lead will never disappear from the environment; some residual lead levels will always remain. To reduce lead uptake, parents can feed their children healthy foods because nutrients like calcium and iron reduce lead uptake (see Figure 17, Appendix I). In addition to drinking water, ATSDR notes children might be exposed to other lead sources such as lead-based paint that was used on the base before 1978. ATSDR recommends concerned parents take steps (like wet mopping floors and removing recalled toys and toy jewelry from children) to make their homes more lead-safe (see Figure18, Appendix I).

ATSDR also understands parents with young children might still be concerned about lead exposures. We recommend parents follow the American Academy of Pediatric Guidelines and have their children tested for blood lead at 1 and 2 years of age (AAP 2012

0. ATSDR can address questions about exposure to lead (toll-free 1-800-CDC-INFO). When contacting ATSDR, please say that you are requesting information about the MCB Camp Lejeune site.

Data Limitations for Lead

ATSDR's public health evaluation of lead in drinking water has several limitations, some of which are noted here.

- ATSDR's evaluation is dependent upon identifying how much, how often, and how long a person might come in contact with some concentration of lead in drinking water. ATSDR does not know the exposure duration for the 14 locations where lead exceeded the 15 ppb action level. The length of time 9 of the 14 locations had elevated lead levels is unclear. At 8 of the 14 locations, tap water sampling data were unavailable before the lead level became elevated. At the Marine Corps Air Station (MCAS) New River location 458 AS 4025, a followup sample had not been collected as of 21 March 2016. And each person's exposure may either increase or decrease depending on her or his lifestyle and individual characteristics. As a conservative measure,

[30] USEPA's 3Ts (Training, Testing, and Telling) help schools implement simple strategies for managing the health risks of lead in school drinking water.

ATSDR evaluated exposure to lead by using USEPA's IEUBK model for lead in children, which assumes daily exposure for a year or longer.

- The IEUBK model depends on reliable estimates of site-specific information for several key parameters which include
  - Lead concentration in outdoor soil (fine fraction) and indoor dust,
  - Soil/dust ingestion rate,
  - Individual variability in child blood lead concentrations affecting the geometric standard deviation and,
  - Rate and extent of lead absorption (i.e., bioavailability).
- If reliable site-specific inputs are not available, the model will use conservatively based default parameters. For its drinking water evaluation, ATSDR used default parameters for all inputs except 1) the drinking water level was set to various lead levels for each model run, 2) the soil level was set to 100 parts per million (ppm) and 3) the BLL reference level for risk estimation was set to 5 µg/dL.
- Another limitation of the IEUBK model is that the model was designed to evaluate relatively stable exposure situations rather than rapidly varying exposures or exposures occurring for less than a year. Because MCB Camp Lejeune's buildings contain copper pipes and lead based solder, the amount of lead found in drinking water likely varies—it depends on how long the water sat in the pipes, whether cold water was used, and whether the cold water was run for 1–2 minutes before use.
- The IEUBK model was also not developed to assess lead risks for age groups older than 7 years.

Overall, ATSDR's evaluation contains recognized uncertainties. Nevertheless, this public health assessment provides a framework that puts site-specific exposures and the potential for harm into perspective (ATSDR 2005).

Conclusions

For those exposed to lead-contaminated drinking water at MCB Camp Lejeune, ATSDR reached the following conclusion.

Conclusion

Based on 2005–2013 sampling data, ATSDR concludes that past exposure to lead found in tap water at 14 locations could have harmed people's health. ATSDR also concludes that for current and future exposures the potential remains for elevated lead levels in drinking water throughout the base that could harm people's health because MCB Camp Lejeune's building's water lines contain copper piping and lead-containing solder that may leach lead into the tap water, especially hot water. Drinking lead-contaminated water, along with exposure to lead from other sources such as lead paint, could cause harmful health effects, especially to children and to a pregnant woman's developing fetus. Because ATSDR recognizes that even low levels of lead in blood have been shown to have harmful effects, we support the additional efforts MCB Camp Lejeune began in 2013 to 1) increase monitoring frequency, 2) collect an immediate followup sample whenever lead is detected, and 3) follow the USEPA 3T guidance[31] as the base's school and daycare sampling strategy. These are voluntary actions undertaken by the base that go beyond regulatory requirements.

Conclusion Basis

Although lead can affect almost every organ and system in the body, the main target for lead toxicity is the nervous system. In general, the level of lead in a person's blood gives a good indication of recent exposure to lead and correlates with harmful health effects. ATSDR notes that for some of the more sensitive health effects associated with lead exposure, no clear threshold is available.

The 2005–2013 site-specific lead data show 14 of 382 drinking water samples exceeded USEPA's 15 ppb action level[32] for lead in the past. ATSDR finds there was a past potential for elevated blood lead levels (BLLs) above 5 micrograms per deciliter[33] (µg/dL) in children who drank water from the tap at these 14 locations. In addition, tap water from these 14 locations indicated the potential for elevating BLLs in the developing fetuses of pregnant women in the past. The length of time 9 of the 14 locations had elevated lead levels is unclear. At 8 of the 14 locations, tap water sampling data were unavailable before the lead level became elevated. At the Marine Corps Air Station (MCAS) New River location 458 AS 4025, a followup sample had not been collected as of 21 March 2016.

[31] USEPA's 3Ts (Training, Testing, and Telling) help schools use simple strategies for managing the health risks of lead in school drinking water

[32] USEPA's regulation to control lead in drinking water is known as the Lead and Copper Rule (also referred to as the LCR or 1991 Rule). If lead concentrations exceed an action level of 15 ppb in more than 10% of customer taps sampled, the system 1) must take a number of additional actions to control corrosion, 2) must inform the public about steps they should take to protect their health, and 3) may have to replace lead service lines under their control.

[33] Until 2012, children were identified as having a blood lead level of concern if the test result was 10 µg/dL or more of lead in blood. Experts now use a reference value of 5 µg/dL based on the U.S. population of children 1 to 5 years of age in National Health and Nutrition Examination Survey (NHANES) (ACCLPP 2012; CDC 2012b).

The site-specific lead data show 284 of the 382 drinking water samples (about 75%) did not detect lead at the minimum level of detection (3 ppb). However, MCB Camp Lejeune personnel found buildings with copper pipes and lead-containing solder indicating the potential for lead to leach into base tap water. Therefore, ATSDR finds the potential for elevated BLLs above 5 µg/dL in children who drink base water.

In October 2015, the Navy and Marine Corps Public Health Center (NMCPHC) reviewed BLL tests ordered at medical treatment facilities in the Camp Lejeune area (Camp Lejeune and Cherry Point) for Department of the Navy beneficiary children (NMCPHC 2015). Although the evaluation has limitations, from March 30, 2004 through October 1, 2015, only a few elevated BLLs[34] in children (i.e., 5 of 4,354 children tested) were found. These data may not necessarily be representative of all children in the site area because 1) the BLL program endeavors to test children with the highest risk for elevated blood lead levels and not all children, and 2) the evaluation did not include data from all sources like purchased care providers.

Other indoor and outdoor lead sources (e.g., lead-based paint) might also result in elevated BLLs. Therefore, ATSDR considers that people's (especially children's) daily exposure to drinking water with elevated lead concentrations could have in the past and could currently harm their health.

Next Steps After its review of available information, ATSDR recommends

- People take measures to reduce exposures to lead in drinking water by using cold water for consumption and running the cold water 1–2 minutes before using it for drinking water purposes (CDC 2013d).
- People take steps to reduce lead uptake (see Figure 17, Appendix I).
- People take measures to reduce exposure to lead from other possible sources (see Table 12 and Figure 18, Appendix I).
- Parents follow the American Academy of Pediatric Guidelines and have their children tested for blood lead at 1 and 2 years of age (AAP 2012).
- MCB Camp Lejeune follow its 2013 Environmental Standard Operating Procedure (MCB Camp Lejeune 2013), USEPA's 3T guidance (USEPA 2013b), and USEPA's Lead and Copper Rule (USEPA 2012c).
- MCB Camp Lejeune retest MCAS New River location 458 AS 4025.

[34] Elevated BLL is based on the reference level in place at the time of testing. NMCPHC used a BLL reference value of 10 µg/dL for the years 2004 through 2013 and found two children with elevated BLLs. NMCPHC used the current BLL reference value of 5 µg/dL for the years 2014 through 2015 and found 3 children with elevated BLLs (NMCPHC 2015).

MCB Camp Lejeune Public Health Action Plan

A Public Health Action Plan (PHAP) ensures that this health assessment not only identifies public health hazards, but also provides a plan of action designed to mitigate and prevent adverse human health effects resulting from exposure to hazardous substances in the environment. The PHAP includes undertaken, planned, and recommended public health actions.

Public Health Actions Undertaken

1. In 1985, MCB Camp Lejeune took the most heavily contaminated wells offline.
2. ATSDR conducted historical reconstruction modeling to estimate the past contaminant concentrations in MCB Camp Lejeune's water supplies.
3. Under the Special Notice for Distribution System Samples Rule, MCB Camp Lejeune notifies building occupants whenever an individual sample exceeds an action level. Educational material is included in this notice.
4. MCB Camp Lejeune includes educational materials in its annual water quality report mailings.
5. In 1997, ATSDR completed a public health assessment.
6. ATSDR completed 1) two MCB Camp Lejeune mortality studies, 2) a birth defects and childhood cancer study, 3) a study of adverse birth outcomes such as small for gestational-age and preterm birth, and 4) a male breast cancer study.
7. MCB Camp Lejeune sampled schools and daycare drinking water in 1994 and 2002. Beginning in 2014, they followed the USEPA 3T sampling guidance.
8. In 2013, MCB Camp Lejeune developed a more protective Environmental Standard Operating Procedure, which requires increased monitoring frequency and collection of an immediate followup sample on any detection of an inorganic contaminant, including lead.

Planned Public Health Actions

1. ATSDR is nearing completion of a health survey of active duty personnel stationed at MCB Camp Lejeune anytime between April 1975 and December 1985, and civilian employees who worked at the base anytime between October 1972 and December 1985.
2. ATSDR is evaluating—to the extent possible—any suspected vapor intrusion exposure pathway to determine whether past or current Marine or naval personnel were or are exposed to harmful levels of contaminants in indoor air originating from groundwater or soil contamination.
3. ATSDR is developing a cancer incidence study that will include Marine and naval personnel as well as civilian workers.

Recommended Public Health Actions

1. Ongoing water monitoring efforts help ensure that MCB Camp Lejeune drinking water meets all current federal and state drinking water requirements for contaminants of concern. But historical reconstruction produced modeled concentrations for VC, TCE, and PCE that are of concern. If former residents and workers are concerned about past exposures, they should discuss those concerns with their healthcare providers.
2. By working with ATSDR's Camp Lejeune Community Assistance Panel and U.S. Department of Veterans Affairs, ATSDR will continue to provide health education and followup materials to persons concerned about any increased cancer and noncancer risk. ATSDR will also provide educational materials on the ATSDR Camp Lejeune Web site at http://www.atsdr.cdc.gov/sites/lejeune/index.html.
3. People should take measures to reduce exposures to lead in drinking water, reduce exposure to other sources of lead, and reduce lead uptake (see Table 12 and Figures 17 and 18, Appendix I).

4. Parents should follow the American Academy of Pediatric Guidelines and have their children tested for blood lead at 1 and 2 years of age [AAP 2012].
5. MCB Camp Lejeune should continue following its 2013 Environmental Standard Operating Procedure and EPA's 3T guidance. Information on USEPA's 3T guidance can be found in Appendix J and here: http://water.epa.gov/infrastructure/drinkingwater/schools/guidance.cfm.
6. The MCAS New River location 458 AS 4025 detected lead at 17 ppb in August 2013 and does not appear to have had a followup sample collected. Because subchronic and chronic exposure at that concentration could be pose health risks, MCB Camp Lejeune should resample this location.
7. If elevated lead levels are found in drinking water, we advise MCB Camp Lejeune to take the necessary measures to prevent exposure, such as, but not limited to, replacement of lead containing fixtures or plumbing, acid reduction, or effective educational efforts. Educational outreach might include, but is not limited to, notices to building occupants, lead prevention literature (http://www.cdc.gov/nceh/lead/infographic.htm), and guidance on flushing the lines and using cold water to for prepare food and formula. Recent CDC guidance motivated this recommendation, which guidance states that there is no proven safe level of lead in the blood, and CDC/ATSDR recommends reducing lead exposure wherever possible.
8. Copies of this public health assessment will be provided to local health and public officials, as well as other interested parties in the vicinity of MCB Camp Lejeune. Copies will also be available on ATSDR's Camp Lejeune Web site. http://www.atsdr.cdc.gov/sites/lejeune/

New environmental, toxicological, health outcome data, or the results of putting recommendations and proposed actions in place, might determine the need for additional actions at this site. ATSDR will re-evaluate and expand the PHAP as warranted.

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Appendices

Appendix A. ATSDR's Screening Analysis

Appendix B. Examples of Dose Calculation Results for Specific Concentrations of Chemicals in Water

Appendix C. Dose Equations used in Exposure Analysis

Appendix D. Derivation of ATSDR and USEPA Toxicological Guidelines

Appendix E. Additional Exposure Scenarios

Appendix F. ATSDR Health Studies

Appendix G. Modeled Contaminants of Concern in Drinking Water

Appendix H. EPA's Lead and Copper Rule

Appendix I. Additional Information About Lead

Appendix J. 3Ts for Reducing Lead in School Drinking Water

Appendix K. Peer Reviewer Comments and ATSDR Responses

Appendix A. ATSDR's Screening Analysis

ATSDR gathers information for the exposure evaluation to gain an understanding of the site and community health concerns, the nature and extent of contamination, and exposure pathways, and begins performing the other scientific component of the public health assessment process—the health effects evaluation. The health effects evaluation consists of two pieces: a screening analysis and, at some sites, based on the results of the screening analysis and community health concerns, a more in-depth analysis to determine possible public health implications of site-specific exposures.

Screening Process

In evaluating these data, ATSDR used comparison values (CVs) to determine which chemicals to examine more closely. CVs are health-based contaminant concentrations found in a specific media (air, soil, or water) and are used to screen contaminants for further evaluation. CVs incorporate assumptions of daily exposure to the chemical and a standard amount of air, water, and soil that someone might inhale or ingest each day.

As health-based thresholds, CVs are set at a concentration below which no known or anticipated adverse human health effects are expected to occur. Different CVs are developed for cancer and noncancer health effects. Noncancer levels are based on valid toxicological studies for a chemical, with appropriate uncertainty factors included, and the assumption that small children (22 pounds) and adults are exposed every day. Cancer levels are based on an adult exposed to contaminated soil or drinking contaminated water every day for 78 years. For chemicals for which both cancer and noncancer levels exist, we use the lower level to be protective. Exceeding a CV does not mean that health effects will occur, just that more evaluation is needed.

CVs used in preparing this document are listed below:

- *Environmental Media Evaluation Guides (EMEGs)* are estimated contaminant concentrations in a media where noncarcinogenic health effects are unlikely. EMEGs are derived from the Agency for Toxic Substances and Disease Registry (ATSDR) minimal risk level (MRL).
- *Cancer Risk Evaluation Guides (CREGs)* are estimated contaminant concentrations that would be expected to cause no more than one additional excess cancer in one million persons exposed over a lifetime. CREGs are calculated from U.S. Environmental Protection Agency (EPA) cancer slope factors (CSFs).
- *Reference Media Evaluation Guides (RMEGs)* are estimated contaminant concentrations in a media where noncarcinogenic health effects are unlikely. RMEGs are derived from EPA's reference dose (RfD).
- *Maximum Contaminant Levels (MCLs)* are enforceable standards set by EPA for the highest level of a contaminant allowed in drinking water. MCLs are set as close to MCL goals (MCLGs, the level of a contaminant in drinking water below which there is no known or expected risk to health) as feasible using the best available might be based on different durations of exposure. Acute duration is defined as exposure lasting 14 days or less. Intermediate duration exposure lasts between 15 and 364 days, and chronic exposures last 1 year or more. Comparison values based on chronic exposure studies are used whenever available. If an intermediate or acute comparison value is used, it may be denoted with a small *i* or *a* before the CV (e.g., iEMEG refers to the intermediate duration EMEG).

Determination of Exposure Pathways

ATSDR identifies human exposure pathways by examining environmental and human components that might lead to contact with contaminants of concern. A pathway analysis considers five principal elements: a source of contamination, transport through an environmental medium, a point of exposure, a route of human exposure, and a receptor population. Completed exposure pathways are those for which

the five elements are evident, and indicate that exposure to a contaminant has occurred in the past, is now occurring, or will occur in the future. Potential exposure pathways are those for which exposure seems possible, but one or more of the elements is not clearly defined. Potential pathways indicate that exposure to a contaminant could have occurred in the past, could be occurring now, or could occur in the future. The identification of an exposure pathway does not imply that health effects will occur. Exposures might be, or might not be, substantive. Therefore, even if exposure has occurred, is now occurring, or is likely to occur in the future, human health effects might not result.

ATSDR reviewed site history, information on site activities, the available sampling data, and historical reconstruction data. This review identified household use of drinking water as the main pathway of concern at MCB Camp Lejeune.

Evaluation of Public Health Implications

The next step is to take those contaminants present at levels above the CVs and further identify which chemicals and exposure situations need to be evaluated further to determine if they pose a health hazard. Child and adult exposure doses are calculated for the site-specific exposure scenario, using our assumptions of who goes on the site and how often they contact the site contaminants. The exposure dose is the amount of a contaminant that gets into a person's body. Appendix C contains the equations used to calculate a dose.

Noncancer Health Effects

The calculated exposure doses are then compared with an appropriate health guideline for that chemical. Health guideline values are considered safe doses; that is, health effects are unlikely below this level. The health guideline value is based on valid toxicological studies for a chemical, with appropriate safety factors built in to account for human variation, animal-to-human differences, and/or the use of the lowest study doses that resulted in harmful health effects (rather than the highest dose that did not result in harmful health effects). For noncancer health effects, the following health guideline values are used.

Minimal Risk Level (MRLs)—Developed by ATSDR

An MRL is an estimate of daily human exposure – by a specified route and length of time – to a dose of chemical that is likely to be without a measurable risk of adverse, noncancerous effects. An MRL should not be used as a predictor of adverse health effects. A list of MRLs can be found at http://www.atsdr.cdc.gov/mrls.html.

Reference Dose (RfD)—Developed by EPA

An RfD is the amount of a chemical that one can ingest every day for a lifetime that is not anticipated to cause harmful noncancer health effects. The RfD can be compared with an estimate of exposure in mg/kg-day. RfDs can be found at http://www.epa.gov/iris.

Reference Concentration (RfC)–Developed by U.S. EPA

An RfC is the concentration of a chemical that one can breathe every day for a lifetime that is not anticipated to cause harmful noncancer health effects. The RfC can be compared with an estimate of exposure concentration in mg/m^3. RfCs can be found at http://www.epa.gov/iris.

If the estimated exposure dose for a chemical is less than the health guideline value, then the exposure is unlikely to cause a noncarcinogenic health effect in that specific situation. If the exposure dose for a chemical is greater than the health guideline, then the exposure dose is compared to known toxicologic values for that chemical and is discussed in more detail in the public health assessment (see Discussion section). These toxicologic values are doses derived from human and animal studies that are summarized in the ATSDR *Toxicological Profiles* and EPA's Integrated Risk Information System (IRIS). A direct comparison of site-specific exposure and doses to study-derived exposures and doses that cause adverse health effects is the basis for deciding whether health effects are likely or not.

Cancer Health Effects

The estimated risk of developing cancer resulting from exposure to the contaminants was calculated by multiplying the site-specific child and adult exposure dose by EPA's corresponding Cancer Slope Factor or exposure concentration by the Inhalation Unit Risk (which can be found at http://www.epa.gov/iris). The results estimate the maximum increase in risk of developing cancer after 78 years of exposure to the contaminant. For this site, we assumed 3 years of exposure for the active Marine and civilian population and 15 years for the civilian worker population. Therefore, the maximum increased cancer risk of exposure was multiplied by the factor (3/78 or 15/78) to account for a less-than lifetime exposure.

Because of the uncertainties and conservatism inherent in deriving the CSFs and IURs, this is only an estimate of risk; the true risk is unknown and could be as low as zero (EPA 2003). Although ATSDR recognizes the utility of numerical risk estimates in risk analysis, the agency considers such estimates in the context of the variables and assumptions involved in their derivation and in the broader context of biomedical opinion, host factors, and actual exposure conditions. The actual parameters of environmental exposures must be considered carefully in evaluating the assumptions and variables relating to both toxicity and exposure (ATSDR 1993).

Appendix B. Examples of Dose Calculation Results for Specific Concentrations of Chemicals in Water

Age: 0-3 year; 3-year exposure duration

Chemical	Chemical Concentration (ppb)	Noncancer Dose			Cancer Dose		
		Ingestion Dose (mg/kg-day)	Dermal Dose (mg/kg-day)	Inhalation Concentration (mg/m^3)	Ingestion Dose (mg/kg-day)	Dermal Dose (mg/kg-day)	Inhalation Concentration (mg/m^3)
Benzene	8	7.0E-04	1.0E-04	1.7E-02	2.7E-05	3.9E-06	6.5E-04
trans-1,2-Dichloroethylene	272	2.3E-02	2.7E-03	5.6E-01	8.7E-04	1.0E-04	2.1E-02
Tetrachloroethylene	25	2.1E-03	1.1E-03	5.1E-02	8.0E-05	4.3E-05	2.0E-03
Trichloroethylene	519	4.3E-02	6.5E-03	1.1E+00	1.5E-03	2.3E-04	4.0E-02
Vinyl Chloride	41	3.4E-03	2.6E-04	8.3E-02	3.7E-03	2.0E-04	2.6E-01

Age: 3-6 year old; 3-year exposure duration

Chemical	Chemical Concentration (ppb)	Noncancer Dose			Cancer Dose		
		Ingestion Dose (mg/kg-day)	Dermal Dose (mg/kg-day)	Inhalation Concentration (mg/m^3)	Ingestion Dose (mg/kg-day)	Dermal Dose (mg/kg-day)	Inhalation Concentration (mg/m^3)
Benzene	8	4.5E-04	9.5E-05	1.2E-02	1.7E-05	3.7E-06	4.4E-04
trans-1,2-Dichloroethylene	272	1.5E-02	2.5E-03	3.9E-01	5.6E-04	9.7E-05	1.4E-02
Tetrachloroethylene	25	1.4E-03	1.1E-03	3.6E-02	5.2E-05	4.1E-05	1.3E-03
Trichloroethylene	519	2.8E-02	6.2E-03	7.4E-01	1.1E-03	2.4E-04	2.7E-02
Vinyl Chloride	41	2.2E-03	2.5E-04	5.8E-02	2.4E-03	1.9E-04	6.0E-02

Age: 6-16 year old; 3-year exposure duration

Chemical	Chemical Concentration (ppb)	Noncancer Dose			Cancer Dose		
		Ingestion Dose (mg/kg-day)	Dermal Dose (mg/kg-day)	Inhalation Concentration (mg/m^3)	Ingestion Dose (mg/kg-day)	Dermal Dose (mg/kg-day)	Inhalation Concentration (mg/m^3)
Benzene	8	3.1E-04	5.4E-05	1.1E-02	1.2E-05	2.1E-06	3.9E-04
trans-1,2-Dichloroethylene	272	1.0E-02	1.5E-03	3.4E-01	3.8E-04	5.6E-05	1.3E-02
Tetrachloroethylene	25	9.2E-04	6.4E-04	3.2E-02	3.5E-05	2.5E-05	1.2E-03
Trichloroethylene	519	1.9E-02	3.7E-03	6.5E-01	7.3E-04	1.4E-04	2.4E-02
Vinyl Chloride	41	1.5E-03	1.4E-04	5.2E-02	5.8E-05	4.5E-06	1.9E-03

Age: >16-year old; 3-year exposure duration

Chemical	Chemical Concentration (ppb)	Noncancer Dose			Cancer Dose		
		Ingestion Dose (mg/kg-day)	Dermal Dose (mg/kg-day)	Inhalation Concentration (mg/m^3)	Ingestion Dose (mg/kg-day)	Dermal Dose (mg/kg-day)	Inhalation Concentration (mg/m^3)
Benzene	8	3.1E-04	4.1E-05	5.2E-03	1.2E-05	1.6E-06	1.9E-04
trans-1,2-Dichloroethylene	272	1.0E-02	1.1E-03	1.7E-01	3.9E-04	4.3E-05	6.2E-03
Tetrachloroethylene	25	9.3E-04	4.8E-04	1.5E-02	3.6E-05	1.9E-05	5.7E-04
Trichloroethylene	519	2.9E-02	4.2E-03	4.8E-01	7.4E-04	1.1E-04	1.2E-02
Vinyl Chloride	41	1.5E-03	1.1E-04	2.5E-02	5.8E-05	4.5E-06	9.3E-04

Civilian Adult Worker; 15-year exposure duration

Chemical	Chemical Concentration (ppb)	Noncancer Dose			Cancer Dose		
		Ingestion Dose (mg/kg-day)	Dermal Dose (mg/kg-day)	Inhalation Concentration (mg/m^3)	Ingestion Dose (mg/kg-day)	Dermal Dose (mg/kg-day)	Inhalation Concentration (mg/m^3)
Benzene	8	2.2E-04	2.9E-05	3.6E-03	4.3E-05	5.6E-06	6.8E-04
trans-1,2-Dichloroethylene	272	7.2E-03	7.9E-04	1.2E-01	1.4E-03	1.5E-04	2.2E-02
Tetrachloroethylene	25	6.6E-04	3.5E-04	1.1E-02	1.3E-04	6.7E-05	2.0E-03
Trichloroethylene	519	2.1E-02	3.0E-03	3.3E-01	2.6E-03	3.8E-04	4.2E-02
Vinyl Chloride	41	1.1E-03	7.5E-05	1.7E-02	2.1E-04	1.4E-05	3.3E-03

Marine-in-Training; 3-year exposure duration

Chemical	Chemical Concentration (ppb)	Noncancer Dose			Cancer Dose		
		Ingestion Dose (mg/kg-day)	Dermal Dose (mg/kg-day)	Inhalation Concentration (mg/m^3)	Ingestion Dose (mg/kg-day)	Dermal Dose (mg/kg-day)	Inhalation Concentration (mg/m^3)
Benzene	8	4.4E-04	8.2E-05	2.2E-02	1.7E-05	3.2E-06	8.1E-04
trans-1,2-Dichloroethylene	272	1.4E-02	2.2E-03	7.1E-01	5.4E-04	8.5E-05	2.6E-02
Tetrachloroethylene	25	1.3E-03	9.7E-04	6.5E-02	5.0E-05	3.7E-05	2.4E-03
Trichloroethylene	519	4.1E-02	8.4E-03	2.0E+00	1.0E-03	2.1E-04	5.0E-02
Vinyl Chloride	41	2.1E-03	2.1E-04	1.1E-01	8.2E-05	6.4E-06	3.9E-03

Appendix C. Dose Equations used in Exposure Analysis

Chronic Daily Intake- Noncancer Dose

Ingestion

$$CDI_{ing}(mg/kg-day) = \frac{C_{water}\left(\frac{\mu g}{L}\right) \times \left(\frac{0.001\ mg}{\mu g}\right) \times EF\left(\frac{days}{yr}\right) \times ED(yrs) \times IR\left(\frac{L}{day}\right)}{AT_{resw}\left(\frac{365\ days}{yr} \times ED(yrs)\right) \times BW(kg)}$$

Dermal

$$CDI_{derm}(mg/kg\text{-}day) = \frac{DA_{Event}\left(\frac{\mu g}{cm^2 \times event}\right) \times EV\left(\frac{1\ event}{day}\right) \times ED(yrs) \times EF\left(\frac{days}{yr}\right) \times SA(cm^2)}{AT\left(\frac{365\ days}{yr} \times ED(yrs)\right) \times BW(kg) \times \left(\frac{\mu g}{0.001\ mg}\right)}$$

where:

$$ET\left(\frac{1\ hr}{event}\right) \leq t^*(hr) \text{ then } DA_{event}\left(\frac{\mu g}{cm^2 \times event}\right) = 2 \times FA \times K_P\left(\frac{cm}{hr}\right) \times C_{water}\left(\frac{\mu g}{L}\right) \times \left(\frac{L}{1000\ cm^3}\right) \times \sqrt{\frac{6 \cdot \tau_{event}\left(\frac{hrs}{event}\right) \times ET\left(\frac{1\ hr}{event}\right)}{\pi}}$$

or ,

$$ET\left(\frac{1\ hr}{event}\right) > t^*(hr) \text{ then } DA_{event}\left(\frac{\mu g}{cm^2 \times event}\right) = FA \times K_P\left(\frac{cm}{hr}\right) \times C_{water}\left(\frac{\mu g}{L}\right) \times \left(\frac{L}{1000\ cm^3}\right) \times \left[\frac{ET\left(\frac{1\ hr}{event}\right)}{1+B} + 2 \times \tau_{event}\left(\frac{hrs}{event}\right) \times \left(\frac{1+3B+3B^2}{(1+B)^2}\right)\right]$$

Inhalation

$$CDI_{inh}(mg/m^3) = \frac{C_{water}\left(\frac{\mu g}{L}\right) \times \left(\frac{0.001\ mg}{\mu g}\right) \times k \times F_w \times T_s \times CF \times InR_{min} \times BT \times EF\left(\frac{days}{yr}\right) \times ED(yrs)}{AT\left(\frac{365\ days}{year} \times ED(yrs)\right) \times V_a \times InR_{day}}$$

Chronic Daily Intake- Cancer Dose

Ingestion

$$\mathbf{C}DI_{ing}(mg/kg-day) = \frac{C_{water}\left(\frac{\mu g}{L}\right) \times \left(\frac{0.001mg}{\mu g}\right) \times IR\left(\frac{L}{day}\right) \times EF\left(\frac{days}{year}\right)}{AT\left(\frac{365days}{year} \times LT(yrs)\right) \times BW(kg)}$$

Dermal

$$CDI_{derm}(mg/kg-day) = \frac{DA_{event}\left(\frac{ug}{cm^2-event}\right) \times SA(cm^2)}{AT_{resw}\left(\frac{365days}{year} \times LT(yrs)\right) \times \left(\frac{\mu g}{0.001mg}\right) \times BW(kg)}$$

where:

$$ET\left(\frac{hours}{event}\right) \leq t^*(hr), \text{ then } DA_{event}\left(\frac{ug}{cm^2-event}\right) = 2 \times FA \times K_p\left(\frac{cm}{hr}\right) \times C_{water}\left(\frac{\mu g}{L}\right) \times \left(\frac{L}{1000cm^3}\right) \times \sqrt{\frac{6 \times \tau_{event}\left(\frac{hrs}{event}\right) \times ET\left(\frac{hrs}{event}\right)}{\pi}}$$

or,

$$ET\left(\frac{hrs}{event}\right) > t^*(hr), \text{ then } DA_{event}\left(\frac{ug}{cm^2-event}\right) = FA \times K_p\left(\frac{cm}{hr}\right) \times C_{water}\left(\frac{\mu g}{L}\right) \times \left(\frac{L}{1000cm^3}\right) \times \left[\frac{ET\left(\frac{hrs}{event}\right)}{1+B} + 2 \times \tau_{event}\left(\frac{hrs}{event}\right) \times \left(\frac{1+3B+3B^2}{(1+B)^2}\right)\right]$$

Inhalation

$$CDI_{inh}(mg/m^3) = \frac{C_{water}\left(\frac{\mu g}{L}\right) \times \left(\frac{0.001\ mg}{\mu g}\right) \times k \times F_w \times T_s \times CF \times InR_{min} \times BT \times EF\left(\frac{days}{yr}\right) \times ED(yrs)}{AT\left(\frac{365\ days}{year} \times LT(yrs)\right) \times V_a \times InR_{day}}$$

Chronic Daily Intake- Mutagenic Cancer Dose- TCE

Ingestion

$$\mathrm{CDI_{ing}(mg/kg-day)} = \frac{\mathrm{C_{water}}\left(\frac{\mu g}{L}\right) \times \left(\frac{0.001 mg}{\mu g}\right) \times \mathrm{ED(yr)} \times \mathrm{EF} \quad \left(\frac{days}{yr}\right) \times \mathrm{IR}\left(\frac{L}{day}\right) \times \mathrm{ADAF}}{\mathrm{AT}\left(\frac{365 days}{year} \times \mathrm{LT(yrs)}\right) \times \mathrm{BW(kg)}}$$

Dermal

$$\mathrm{CDI_{derm}}\left(\frac{mg}{kg}-day\right) = \frac{\mathrm{DA_{event}}\left(\frac{ug}{cm^2-event}\right) \times \ \mathrm{SA}\ (cm^2)}{\mathrm{AT_{resw}}\left(\frac{365 days}{year} \times \mathrm{LT(yrs)}\right) \times \left(\frac{\mu g}{0.001 mg}\right) \times \mathrm{BW(kg)}}$$

where:

$$\mathrm{ET}\left(\frac{hrs}{event}\right) \leq t^*(hr), \text{ then } \mathrm{DA_{event}}\left(\frac{ug}{cm^2-event}\right) = 2 \times \mathrm{FA} \times \mathrm{K_p}\left(\frac{cm}{hr}\right) \times \mathrm{C_{g-water}}\left(\frac{\mu g}{L}\right) \times \left(\frac{L}{1000 cm^3}\right) \times \sqrt{\frac{6 \times \tau_{event}\left(\frac{hrs}{event}\right) \times \mathrm{ET}\left(\frac{hrs}{event}\right)}{\pi}}$$

or,

$$\mathrm{ET}\left(\frac{hrs}{event}\right) > t^*(hr), \text{ then } \mathrm{DA_{event}}\left(\frac{ug}{cm^2-event}\right) = \mathrm{FA} \times \mathrm{K_p}\left(\frac{cm}{hr}\right) \times \mathrm{C_{g-water}}\left(\frac{\mu g}{L}\right) \times \left(\frac{L}{1000 cm^3}\right) \times \left[\frac{\mathrm{ET}\left(\frac{hrs}{event}\right)}{1+B} + 2 \times \tau_{event}\left(\frac{hrs}{event}\right) \times \left(\frac{1+3B+3B^2}{(1+B)^2}\right)\right]$$

Inhalation

$$\mathrm{CDI_{inh}(mg/m^3)} = \frac{\mathrm{C_{water}}\left(\frac{\mu g}{L}\right) \times \left(\frac{0.001\ mg}{\mu g}\right) \times k \times F_w \times T_s \times CF \times InR_{min} \times BT \times EF\left(\frac{days}{yr}\right) \times ED(yrs)}{\mathrm{AT}\left(\frac{365\ days}{year} \times LT(yrs)\right) \times V_a \times InR_{day}}$$

Chronic Daily Intake- Cancer Dose-Vinyl Chloride

Ingestion

$$\mathrm{CDI_{ing}(mg/kg-day)} = \mathrm{C_{water}}\left(\frac{\mu g}{L}\right) \times \left(\frac{0.001 mg}{\mu g}\right) \times \left(\left(\frac{\mathrm{IR}\left(\frac{L}{kg}\right)}{\mathrm{AT}\left(\frac{365 days}{yr} \times \mathrm{LT(yrs)}\right)}\right) + \left(\frac{\mathrm{IR}\left(\frac{L}{day}\right)}{\mathrm{BW(kg)}}\right)\right)$$

Dermal

$$\mathrm{CDI_{derm}}\left(\frac{mg}{kg}-day\right) = \left(\frac{\mathrm{DA_{event}}\left(\frac{ug}{cm^2-event}\right) \times \mathrm{EV}\left(\frac{1event}{day}\right) \times \mathrm{ED(yrs)} \times \mathrm{EF}\left(\frac{days}{year}\right) \times \mathrm{SA}(cm^2)}{\mathrm{AT}\left(\frac{365days}{year} \times \mathrm{LT(yrs)}\right) \times \left(\frac{\mu g}{0.001mg}\right) \times \mathrm{BW(kg)}}\right)$$

$$\mathrm{ET}\left(\frac{hrs}{event}\right) \leq t^*(hr), \text{ then } \mathrm{DA_{event}}\left(\frac{ug}{cm^2-event}\right) = 2 \times \mathrm{FA} \times \mathrm{K_p}\left(\frac{cm}{hr}\right) \times \mathrm{C_{water}}\left(\frac{\mu g}{L}\right) \times \left(\frac{L}{1000cm^3}\right) \times \sqrt{\frac{6 \times \tau_{event}\left(\frac{hrs}{event}\right) \times \mathrm{ET}\left(\frac{hrs}{event}\right)}{\pi}}$$

$$\mathrm{ET}\left(\frac{hrs}{event}\right) > t^*(hr), \text{ then } \mathrm{DA_{event}}\left(\frac{ug}{cm^2-event}\right) = \mathrm{FA} \times \mathrm{K_p}\left(\frac{cm}{hr}\right) \times \mathrm{C_{g-water}}\left(\frac{\mu g}{L}\right) \times \left(\frac{L}{1000cm^3}\right) \times \left[\frac{\mathrm{ET}\left(\frac{hrs}{event}\right)}{1+B} + 2 \times \tau_{event}\left(\frac{hrs}{event}\right) \times \left(\frac{1+3B+3B^2}{(1+B)^2}\right)\right]$$

Inhalation

$$\mathrm{CDI_{inh}(mg/m^3)} = \frac{\mathrm{C_{water}}\left(\frac{\mu g}{L}\right) \times \left(\frac{0.001\ mg}{\mu g}\right) \mathrm{x\ k\ x\ F_w\ x\ T_s\ x\ CF\ x\ InR_{min}\ x\ BT}}{\mathrm{V_a\ x\ InR_{day}}} \mathrm{x} \left(1 + \frac{\mathrm{EF}\left(\frac{days}{yr}\right) \times \mathrm{ED(yrs)}}{\mathrm{AT}\left(\frac{365\ days}{year} \times \mathrm{LT(yrs)}\right)}\right)$$

Dose Equation Glossary

Term	Definition
ADAF	Age-dependent adjustment factor (unitless)
AT	Averaging time (days)
B	Dimensionless ratio of the permeability coefficient of a chemical through the stratum corneum relative to its permeability coefficient across the viable epidermis (unitless)
BT	Total time in bathroom (min/day)
BW	Body weight (kg)
CDI_{derm}	Chronic daily dose-dermal (mg/kg-day)
CDI_{ing}	Chronic daily dose-ingestion (mg/kg-day)
CDI_{inh}	Chronic daily dose-inhalation (mg/kg-day)
C_{water}	Chemical concentration in water (ppb)
CF	Conversion factor (1000 L/m^3)
DA_{event}	Absorbed dose per event (mg/cm^2-event)
ED	Exposure duration (days)
EF	Exposure frequency (days/year)
ET	Exposure time (hrs/event)
FA	Fraction absorbed water (dimensionless)
IR	Water ingestion rate (liters per day)
InR_{day}	Inhalation rate-daily (m^3/day)
InR_{min}	Inhalation rate-minute (m^3/min)
K	Constant for chemical volatilization from water to air
K_p	Dermal permeability coefficient of compound in water (cm/hr)
LT	Lifetime (yrs)
SA	Surface area of skin (cm^2)
t*	Time to reach steady-state (hr)
t_{event}	Event duration (hr/event)
τ_{event}	Lag time per event (hr/event)
T_s	Time in shower (min)
V_a	Volume of air for showering scenario

Appendix D. Derivation of ATSDR and USEPA Toxicological Guidelines

TCE toxicity

Noncancer–Review of available human and animal studies shows that exposure to TCE has been associated with toxicity to the central nervous system, kidney, liver, immune system, male reproductive system, and developing fetus. The ATSDR MRL and the U.S. EPA Reference Dose (RfD) estimate the daily chronic exposure of human populations to a chemical unlikely to cause noncancerous health effects. The RfD is based on the determination of the lowest dose associated with the most sensitive physiological endpoint. For TCE, the RfD is based on three studies that found developmental effects on fetal cardiac abnormalities and adverse effects on the immune system function in young and adult animals:

- **Cardiac effects during fetal development**–Johnson et al., (2003) observed increased heart defect rates in newborn rats born to mothers exposed to TCE in drinking water during pregnancy. A Physiologically Based Pharmacokinetic (PBPK) model that compares TCE metabolism of rats and humans was used to derive a 99th percentile human equivalent dose (HED_{99}) of 0.0051 mg/kg/day. PBPK modeling is a mathematical modeling technique that helps predict the movement of chemicals through the body. Thus at an ingested TCE dose of 0.0051 mg/kg/day, a 1% response rate is theoretically expected for fetal heart malformations in humans. An uncertainty factor of 10 (3.16*x* for interspecies extrapolation; 3.16*x* for human variability) was applied to the HED_{99}, resulting in a candidate RfD of 0.00051 mg/kg/day.
- **Immune effects in animals**–A study in female adult mice showed immune system effects (decreased thymus weight) after exposure to TCE in a 30-week drinking water study (Keil et al., 2009). U.S. EPA converted the study findings to obtain a HED_{99} of 0.048 mg/kg/day. An uncertainty factor of 100 (10*x* for use of LOAEL; 3.16*x* for interspecies extrapolation; 3.16*x* for human variability) was applied to the HED_{99}, resulting in a candidate RfD of 0.00048 mg/kg/day
- **Immune effects during fetal development and young animals**–A study in mice exposed to TCE in drinking water during fetal development and during lactation periods showed problems with immune system development (Peden-Adams et al., 2006). U.S. EPA used the lowest study effect level of 0.37 mg/kg/day as a point of departure. An uncertainty factor of 1,000 (10*x* for use of LOAEL; 10*x* for interspecies extrapolation; 10*x* for human variability) was applied to this value, resulting in a candidate RfD of 0.00037 mg/kg/day.

This RfD is supported by the toxic effects of TCE on the kidney, including toxic nephropathy (NTP 1988) and increased kidney weight (Woolhiser et al., 2006). Integrating the appropriate dose from each of these studies and the application of specific uncertainty factors, U.S. EPA derived the following TCE RfD value (USEPA 2011c, 2011d):

USEPA RfD for TCE: **0.0005 mg/kg/day**

The U.S. EPA Reference Concentration (RfC) was also based on the cardiac effects during fetal development in rats (Johnson 2003) and the immune effects in mice (Keil 2009). The evidence of toxic nephropathy (NTP 1988) is also supportive of the RfC based on developmental and immune effects. Using a PBPK model, the oral doses were converted into an inhalation dose. Applying the same uncertainty factors as for the RfD, the RfC for TCE is

USEPA RfC for TCE: **0.002 mg/m^3**.

ATSDR has adopted the U.S. EPA RfD and RfC values for TCE as our Minimum Risk Levels (MRLs) for oral and inhalation exposures. Given the narrow window of susceptibility for the development of the cardiac system, ATSDR applies the RfD and RfC values when considering women exposed to TCE during their first trimester of pregnancy.

Cancer–The National Toxicology Program (NTP) states that TCE is a *known human carcinogen*[35] based on sufficient evidence of carcinogenicity from humans (NTP, 2015). The human studies were epidemiological studies that showed increased rates of kidney cancer, liver cancer, and non-Hodgkin lymphoma, primarily in workers exposed to TCE on the job. The animal studies showed increased numbers of liver, kidney, testicular, and lung tumors by two different routes of exposure (NTP 2011). The International Agency for Research on Cancer (IARC) considers TCE as carcinogenic to humans.[36] USEPA characterizes TCE as carcinogenic to humans by all routes of exposure, based on convincing evidence that trichloroethylene exposure can cause kidney cancer. (USEPA 2011d).

By a weight-of-evidence evaluation, USEPA concluded that TCE is carcinogenic by a mutagenic mode of action for induction of kidney tumors. From the critical study, the adult-based LEC01 (lower 95% bound on exposure at 1% extra risk) is 2.4 mg/m^3. The inhalation unit risk estimate for TCE is calculated from the inhalation unit risk estimate for kidney cancer with a factor of 4 applied to include NHL and liver cancer risks (http://www.epa.gov/iris/subst/0199.htm). Based on this level, the Inhalation Unit Risk value is:

USEPA Inhalation Unit Risk for TCE: **4.1E-06 (µg/m^3)$^{-1}$**

However, because the inhalation unit risk is calculated from data from adult exposure, it does not reflect presumed increased early-life susceptibility to kidney tumors for this chemical. As a result, increased early-life susceptibility is assumed for kidney cancer. Thus when estimating age-specific cancer risks, ATSDR used age-dependent adjustment factors (ADAFs) for the kidney cancer component of the total cancer risk. ADAFs are factors by which cancer risk is multiplied to account for increased susceptibility to chemicals that act by a mutagenic mode of action early in life. Standard ADAFs are 10 (for ages below 2 years), 3 (for ages 2 up to 16 years), and 1 (for ages more than 16) (USEPA 2005).[37] The rationale for the ADAF is that because the rate of cell replication is more rapid in young children compared with adults, children have a greater likelihood of DNA damage resulting from exposure to a chemical that acts by a mutagenic mode of action. Because the Camp Lejeune assessment evaluated specific age groups, that ADAFs were applied using the following formula:

Age-specific Inhalation Unit Risk = [1E-06 (kidney) x ADAF] + 3E-06 (NHL and liver)

	IUR(µg/m^3)$^{-1}$
Ages 0-2:	**1.3E-05**
Ages 2-16:	**6E-06**
Ages >16:	**4E-06**

To evaluate the cancer risk for the oral pathway, USEPA used a PBPK model-based route-to-route extrapolation of the inhalation unit risk estimate for kidney cancer, with a factor of 5 applied to include non-Hodgkin lymphoma and liver cancer risks (USEPA 2011c). Individual cancer slope factors were calculated for specific tissues: for kidney cancer, the oral slope factor is 9.33×10^{-3} (mg/kg/day)$^{-1}$; for non-Hodgkin lymphoma, the slope factor is 2.16×10^{-2} (mg/kg/day)$^{-1}$; and for liver cancer, the slope factor is 1.55×10^{-2} (mg/kg/day)$^{-1}$ (USEPA, 2011c). From these values, this integrated oral slope factor was calculated for combined cancer risk:

USEPA Oral Slope Factor for TCE: **0.046 (mg/kg/day)$^{-1}$**

Because TCE is also considered to be carcinogenic via ingestion route through a mutagenic mode and action, the same ADAF strategy applies to the derivation of age-specific oral cancer slope factors (CSF).

[35] http://ntp.niehs.nih.gov/ntp/roc/monographs/finaltce_508.pdf

[36] http://monographs.iarc.fr/ENG/Monographs/vol106/mono106-001.pdf

[37] http://www.epa.gov/oswer/riskassessment/sghandbook/riskcalcs.htm

Age-specific CSF = [9.33E-03 (Kidney) x ADAF] + 2.16E-02 (NHL) + 1.55E-02 (liver)

	CSF(mg/kg/day)$^{-1}$
Ages 0-2:	**0.13**
Ages 2-16:	**0.065**
Ages >16:	**0.046**

To obtain an increased cancer risk for a given exposure period, the component oral cancer slope factor is multiplied by the daily exposure dose, the appropriate ADAF, and a fraction corresponding to the fraction of the 78-year average lifetime. Table 3 shows the specific assumptions used for the exposure dose calculations.

Get more details about the toxicology of TCE from the ATSDR Toxicological Profile/Addendum for TCE, and the USEPA Integrated Risk Information System (IRIS) file and Toxicological Review, available online at:

http://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=173&tid=30
http://www.epa.gov/iris/subst/0199.htm

PCE toxicity

Noncancer–Available human and animal studies have shown that exposure to PCE has been associated with toxicity to the central nervous system, the kidney, liver, immune and hematologic (blood or circulatory) systems, and to development and reproduction toxicity. Neurotoxic effects have been characterized in human controlled exposure, occupational and residential studies, as well as in experimental animal studies. The studies provide evidence of an association between PCE exposure and neurological deficits. PCE exposure primarily results in visual changes, increased reaction time, and cognitive decrements in humans. Animal studies found effects on vision, visual-spatial function, and reaction time, as well as brain weight changes. An animal study (Chen et al., 2002) showed neurological impacts at a Human Equivalent Dose of 1.8 mg/kg-day, based on PBPK modeling (displayed in Figure 13). Numerous animal studies have reported adverse effects on the kidney in the form of tubular toxicity. Although human studies have not systematically investigated nephrotoxicity, measurement of urinary excretion of renal proteins and end-stage renal disease support an association between PCE exposure via inhalation and chronic kidney disease (USEPA 2012a). A study of dry cleaning workers (Mutti et al., 1992) showed the inhalation dose associated with kidney toxicity was 34 ppm (as derived in USEPA, 2012a). The equivalent ingestion dose from the Mutti, 1992 study was calculated to be 5.4 mg/kg-day (displayed in Figure 13), based on route-to-route extrapolation using PBPK modeling (USEPA, 2012a). Another study of dry cleaners showed hematologic effects (Emara et al., 2010) at an inhalation dose of 43 ppm (as derived in USEPA, 2012a). The equivalent ingestion dose from Emara, 2010 study was calculated to be 6.8 mg/kg-day (displayed in Figure 13), based on route-to-route extrapolation using PBPK modeling (USEPA, 2012a). The developmental and reproductive toxicity database for PCE includes a range of data from appropriate, well-conducted studies in several laboratory animal species plus limited human data. The developmental effects include fetal malformations of bone and soft tissue, delayed ossification, and decreased fetal weight. Reproductive effects include increased incidence of fetal resorptions and preimplantation losses. Evidence of liver toxicity is primarily from several well-conducted rodent studies, including chronic bioassays (ATSDR 2014b; USEPA 2012a).

The USEPA RfC incorporates neurotoxic effects found in studies of workers exposed to PCE vapors (Echeverria et al., 1995; Cavalleri et al., 1994). The LOAEL in these studies was 15–56 mg/m^3. With the application of an uncertainty factor of 1,000 (10*x* for use of LOAEL; 10*x* for human variability; 10*x* for database deficiencies), the resulting RfC is

USEPA RfC for PCE: **0.04 mg/m^3 (0.006 ppm)**

ATSDR has an Inhalation MRL for assessment of both short-term and chronic exposures. It draws on an epidemiological study of drycleaner workers exposed to PCE for an average of 2 years, showing a loss of color vision resulting from PCE exposure (Cavalleri et al., 1994; Gobba et al., 1998). The exposure time-adjusted LOAEL in the study was 1.7 ppm. With the application of an uncertainty factor of 300 (10*x* for use of LOAEL; 10*x* for human variability; 3*x* for database deficiencies), the resulting MRL is

ATSDR Acute, Intermediate, Chronic Inhalation MRL for PCE: **0.04 mg/m^3 (0.006 ppm)**

The USEPA derives its RfD by route-to-route extrapolation from inhalation exposure cited for the RfC (Echeverria et al., 1995; Cavalleri et al., 1994) using Chiu and Ginsberg's (2011) PBPK model. The LOAEL estimated for the oral pathway from these studies was 2.6–9.7 mg/kg-day. With the application of an uncertainty factor of 1,000 (10*x* for use of LOAEL; 10*x* for human variability; 10*x* for database deficiencies), the resulting RfD is:

USEPA RfD for PCE: **0.006 mg/kg-day**.

ATSDR has an Oral MRL for assessment of both short-term and chronic exposures. Its derivation is by route-to-route extrapolation from inhalation exposure in workers cited for the Inhalation MRL, based on loss of color vision. The LOAEL was 2.3 mg/kg-day. With the application of an uncertainty factor of 300 (10*x* for use of LOAEL; 10*x* for human variability; 3*x* for database deficiencies), the resulting MRL is:

ATSDR Acute, Intermediate, Chronic Oral MRL for PCE: **0.008 mg/kg-day**

Cancer–PCE is considered a likely human carcinogen by all routes of exposure (USEPA 2012a). The National Toxicology Program considers PCE a reasonably anticipated human carcinogen (NTP 2011). Regarding cancer, PCE is associated with tumors of liver, kidney, brain, and testes, and in laboratory animal studies, leukemia and hemangiosarcomas (USEPA 2012a). Epidemiologic studies of occupational exposure show an association with several types of cancer, specifically bladder cancer, non-Hodgkin lymphoma, and multiple myeloma. Suggested associations have also been found for esophageal, kidney, lung, cervical, and breast cancer (USEPA 2012a).

In 2012, the International Agency for Research on Cancer (IARC) convened an expert working group that assessed the evidence for PCE and cancers and concluded that PCE was "probably carcinogenic to humans" (Group 2A) (IARC 2014). Subsequent to the assessments of evidence for PCE and cancers by IARC, EPA and NTP, the IARC working group and additional researchers conducted a meta-analysis of studies of dry cleaning workers and PCE workers and bladder cancer (Vlaanderen et al. 2014). The meta-analysis concluded: "Our meta-analysis demonstrates an increased risk of bladder cancer in dry cleaners, reported in both cohort and case-control studies, and some evidence for an exposure-response relationship. Although dry cleaners incur mixed exposures, tetrachloroethylene could be responsible for the excess risk of bladder cancer because it is the primary solvent used and it is the only chemical commonly used by dry cleaners that is currently identified as a potential bladder carcinogen." The researchers noted that the excess risk of bladder cancer did not appear to be confounded by smoking.

The USEPA Inhalation Unit Risk value (IUR) is based on a study of rats exposed to PCE via inhalation, resulting in the induction of hepatocellular adenomas or carcinomas. The IUR for PCE is

USEPA Inhalation Unit Risk for PCE: **2.6E-07 per µg/m^3**

The USEPA Oral Slope Factor is based on the same study cited for the IUR, with an extrapolation to the ingestion pathway using the PBPK model of Chiu and Ginsberg (2011). The Oral Slope Factor for PCE is

USEPA Oral Slope Factor for PCE: **2 × 10^{-3} per mg/kg-day**

Get more details about the toxicology of PCE from the ATSDR Toxicological Profile for PCE and the USEPA IRIS file and Toxicological Review, available online at:

http://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=265&tid=48

http://www.epa.gov/iris/subst/0106.htm

Trans-1,2-DCE Toxicity

Noncancer–The two forms of 1,2-dichloroethene (DCE) are cis-1,2-DCE and trans-1,2-DCE. The trans form of 1,2- DCE was detected in the drinking water supplies at MCB Camp Lejeune. At very high acute oral exposure levels (>1,000 mg/kg/day) trans-1,2-dichloroethene caused serious heart and lung effects. Lower levels (100 mg/kg/day) of longer term exposure are associated with decreased numbers of red blood cells, and effects on the liver and immune system.

The ATSDR Intermediate Oral MRL is based on a NOAEL for altered liver enzyme levels of 17 mg/kg/day. Applying an uncertainty factor of 100 (10*x* for animal to human; 10*x* for sensitive populations), the resulting Oral MRL is

ATSDR Intermediate Oral MRL: **0.2 mg/kg/day**

The USEPA bases its RfD on immune effects in mice, using a Benchmark Dose of 65 mg/kg/day. Applying an uncertainty factor of 3,000 (10*x* for use of LOAEL; 10*x* for interspecies extrapolation; 10*x* for human variability; 3*x* database deficiencies), the Oral RfD is

USEPA RfD: **0.02 mg/kg/day**

The long-term effects of exposure to trans-1,2-DCE have not been well studied in either animals or humans. At high concentrations (>1,000 ppm), inhalation of trans-1,2- DCE has been associated with serious heart toxicity. Lower concentrations (>200 ppm), have resulted in adverse effects on the liver, lungs, and immune system. A 16-week subchronic rat inhalation toxicity study (Freundt et al., 1977) identified lung, liver, and cardiac effects as the critical toxic effects; the study was used as the critical study for the development of a provisional RfC value issued by USEPA in 2002, referred to as a Provisional Peer-Review Toxicity value (PPRTV; http://hhpprtv.ornl.gov/issue_papers/Dichloroethylene12MixedIsomers.pdf). Using a LOAEL (human equivalent) of 189 mg/m^3 and the application of a 3,000 uncertainty factor (10*x* for use of LOAEL; 10*x* for interspecies extrapolation; 10*x* for human variability; 3*x* database deficiencies), the resulting RfC for the mixture of cis and trans isomers of 1,2-DCE is

USEPA Provisional RfC for 1,2 DCE: **0.06 mg/m^3**

Cancer–No animal laboratory studies have been done to determine whether trans-1,2-DCE can cause cancer. And to our knowledge no one has found any evidence indicating that exposure to trans-1,2-DCE can cause cancer in humans. USEPA says there is “inadequate information to assess the carcinogenic potential” of trans-1,2-DCE.

Get more details about trans-1,2-DCE toxicology from the ATSDR Toxicological Profile, the USEPA IRIS file and Toxicological Review, and the USEPA PPRTV document, each of which is available online at:

http://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=464&tid=82

http://www.epa.gov/iris/subst/0314.htm

http://hhpprtv.ornl.gov/issue_papers/Dichloroethylenetrans12.pdf

Vinyl Chloride Toxicity

Noncancer–Animal studies show that extremely high VC levels can damage the liver, lungs, and kidneys. These high levels also can damage the heart and prevent blood clotting. The effects of ingesting VC are unknown. Some people who have breathed very high levels of VC for several years have changes in the structure of their livers. Some people who have worked with VC have nerve damage, and others develop an immune reaction. Animal studies have shown long-term VC exposure can damage the sperm and testes.

Studies using pregnant animals have shown that breathing very high VC levels (5,000 ppm) can harm unborn baby animals. Animal studies have also shown that VC can produce more miscarriages early in

pregnancy and can decrease weight and delay skeletal development in fetuses. These same very high VC levels also caused harmful effects in the pregnant animals. Inhalation studies with animals have suggested that VC might affect growth and development. Animal studies have also suggested that infants and young children might be more susceptible than are adults to VC-induced cancer.

Both the ATSDR Chronic Oral MRL and the USEPA's RfD for VC use a study that demonstrated liver toxicity in animals (Til et al., 1983, 1991). USEPA applied a PBPK model (Clewell et al., 1995a,b) to convert the animal dose into a human equivalent dose when developing the RfD (USEPA 2011c, 2011d). Applying an uncertainty factor of 30 (10*x* for human variability; 3*x* for interspecies extrapolation) resulted in an oral MRL/RfD of

ATSDR Chronic Oral MRL and USEPA RfD for VC: **0.003 mg/kg/day**

ATSDR applied the results of an inhalation study in laboratory animals where liver toxicity was observed in laboratory animals exposed during embryonic development and lactation. Using Benchmark Dose Analysis and adjusting for a continuous exposure, the lowest effect level for a response in 10% of the animals was 2.6 mg/m^3. Applying an uncertainty factor of 30 (10*x* for human variability; 3*x* for interspecies extrapolation) resulted in an inhalation MRL of

ATSDR Chronic Inhalation MRL**: 0.077 mg/m^3**

Cancer–Finding sufficient evidence of carcinogenicity from human studies, **t**he National Toxicology Program declares VC a known human carcinogen (NTP 2011). The USEPA has also characterized VC as a known human carcinogen (USEPA 2000). The strongest evidence that VC causes cancer in humans comes from numerous epidemiological studies and case reports that show its association with cancer of the blood vessels of the liver (hepatic angiosarcoma), a very rare tumor. Several studies have also reported that VC exposure causes cancer at other tissue sites, including the liver (hepatocellular carcinoma), brain, lung, lymphatic system, and hematopoietic system (NTP 2011). Given such evidence for carcinogenicity in human epidemiology studies, USEPA has classified VC as a known human carcinogen. Positive evidence for carcinogenicity in animal bioassays, including several species and strains and strong evidence for genotoxicity, supports this classification (USEPA 2000).

Derivation of a cancer slope factor for VC uses induction of liver angiosarcoma, hepatocellular carcinoma, and neoplastic nodules found in an oral feeding study in rats (Feron et al., 1981).

USEPA Oral Slope Factor: **0.72 $(mg/kg\text{-}day)^{-1}$**

An additional basis for derivation of the inhalation unit risk value is animal research that found liver effects, specifically liver angiosarcomas, angiomas, hepatomas, and neoplastic nodules in inhalation studies in rats (Maltoni et al., 1981, 1984).

USEPA Inhalation Unit Risk: **4.4E-06 ($\mu g/m^3$)**

Animal studies have demonstrated that compared with adult VC exposures, tumor incidence is higher when VC exposure begins at a young age. This apparent increased cancer sensitivity to vinyl chloride for younger persons has led to a separate assessment of cancer risk for the youngest age groups (see excerpt from USEPA 2000; Section 5.3.5.1 in the box below for description and example calculations). The calculation of cancer risk for children exposed from birth through age 6 incorporates a term in the risk equation that, in addition to the term based on exposure duration, is independent of such exposure duration (Appendix C). This incorporation results in a higher level of estimated cancer risk when exposure begins at a very young age.

Get more information about the adverse health effects of VC in humans and animals in the ATSDR toxicological profile for vinyl chloride (ATSDR 2006) and the USEPA IRIS file:

http://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=282&tid=51

http://www.epa.gov/iris/subst/1001.htm

Calculation of less-than-lifetime cancer risk for vinyl chloride exposure for exposures starting at birth; taken from Section 5.3.5.1 of US Environmental Protection Agency. 2000. IRIS toxicological review of vinyl chloride. Washington DC: Office of Research and Development. May 2000. Available at:http://www.epa.gov/iris/toxreviews/1001tr.pdf

In applying these results to partial lifetime exposure, the later-life portion can be apportioned according to a curve that declines with age (Cogliano, 1989, 1990; Cogliano and Parker, 1992; Cogliano et al., 1996; Hiatt et al., 1994). In contrast, early-life exposures would not be prorated over a longer duration. (A simpler approach would be to prorate later-life exposures over the life span, while not prorating early-life exposures.) The following examples illustrate these adjustments.

Example 1. Full lifetime exposure (birth through death) to 1 ug/m^3.
Continuous lifetime exposure during childhood: $8.8 \times 10^{-6} \times (1\ ug/m^3) = 8.8 \times 10^{-6}$
Total risk: 8.8×10^{-6}
Here the total risk is a single unit risk estimate.

Example 2. Exposure to 2 ug/m^3 from ages 30 to 60.
Early-life risk: Not applicable.
Later-life risk: $(4.4 \times 10^{-6}$ per ug/m$^3) \times (2$ ug/m$^3) \times (30/70) = 3.8 \times 10^{-6}$
Total risk: 3.8×10^{-6}

Here exposure begins at age 30, so there is no early-life component. The later-life component is prorated as a duration of 30 years over an assumed life span of 70 years.

Example 3. Exposure to 5 ug/m^3 from ages 0 to 10.
Early-life risk: $(4.4 \times 10^{-6}$ per ug/m$^3) \times (5$ ug/m$^3) = 22 \times 10^{-6}$
Later-life risk: $(4.4 \times 10^{-6}$ per ug/m$^3) \times (5$ ug/m$^3) \times (10/70) = 3.1 \times 10^{-6}$
Total risk: $25 \times 10^{-6} = 2.5 \times 10^{-5}$

In this instance, both "continuous lifetime exposure from birth" and "continuous exposure during adulthood" components of risk would apply. The first component would be the early-life risk, which can be apportioned from the "exposure from birth" minus "exposure during adulthood" components at $8.8 - 4.4 = 4.4 \times 10^{-6}$. A second component of risk would be another apportionment from "exposure during adulthood" for later-life risk. Because the exact age window of susceptibility in humans is not known, but is likely to be much shorter in duration than 10 years, risk outside this window of susceptibility should be considered, but at the level of later-life risk, 4.4×10^{-6}. Furthermore, this risk would have to be apportioned based on the fractional life span of the exposure, i.e., 10/70 years. The total risk would be summed from these two components to be $25 \times 10^{-6} = 2.5 \times 10^{-5}$. It is recognized that the period of susceptibility is accounted for in both of these components. It should be noted, however, that the total risk in this instance is far less than what it would be from continuous lifetime exposure from birth at $(8.8 \times 10^{-6}) \times (5$ ug/m$^3) = 44 \times 10^{-6}$.

In general, the potential for added risk from early-life exposure to VC is accounted for in the quantitative cancer risk estimates by a twofold uncertainty factor. If exposure occurs only during adult life, the twofold factor need not be applied.

Benzene Toxicity

Noncancer–Health concerns about long-term benzene exposure mainly relate to effects on the bone marrow and immune system. Exposure during pregnancy can also result in effects on the developing fetus, resulting in low birth weight, delayed bone formation, and bone marrow damage. Drawing on Lan et al.,'s (2004) work on detection of a diminished immune function found during an epidemiological study of workers exposed to benzene, ATSDR used Benchmark Dose Modeling to identify a benchmark dose lower bound $(BMDL)_{0.25sd}$ of 0.1 ppm. Adjusting for continuous exposure and applying an uncertainty factor of 10 (human variability), the chronic inhalation MRL is

ATSDR Chronic Inhalation MRL**: 9.6E-03 mg/m^3**

Using the same critical study and toxicological endpoint, ATSDR conducted a route-to-route extrapolation from inhalation to oral pathway to derive $BMDL_{0.25sd\ adj}$ of 0.014 mg/kg/day. After applying an uncertainty factor of 30 (10x for human variability; 3x for route-to-route extrapolation), the resulting Chronic Oral MRL is

ATSDR Chronic Oral MRL: **5.0E-04 mg/kg-day**

Cancer–Finding sufficient evidence in human studies, **t**he National Toxicology Program's Report on Carcinogens recognizes benzene as a known human carcinogen (NTP 2011). Both the International Agency for Cancer Research and the USEPA have determined that benzene is carcinogenic to humans. Case reports and case series have reported leukemia—mostly acute myelogenous leukemia, also known as acute myeloid or myelocytic leukemia—in persons exposed to benzene. The strongest epidemiological evidence that benzene causes cancer is from several cohort studies in various industries and geographical locations. These studies found that occupational exposure to benzene increased the risk of mortality from leukemia (mainly acute myelogenous leukemia) (NTP 2011). USEPA found convincing human evidence as well as supporting evidence from animal studies to classify benzene as a known human carcinogen for all exposure routes (USEPA 1998).

USEPA relied on results from several epidemiological studies of workers exposed to benzene through inhalation, where an increase in the incidence of leukemia was detected. Using a linear multi-stage cancer model, the inhalation unit risk is

USEPA Inhalation Unit Risk: **7.8E-06 (µg/m^3)$^{-1}$**

Using the same critical study and endpoint, USEPA conducted a route-to-route extrapolation from inhalation to oral dose. A linear multi-stage cancer model produced an oral slope factor of

USEPA Oral Slope Factor: **0.055 (mg/kg-day)$^{-1}$**

Note that the USEPA IRIS file provides estimates of a range of oral slope factors and inhalation-unit risk values for benzene. To ensure the most conservative cancer risk estimate in this public health assessment, ATSDR selected the highest risk factor.

Get more information about the adverse health effects of benzene in humans and animals in the ATSDR toxicological profile for benzene and the USEPA IRIS file, each of which is available online at:

http://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=40&tid=14

http://www.epa.gov/iris/subst/0276.htm

Summary Tables from ATSDR Interaction Profiles for Chemical Mixtures (ATSDR 2004)
(note that all citations refer to the Interaction Profile document, not to this PHA)

Effect of Trichloroethylene on Tetrachloroethylene

BINWOE: =IIC (for nervous system effects)

BINWOE: =IIB (for cancer and noncancer liver or kidney effects)

Direction of Interaction - The parent chemicals and trichloroethanol (a metabolite of trichloroethylene) may additively act to produce nervous system effects, but studies designed to test this hypothesis were not located. It is plausible that trichloroethylene may have little influence on tetrachloroethylene metabolism, and that tetrachloroethylene and trichloroethylene metabolites would additively act to produce liver and kidney effects.

Mechanistic Understanding - Like other solvents, the parent chemicals (and the trichloroethylene metabolite, trichloroethanol) depress nervous system functions by reversibly acting on neuronal membranes and sensitize the heart to epinephrine-induced arrhythmias (see Appendices C and D; ATSDR 1997a, 1997b).

Liver or kidney effects in rodents exposed to high levels of tetrachloroethylene are believed to involve reactive metabolic intermediates (see Appendices C and D). Tetrachloroethylene is not a potent liver or kidney toxicant because it is poorly metabolized (Monster et al., 1979; Pegg et al., 1979). Any influence that trichloroethylene may have on tetrachloroethylene metabolism should have little influence on tetrachloroethylene toxicity due to detoxification from downstream metabolism and/or repair of damaged cellular macromolecules. Results from a rat and mouse study suggest that trichloroethylene and tetrachloroethylene act in a less-than-additive manner to cause hepatic and renal peroxisomal proliferation (Goldsworthy and Popp 1987; see Section 2.2.7). This observation may be explained by non-competitive inhibition of CYP isozymes leading to slower rates of trichloroacetic acid formation from trichloroethylene. Other rat studies (see Section 2.2.7) show that the chemicals act additively to increase kidney weight (Jonker et al., 1996), and mixtures of subthreshold doses can produce increased serum ALT (Stacey 1989). The latter observation could be consistent with additive joint action on the liver, but the study design could not definitively rule out greater-than-additive or less-than-additive joint action (Stacey 1989).

Mechanistic understanding was assigned a moderate quality factor (II) to reflect lack of data regarding joint actions on the nervous system, and uncertainties regarding joint actions on the liver and kidney.

Toxicological Significance - Studies designed to examine the joint toxic action of these chemicals on nervous system endpoints were not located. Thus, the lowest possible toxicologic significance data quality factor, C, was assigned for nervous system effects. For liver and kidney effects, a moderate data quality factor, B, was assigned because there are studies on the joint toxic action of these chemicals on liver and kidney endpoints in rats, but results are inconsistent across endpoints (see above and Section 2.2.7).

Additional Uncertainties - Competitive metabolic interactions at CYP catalytic sites are possible, especially at high exposure levels when sites are saturated. CYP induction by ethanol, phenobarbital, or Aroclor 1254 has not produced consistent potentiation of acute high-level tetrachloroethylene hepatotoxicity (Cornish and Adefuin 1966; Cornish et al., 1973; Klaassen and Plaa 1966; Moslen et al., 1977). Any influence that trichloroethylene may have on tetrachloroethylene metabolism (enhancement or inhibition) should have little influence on toxicity, because tetrachloroethylene is poorly metabolized.

Effect of Tetrachloroethylene on Trichloroethylene

BINWOE: =IIC (for nervous system effects)

BINWOE: <IIB (-1 x 0.71 x 0.71= -0.50) **(for cancer and noncancer liver or kidney effects)**

Direction of Interaction - It is plausible that the parent chemicals and trichloroethanol may jointly act in an additive manner to interact with nervous system membranes. There is evidence that tetrachloroethylene inhibits the metabolism of trichloroethylene in humans (Seiji et al., 1989) and evidence of less than-additive joint action on hepatic and renal peroxisomal proliferation in rats and mice (Goldsworthy and Popp 1987). It is plausible that the interaction may antagonize liver and kidney effects from trichloroethylene metabolites.

Mechanistic Understanding -Like other solvents, the parent chemicals (and the trichloroethylene metabolite, trichloroethanol) depress nervous system functions by reversibly acting on neuronal membranes and sensitize the heart to epinephrine-induced arrhythmias (see Appendices C and D; ATSDR 1997a, 1997b). Mechanistic understanding was assigned a moderate quality factor (II) to reflect the lack of direct data on the joint action of these chemicals on the nervous system.

Liver or kidney effects in rodents exposed to high levels of these chemicals are believed to involve reactive metabolic intermediates (see Appendices C and D). Studies of urinary metabolites in workers exposed to trichloroethylene alone, tetrachloroethylene alone, or mixtures of trichloroethylene and tetrachloroethylene indicate that tetrachloroethylene inhibits the metabolism of trichloroethylene at low exposure levels (<20 ppm) (Seiji et al., 1989). Results from a rat and mouse study suggest that trichloroethylene and tetrachloroethylene act in a less-than-additive manner to cause hepatic and renal peroxisomal proliferation (Goldsworthy and Popp 1987). This observation may be explained by noncompetitive inhibition of CYP isozymes leading to slower rates of trichloroacetic acid formation. Other rat studies show that the chemicals act additively to increase kidney weight (Jonker et al., 1996), and mixtures of subthreshold doses can produce increased serum ALT in rats (Stacey 1989; see Section 2.2.7). A moderate quality factor (II) was selected to reflect ambiguities (i.e., inconsistency of the database) regarding the projection of less-than-additive joint action on the liver and kidney.

Toxicological Significance - Studies designed to examine the joint toxic action of these chemicals on nervous system endpoints were not located. Thus, the lowest possible toxicologic significance data quality factor, C, was applied for nervous system effects. For liver and kidney effects, a moderate data quality factor, B, was selected. Evidence exists for tetrachloroethylene inhibition of trichloroethylene metabolism in humans (Seiji et al., 1989), but evidence for less-than-additive joint action on liver and kidney endpoints in rats is inconsistent across endpoints (see above and Section 2.2.7).

Additional Uncertainties - Data for humans exposed to low levels of these chemicals indicate that tetrachloroethylene inhibits trichloroethylene metabolism (Seiji et al., 1989). PBPK simulations of trichloroethylene and vinyl chloride indicate that competitive metabolic interactions between halogenated hydrocarbons only occur at high concentrations (Barton et al., 1995). Thus, tetrachloroethylene may inhibit trichloroethylene metabolism by a non-competitive mechanism. The design of the study observing joint action to increase serum ALT in rats (Stacey 1989) could not discern additive from greater-than-additive or less-than-additive joint action.

Effect of Trichloroethylene on Vinyl Chloride

BINWOE: <IB for hepatic effects

BINWOE: <IB for renal effects

BINWOE: <IB for immunological effects

BINWOE: <IB for developmental effects

BINWOE: <IB for carcinogenic effects

Direction of Interaction – Because both trichloroethylene and vinyl chloride are metabolized to reactive metabolites by the same enzyme, once metabolism is saturated, the effects of each will be lessened because of a limitation on the rate of production of new metabolites. A less-than-additive interaction at the level of metabolism has been verified in high-dose animal studies. This would be expected to result in less-than-additive toxicity at high doses of trichloroethylene and vinyl chloride.

Mechanistic Understanding – Many of the effects of vinyl chloride are believed to be the result of metabolism by CYP2E1 to a reactive metabolite, which then can bind to tissue molecules to produce cellular damage (Appendix D). Trichloroethylene is also metabolized primarily by CYP2E1 to form reactive products (Appendix C), so competition for the active enzyme at high doses is possible. A five-compartment joint rat PBPK model for vinyl chloride and trichloroethylene has been developed (Barton et al., 1995) and compared with high-dose inhalation data. A comparison of model simulations with experimental co-exposure data indicated that a competitive model of metabolism, where the two chemicals are assumed to independently compete for the active site of the enzyme, best fit the available metabolic data. It was also noted that at concentrations below 30 ppm, there was no noticeable effect of either compound on the uptake or metabolism of the other. Because a direct demonstration of the mechanism by which the interactions could occur exists, a rating of "I" for mechanistic understanding was assigned.

Toxicological Significance – Relevant interaction data on pertinent health effects following simultaneous exposure were not located. No studies were located in which pretreatment with trichloroethylene before vinyl chloride exposure was examined. Because the toxicological significance of the metabolic interaction can be inferred, and has been demonstrated for related binary mixtures (chloroform and trichloroethylene, 1,1-dichloroethylene and trichloroethylene), a rating of "B" was assigned.

Additional Uncertainties – Uncertainties have been addressed in the above discussion.

Effect of Vinyl Chloride on Trichloroethylene

BINWOE: <IB for hepatic effects

BINWOE: <IB for renal effects

BINWOE: <IB for immunological effects

BINWOE: uncertain for neurological effects

BINWOE: <IB for developmental effects

BINWOE: <IB for carcinogenic effects

Direction of Interaction – Because both vinyl chloride and trichloroethylene are metabolized to reactive metabolites by the same enzyme, once metabolism is saturated, the effects of each are anticipated to be lessened because of a limitation on the rate of production of new metabolites. A less-than-additive interaction at the level of metabolism has been verified in high-dose animal studies. This would be expected to result in less-than-additive toxicity at high doses of trichloroethylene and vinyl chloride. Because the neurological effects of trichloroethylene may be caused by both the parent compound and the metabolite trichloroethanol, the possible effects of vinyl chloride on trichloroethylene-induced neurological effects cannot be determined.

Mechanistic Understanding – Many of the effects of trichloroethylene are believed to be the result of metabolism by CYP2E1 to a reactive metabolite, which then can bind to tissue molecules to produce cellular damage (Appendix C). Vinyl chloride is also metabolized primarily by CYP2E1 to form reactive products (Appendix D), so competition for the active enzyme at high doses is possible. A five-compartment joint rat PBPK model for vinyl chloride and trichloroethylene has been developed (Barton et al., 1995) and compared with high-dose inhalation data. A comparison of model simulations with experimental co-exposure data indicated that a competitive model of metabolism, where the two chemicals are assumed to independently compete for the active site of the enzyme, best fit the available metabolic data. It was also noted that at concentrations below 30 ppm, there was no noticeable effect of either compound on the uptake or metabolism of the other. Because a direct demonstration of the mechanism by which the interactions could occur exists, a rating of "I" for mechanistic understanding was assigned. Because the neurological effects of trichloroethylene may be caused by both the parent compound and to the metabolite trichloroethanol (Appendix C), how competitive interaction for CYP2E1 would affect this endpoint is unknown.

Toxicological Significance – Relevant interaction data on pertinent health effects following simultaneous exposure were not located. No studies were located in which pretreatment with vinyl chloride before trichloroethylene exposure was examined. Because the toxicological significance of the metabolic interaction can be inferred, and has been demonstrated for related binary mixtures (chloroform and trichloroethylene, 1,1-dichloroethylene and trichloroethylene), a rating of "B" was assigned.

Additional Uncertainties – Uncertainties have been addressed in the above discussion

Table D-1: Specific Target-organ Toxicity Doses (TTD) for Ingestion

D-1a: Calculation of Target-organ Toxicity Dose (TTD) for Renal Effects-Ingestion

	HED-NOAEL (mg/kg-day)	HED-LOAEL (mg/kg-day)	UF	MRL (mg/kg-day)	TTD_{renal} (mg/kg-day)	Effect
Benzene	15		100		0.15	
Dichloroethylene, 1,2-trans-						
Tetrachloroethylene	3.9	400	100		0.04	increased kidney weight
Trichloroethylene	14	250	100		0.14	increased urinary protein
Vinyl Chloride						

D-1b: Calculation of Target-organ Toxicity Dose (TTD) for Liver Effects-Ingestion

	HED-NOAEL (mg/kg-day)	HED-LOAEL (mg/kg-day)	UF	MRL (mg/kg-day)	TTD_{liver} (mg/kg-day)	Effect
Benzene	15		100		0.15	
Dichloroethylene, 1,2-trans-	2.6		100		0.026	increased liver enzymes
Tetrachloroethylene	3	100	100		0.03	increased liver weight
Trichloroethylene	316	400	100		3.2	enlarged hepatocytes
Vinyl Chloride	0.05	1.7	30		0.0016	liver cell polymorphism

D-1c: Calculation of Target-organ Toxicity Dose (TTD) for Lymphatic System Effects-Ingestion

	HED-NOAEL (mg/kg-day)	HED-LOAEL (mg/kg-day)	BMD	UF	MRL (mg/kg-day)	TTD_{lymph} (mg/kg-day)	Effect
Benzene		3.8		1000		0.0038	lymphocytopenia
Dichloroethylene, 1,2-trans-			65	3000	0.02		increased WBC, decreased thymic weight
Tetrachloroethylene							
Trichloroethylene					4.30E-04		altered immune response
Vinyl Chloride							

D-1d: Calculation of Target-organ Toxicity Dose (TTD) for Hematopoietic Effects-Ingestion

	HED-NOAEL (mg/kg-day)	HED-LOAEL (mg/kg-day)	BMD	UF	MRL (mg/kg-day)	$TTD_{hematto}$ (mg/kg-day)	Effect
Benzene			0.014	30	0.0005		decreased white blood cell count
Dichloroethylene, 1,2-trans-		134		1000		0.13	decreased white blood cell count, hemoglobin, and hematocrit
Tetrachloroethylene	392	3000		100		3.92	Decreased hemoglobin, hematocrit, red blood cell, platelet
Trichloroethylene	71	660		100		0.7	decreased red blood cell count
Vinyl Chloride	1.6	17		100		0.016	decreased clotting time

D-1e: Calculation of Target-organ Toxicity Dose (TTD) for Neurological Effects-Ingestion

	HED-NOAEL (mg/kg-day)	HED-LOAEL (mg/kg-day)	UF	MRL (mg/kg-day)	TTD_{neuro} (mg/kg-day)	Effect
Benzene	15		100		0.15	
Dichloroethylene, 1,2-trans-	336	784	100		3.36	ataxia-acute
Tetrachloroethylene		6.2	1000	0.006		Loss of color vision
Trichloroethylene		1000	1000		1	decreased dopaminergic neurons
Vinyl Chloride						

D-1f: Calculation of Target-organ Toxicity Dose (TTD) for Developmental Effects-Ingestion

	HED-NOAEL (mg/kg-day)	HED-LOAEL (mg/kg-day)	UF	MRL (mg/kg-day)	TTD_{devel} (mg/kg-day)	Effect
Benzene						
Dichloroethylene, 1,2-trans-						
Tetrachloroethylene						
Trichloroethylene		0.005	10	5E-04		cardiac abnormalities
Vinyl Chloride						

Table D-2: Target-organ Toxicity Doses for Inhalation

D-2a: Calculation of Target-organ Toxicity Dose (TTD) for Renal Effects-Inhalation

	HEC-NOAEL (µg/m^3)	HEC-LOAEL (µg/m^3)	UF	MRL (µg/m^3)	TTD_{renal} (µg/m^3)	Effect
Benzene	227,860		100		2,279	
Dichloroethylene, 1,2-trans-	189,048		100		1,890	
Tetrachloroethylene		24,214	100		242	nephrotoxicity
Trichloroethylene		47,307	100		473	increased kidney weight
Vinyl Chloride	5,486		100		55	increased kidney weightt

D-2b: Calculation of Target-organ Toxicity Dose (TTD) for Liver Effects-Inhalation

	HEC-NOAEL (µg/m^3)	HEC-LOAEL (µg/m^3)	UF	MRL (µg/m^3)	TTD_{liver} (µg/m^3)	Effect
Benzene	170,890		100		1,709	
Dichloroethylene, 1,2-trans-		189,050	1,000	189		increased liver enzymes
Tetrachloroethylene		61,020	1,000		61	increased liver weight
Trichloroethylene	47,310		100		473	increased cholinesterase activity
Vinyl Chloride		3,200	30	107		liver hypertrophy

D-2c: Calculation of Target-organ Toxicity Dose (TTD) for Lymphatic System Effects-Inhalation

	HEC-NOAEL (µg/m^3)	HEC-LOAEL (µg/m^3)	BMD	UF	MRL (µg/m^3)	TTD_{lymph} (µg/m^3)	Effect
Benzene			96	10	9.6		lymphocytopenia
Dichloroethylene, 1,2-trans-		189,050		1,000		189	Increased white blood cells, decreased thymic weight
Tetrachloroethylene							
Trichloroethylene		20		10	2		increased autoantibodies
Vinyl Chloride		4,571		1,000		4.6	increased lymphocyte proliferation

D-2d: Calculation of Target-organ Toxicity Dose (TTD) for Hematopoietic Effects-Inhalation

	HEC-NOAEL ($\mu g/m^3$)	HEC-LOAEL ($\mu g/m^3$)	BMD	UF	MRL ($\mu g/m^3$)	$TTD_{hematо}$ ($\mu g/m^3$)	Effect
Benzene		433		100		4.3	Decreased white blood cell and platelet count
Dichloroethylene, 1,2-trans-							
Tetrachloroethylene	32,290			10		3,229	
Trichloroethylene							
Vinyl Chloride		1.2e07		1,000		12,190	Decreased white blood cells

D-2e: Calculation of Target-organ Toxicity Dose (TTD) for Neurological Effects-Inhalation

	HEC-NOAEL ($\mu g/m^3$)	HEC-LOAEL ($\mu g/m^3$)	UF	MRL ($\mu g/m^3$)	TTD_{neuro} ($\mu g/m^3$)	Effect
Benzene						
Dichloroethylene, 1,2-trans-						
Tetrachloroethylene		11,530	300	40		Loss of color vision
Trichloroethylene		63,930	1,000		64	Decreased wakefulness
Vinyl Chloride						

D-2f: Calculation of Target-organ Toxicity Dose (TTD) for Developmental Effects-Inhalation

	HEC-NOAEL ($\mu g/m^3$)	HEC-LOAEL ($\mu g/m^3$)	UF	MRL ($\mu g/m^3$)	TTD_{devel} ($\mu g/m^3$)	Effect
Benzene						
Dichloroethylene, 1,2-trans-						
Tetrachloroethylene		1.7E+06	1,000		1,700	Decreased fetal weight, skeletal abnormalities
Trichloroethylene		20	10	2		Autoantibodies
Vinyl Chloride		37,330	30		1,244	Delayed ossification

Table D-3: Hadnot Point- Child (0-3 yrs old); Hazard Quotients for Specific Target Organs- Ingestion Pathway- Upper End Exposure Level

0-3 yrs old	Max 3 yr Total Dose (mg/kg/day)	Renal		Liver		Immune		Hematologic		Neurologic		Developmental	
		RfD or TTD (mg/kg/day)	HQ	RfD or TTD (mg/kg/day)	HQ	RfD or TTD (mg/kg/day)	HQ	RfD or TTD (mg/kg/day)	HQ	RfD or TTD (mg/kg/day)	HQ	RfD or TTD (mg/kg/day)	HQ
Benzene	8.8E-04	0.15	5.9E-03	0.15	5.9E-03	3.8E-03	0.2	4.7E-04	1.9	0.2	5.9E-03		
Dichloroethylene, 1,2-trans-	2.8E-02			0.026	1.1	2.2E-02	1.3	0.1	0.2	3.4	8.3E-03		
Tetrachloroethylene	3.6E-03	0.04	9.1E-02	0.03	0.12			3.9	9.1E-04	6.2E-03	0.6		
Trichloroethylene	5.5E-02	0.14	3.9E-01	3.2	1.7E-02	4.8E-04	115	0.7	0.08	1	5.5E-02	4.8E-4	115
Vinyl Chloride	4.1E-03			1.6E-03	2.6			1.6E-02	0.26				
	Hazard Index		0.5		3.8		116		2.4		0.7		115

Table D-4: Hadnot Point- Marine-in-training; Hazard Quotients for Specific Target Organs- Ingestion Pathway- Upper End Exposure Level

Marine-in-training	Max 3 yr Total Dose (mg/kg/day)	Renal		Liver		Immune		Hematologic		Neurologic		Developmental	
		RfD or TTD (mg/kg/day)	HQ	RfD or TTD (mg/kg/day)	HQ	RfD or TTD (mg/kg/day)	HQ	RfD or TTD (mg/kg/day)	HQ	RfD or TTD (mg/kg/day)	HQ	RfD or TTD (mg/kg/day)	HQ
Benzene	5.2E-04	0.15	3.5E-03	0.15	3.5E-03	3.8E-03	0.1	4.7E-04	1.1	0.2	3.5E-03		
Dichloroethylene, 1,2-trans-	1.6E-02			0.026	0.6	2.2E-02	0.8	0.1	0.1	3.4	4.9E-03		
Tetrachloroethylene	2.3E-03	0.04	5.8E-02	0.03	7.6E-02			3.9	5.8E-04	6.2E-03	0.4		
Trichloroethylene	4.9E-02	0.14	0.4	3.2	1.6E-02	4.8E-04	102	0.7	6.9E-02	1	4.9E-02	5.0E-04	98
Vinyl Chloride	2.3E-03			1.6E-03	1.5			1.6E-02	0.1				
	Hazard Index		0.4		2.2		103		1.5		0.4		98

Table D-5: Hadnot Point- Child (0-3 yrs old); Hazard Quotients for Specific Target Organs- Inhalation Pathway- Upper End Exposure Level

0-3 yrs old	Max 3 yr Inhalation Conc. (µg/m³)	Renal		Liver		Immune		Hematologic		Neurologic		Developmental	
		RfC or TTD (µg/m³)	HQ	RfC or TTD (µg/m³)	HQ	RfC or TTD (µg/m³)	HQ	RfC or TTD (µg/m³)	HQ	RfC or TTD (µg/m³)	HQ	RfC or TTD (µg/m³)	HQ
Benzene	17	2,279	7.5E-03	1,709	9.9E-03	10	1.8	4	3.9				
Dichloroethylene, 1,2-trans-	563	1,890	0.3	189	3.0	189	3.0						
Tetrachloroethylene	51	242	0.2	61	0.8			3,229	1.6E-02	40	1.3		
Trichloroethylene	1,054	473	2.2	473	2.2	2	531			64	16.5	2	595
Vinyl Chloride	83	55	1.5	107	0.8	5	18.1	12,190	6.8E-03				
	Hazard Index		4.3		6.8		554		3.9		17.8		595

Table D-6: Hadnot Point- Marine-in-training; Hazard Quotients for Specific Target Organs- Inhalation Pathway- Upper End Exposure Level

Marine-in-training	Max 3 yr Total Dose (µg/m³)	Renal		Liver		Immune		Hematologic		Neurologic		Developmental	
		RfC or TTD (µg/m³)	HQ	RfC or TTD (µg/m³)	HQ	RfC or TTD (µg/m³)	HQ	RfC or TTD (µg/m³)	HQ	RfC or TTD (µg/m³)	HQ	RfC or TTD (µg/m³)	HQ
Benzene	22	2,279	9.6E-03	1,709	1.3E-02	10	2.3	4	5.1				
Dichloroethylene, 1,2-trans-	709	1,890	0.4	189	3.8	189	3.8						
Tetrachloroethylene	65	242	0.3	61	1.1			3,229	2.0E-02	40	1.6	1,700	0.04
Trichloroethylene	2,039	473	4.3	473	4.3	2	1,151			64	31.9	1.9	1,085
Vinyl Chloride	107	55	1.9	107	1.0	5	23.4	12,190	8.8E-03			1,244	8.6E-02
	Hazard Index		6.9		10.1		1,180		5.1		33.5		1,085

Table D-7: Tarawa Terrace- Child (0-3 yrs old); Hazard Quotients for Specific Target Organs- Ingestion Pathway- Upper End Exposure Level

0-3 yrs old	Max 3 yr Total Dose (mg/kg/day)	Renal		Liver		Immune		Hematologic		Neurologic		Developmental	
		RfD or TTD (mg/kg/day)	HQ	RfD or TTD (mg/kg/day)	HQ	RfD or TTD (mg/kg/day)	HQ	RfD or TTD (mg/kg/day)	HQ	RfD or TTD (mg/kg/day)	HQ	RfD or TTD (mg/kg/day)	HQ
Dichloroethylene, 1,2-trans-	1.2E-03			0.026	4.6E-02	2.2E-02	5.4E-02	0.1	8.7E-03	3.4	3.5E-04		
Tetrachloroethylene	1.1E-02	0.04	0.3	0.03	0.4			3.9	2.9E-03	6.2E-03	1.8		
Trichloroethylene	3.7E-04	0.14	2.6E-03	3.2	1.2E-04	4.8E-04	0.9	0.7	5.2E-04	1	3.7E-04	4.8E-04	0.9
Vinyl Chloride	6.2E-04			1.6E-03	0.4			1.6E-02	3.9E-02				
	Hazard Index		0.3		0.8		0.9		5.2E-02		1.8		0.9

Table D-8: Tarawa Terrace- Marine-in-training; Hazard Quotients for Specific Target Organs- Ingestion Pathway- Upper End Exposure Level

Marine-in-training	Max 3 yr Total Dose (mg/kg/day)	Renal		Liver		Immune		Hematologic		Neurologic		Developmental	
		RfD or TTD (mg/kg/day)	HQ	RfD or TTD (mg/kg/day)	HQ	RfD or TTD (mg/kg/day)	HQ	RfD or TTD (mg/kg/day)	HQ	RfD or TTD (mg/kg/day)	HQ	RfD or TTD (mg/kg/day)	HQ
Dichloroethylene, 1,2-trans-	8.30E-04			0.026	3.3E-02	2.2E-02	3.8E-02	0.1	6.2E-03	3.4	2E-04		
Tetrachloroethylene	9.40E-03	0.04	0.24	0.03	0.3			3.9	2.4E-03	6.2E-03	1.5		
Trichloroethylene	4.14E-04	0.14	3.0E-03	3.2	1E-04	4.8E-04	0.9	0.7	5.9E-04	1	4E-04	5.1E-04	0.8
Vinyl Chloride	4.34E-04			1.6E-03	0.3			1.6E-02	2.8E-02				
	Hazard Index		0.2		0.6		0.9		3.7E-02		1.5		0.8

Table D-9: Tarawa Terrace- Child (0-3 yrs old); Hazard Quotients for Specific Target Organs- Inhalation Pathway- Upper End Exposure Level

0-3 yrs old	Max 3 yr Inhalation Conc (µg/m³)	Renal		Liver		Immune		Hematologic		Neurologic		Developmental	
		RfC or TTD (µg/m³)	HQ	RfC or TTD (µg/m³)	HQ	RfC or TTD (µg/m³)	HQ	RfC or TTD (µg/m³)	HQ	RfC or TTD (µg/m³)	HQ	RfC or TTD (µg/m³)	HQ
Dichloroethylene, 1,2-trans-	27.9	1,890	1.5E-02	189		189	0.1						
Tetrachloroethylene	209	242	0.9	61	3.4			3,229	6.5E-02	40	5.4		
Trichloroethylene	8.6	473	1.8E-02	473	1.8E-02	2	4.3			64	0.1	2	4.6
Vinyl Chloride	15.4	55	0.3	107	0.1	5	3.4	12,190	1.3E-03				
	Hazard Index		1.2		3.6		7.8		0.1		5.6		4.6

Table D-10: Tarawa Terrace- Marine-in-training; Hazard Quotients for Specific Target Organs- Inhalation Pathway- Upper End Exposure Level

Marine-in-training	Max 3 yr Inhalation Conc (µg/m³)	Renal		Liver		Immune		Hematologic		Neurologic		Developmental	
		RfC or TTD (µg/m³)	HQ	RfC or TTD (µg/m³)	HQ	RfC or TTD (µg/m³)	HQ	RfC or TTD (µg/m³)	HQ	RfC or TTD (µg/m³)	HQ	RfC or TTD (µg/m³)	HQ
Dichloroethylene, 1,2-trans-	36	1,890	1.9E-02	189	0.2	189	0.2						
Tetrachloroethylene	269	242	1.1	61	4.4			3,229	8.3E-02	40	7.0	1,700	0.16
Trichloroethylene	17	473	3.6E-02	473	3.6E-02	2	8.6			64	0.3	1.9	9
Vinyl Chloride	20	55	0.4	107	0.2	5	4.3	12,190	1.6E-03			1,244	1.6E-02
	Hazard Index		1.5		4.8		13		0.1		7.3		9.3

Appendix E. Additional Exposure Scenarios

Based on information and concerns provided by the Community Assistance Panel ATSDR evaluated three additional exposure scenarios to estimate individuals' exposure to contaminants of concern and to determine if those exposures may have occurred at levels that could cause adverse health effects. The three exposure scenarios are

1, Swimming/Training Pools

2, Laundry Facilities

3. Food Preparation/Dishwashing Operations

These three exposure scenarios were evaluated separately from the toxicological and exposure assessment contained in the body of this PHA. If an individual fell into an exposure category discussed in the body of this PHA and also engaged in one of the exposure categories discussed in this appendix, that individual should expect to have the cumulative exposure from all the exposure categories that applied to their specific circumstance. Civilian workers in these scenarios would expect to have an increased estimated cancer risk in addition to what they may have experienced in exposure scenarios discussed in the main body of this PHA. Exposures experienced by training swimming and recreational pool users would not contribute to an increased cancer risk as much as the laundry facility and food preparation/dishwashing operations because the swimming scenarios have much shorter exposure durations, whereas the civilian workers of the laundry facility and food preparation/dishwashing operations could have been exposed for a 15-year period.

We used conservative one-compartment models to estimate inhalation exposures from sources. The models tend to over-predict actual exposures that occurred because they do not take clean air ventilation into account. Equations obtained from the EPA SWIMODEL were used to estimate PCE, TCE, 1,2-t DCE, vinyl chloride, and benzene inhalation exposures to indoor swimming pool users. The one-compartment model developed by Andelman (1990) was used to estimate the inhalation exposures to laundry facility and mess hall workers. Results of the models were converted into 24-hour average inhalation exposures in air and compared with intermediate and chronic minimum risk levels (MRLs) for inhalation for each contaminant of concern. An MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk for adverse noncancer health effects over a specified duration of exposure. These substance-specific estimates, which are intended to serve as screening levels, are used by ATSDR health assessors and other responders to identify contaminants and potential health effects that may be of concern at hazardous waste sites. To go one step beyond the screening process, the model's 24-hour average inhalation exposures were also evaluated against applicable studies' points of departure. A point of departure is a dose that can be considered to be in the range of observed responses, without significant extrapolation. A point of departure can be a datum point or an estimated point that is derived from observed dose-response data. A point of departure is used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. Common points of departure are LOAEL, NOAEL, and benchmark dose. The chronic inhalation MRL for PCE, TCE, and benzene are 41 $\mu g/m^3$, 2.1 $\mu g/m^3$, and 9.6 $\mu g/m^3$, respectively, were used to compare the inhalation exposures to laundry facility and mess hall workers. No established chronic inhalation MRLs currently exist for vinyl chloride and 1,2 t-DCE, so the RfC was used for vinyl chloride and the intermediate MRL was used for 1,2 t-DCE, 100 $\mu g/m^3$ and 790 $\mu g/m^3$, respectively.

Indoor Swimming Pool

Inhalation exposures in indoor swimming pools are estimated for enlisted Marines who trained in the pools, as well as for persons who used the pools for recreation. Because air concentrations were not measured at the indoor swimming pools and the chemicals of concern are volatile, Henry's Law constant is used to estimate ambient air concentrations. The indoor swimming pool water temperature was assumed to be 80 degrees Fahrenheit (C. Delaney, electronic communication, August 18, 2014). The estimated ambient vapor concentration is calculated as follows:

$$C_{vp} = H' \times C_w \times (1{,}000\ L/m^3) \quad (1)$$

where:
- C_{vp} = Ambient air concentration (mg/m^3 as vapor)
- H' = Unitless Henry's law constant
- C_w = Concentration of chemical in water (mg/L)

The total inhalation exposure per event is calculated according to the following equation:

$$PDR_{inhalation} = C_{vp} \times ET \times IR \quad (2)$$

where:
- $PDR_{inhalation}$ = Potential dose rate via inhalation exposure per event (mg/event)
- C_{vp} = Ambient air concentration (mg/m^3 as vapor)
- ET = Exposure time (hrs/event)
- IR = Inhalation rate (m^3/hr).

Inhalation exposures from indoor swimming pools are converted to 24-hour air concentrations which can be compared to intermediate and chronic inhalation MRLs. Dermal exposures are also estimated and converted into equivalent 24-hour concentrations. The dermal exposure estimates are negligible when compared to the inhalation estimates; therefore, dermal exposures were excluded from the final results.

Information obtained from Camp Lejeune indicated that four levels of training for enlisted Marines occurred in the indoor swimming pool. Basic and intermediate training each occurred 1 day per year, advanced training occurred 5 days per year, and pre-dive training occurred an additional 14 days per year (C. Delaney, electronic communication, August 18, 2014). The estimated number of training hours for each level was also provided by Camp Lejeune environmental personnel (C. Delaney, electronic communication, August 20, 2014). For every level of training an enlisted Marine accomplished, it was assumed they completed the levels of training below as well. For example, if a Marine completed the 5-day advanced training, it was assumed he also completed the 1-day basic training and the 1-day intermediate training.

Initial water concentrations used to determine inhalation exposures to enlisted Marines during training in the indoor pool are obtained from calculating 3-year running averages of the modeled water concentrations at the Hadnot Point water treatment plant. Chemical specific permeability coefficients, used to calculate dermal exposures, were determined from toxicological reviews conducted by the EPA. All other values (inhalation rates, surface area of exposed skin, etc.) that are needed to calculate an individual's exposure are obtained from the Environmental Protection Agency Exposure Factors Handbook (USEPA 2011d).

Indoor Swimming Pool Results

Table 9(a) lists calculated inhalation exposure concentrations from the four levels of indoor swimming pool training. For basic and intermediate training, TCE exposure to enlisted Marines exceeds the intermediate and chronic inhalation MRL; for advanced and pre-dive training, PCE, TCE, and benzene exposures to enlisted Marines exceed health guidelines. Both advanced and predive training groups exceeded the comparison values for trans-1,2-DCE and VC. See individual inhalation exposure tables for the assessment of each receptor evaluated. Table 9(b) lists calculated total inhalation exposures for enlisted Marines who trained in and used the indoor pool for recreation. For all four levels of training, PCE, TCE, and benzene exposures to enlisted Marines exceed the intermediate and chronic inhalation MRLs and trans-1,2-DCE and VC exposures exceed the intermediate MRL and RfC, respectively. Table 9(c) lists total exposure concentrations for persons who used the pool for recreation only. TCE and benzene exposures exceed the intermediate and chronic inhalation MRLs for all ages that used the pool for recreation only. Trans-1,2-DCE and VC exposures exceed the intermediate MRL and RfC, respectively, for all ages. The TCE exposures exceeded both of its points of departure, or LOAELs, for immune effects and heart malformations, as presented in USEPA's IRIS Web site. The uncertainty factors applied to the immune effects and heart malformation studies are 100 and 10, respectively. Additionally, the points of departure for PCE, vinyl chloride, or benzene were not exceeded.

For those whose values in the following tables are presented in bold font, people could have experienced noncancer health effects described in this PHA's Potential Health Effects from Exposure section. For instance, a Marine who trained in the pool at any of the exposure frequencies (basic, intermediate, advanced, or pre-dive) may experience toxicity to the central nervous system, kidney, liver, immune system, male reproductive system, and developing fetus. Regarding vinyl chloride exposures, the RfC is based on continuous lifetime exposures. The swimming exposures evaluated here are based on our conservative assumptions, such as exposure to the maximum contaminant concentration. In addition, indoor swimming exposures are for less than lifetime and either don't exceed the RfC or only exceed the RfC by one order of magnitude or so. Therefore, adverse health effects are not expected to occur because of exposure to VC. Of note, a linear relationship exists between contaminant concentration and the calculated inhalation exposures below, so if an individual was swimming during a time when the contaminant concentrations were half of the maximum contaminant concentration, their calculated inhalation exposure would be half of the value presented in the following tables.

In addition, the indoor swimming pool inhalation exposures are estimated using calculations that assume volatilization is constantly occurring at the surface of the pool. The pool would have to be continuously filled with new water for volatilization to occur at a constant rate. Continuously filling the pool with new water obviously did not occur, however, the indoor pool was backwashed 8–10 inches every 100 hours (C. Delaney, electronic communication, Dec. 2014). Backwashing is the process of cleaning the pool filter by a method of reversing the flow of water until the water runs clear through the waste line. During the backwashing process, new water is added to the pool as existing water is drained from it. Measured air concentrations taken from inside the indoor swimming pool facility during the time of interest would give the best estimate of how much inhalation exposure actually occurred. Because air measurements do not exist, overly conservative inputs and equations are used to calculate estimated exposures from the indoor swimming pool water. Actual inhalation exposures are expected to be much less than the exposures calculated from using the overly conservative inputs and equations. Another reason actual inhalation exposures at the surface of the indoor swimming pool water are expected to be much less than the estimated exposures is because contaminants of concern would most likely volatize from the swimming pool water during the time the pool is filled and the day or two after, when chemicals are added to get the pool to safe swimming conditions. By the time the pool water was chemically balanced and ready for swimmers to enter, most of the contaminants of concern would have volatized from the water.

Table 9a: Inhalation Exposure for Enlisted Marines Who Trained in the Indoor Swimming Pool

Chemical	Health Guideline	Calculated Inhalation Exposure in Air, in µg/m³			
		Training Level			
		Basic	Intermediate	Advanced	Pre-Dive
PCE	40*	27	45	313	813
TCE	2Ω	308	513	3594	9344
t-1,2-DCE	790β	145	242	1696	4410
Vinyl chloride	100¥	54	90	627	1629
Benzene	9.6*	3	4	30	78

* Acute, Intermediate, and Chronic MRL
Ω Intermediate and Chronic MRL
β Intermediate MRL
¥ RfC

Table 9b: Inhalation Exposure for Enlisted Marines Who Trained in and Used Indoor Swimming Pool for Recreation

Chemical	Health Guideline	Calculated Inhalation Exposure in Air, in µg/m³			
		Training Level			
		Basic	Intermediate	Advanced	Pre-Dive
PCE	40*	286	304	572	1072
TCE	2Ω	3286	3491	6571	12,321
trans-1,2-DCE	790β	1551	1648	3102	5816
Vinyl chloride	100¥	573	609	1146	2149
Benzene	9.6*	27	29	55	102

* Acute, Intermediate, and Chronic MRL
Ω Intermediate and Chronic MRL
β Intermediate MRL
¥ RfC

Table 9c: Inhalation Exposure, by Age, for Persons Who Used the Indoor Swimming Pool for Recreation

Chemical	Health Guideline	Calculated Inhalation Exposure in Air, in µg/m³			
		Age when exposed			
		0-3 years	3-6 years	6-16 years	>16 years
PCE	40*	210	260	247	206
TCE	2Ω	2418	2989	2843	2370
trans-1,2-DCE	790β	1141	1411	1342	1119
Vinyl chloride	100¥	422	521	496	413
Benzene	9.6*	20	25	24	20

* Acute, Intermediate, and Chronic MRL
Ω Intermediate and Chronic MRL
β Intermediate MRL
¥ RfC

Laundry Facility Workers

Inhalation exposures are estimated for civilians who worked in laundry facilities where industrial size steam presses and washing machines were operated. Because air concentrations were not measured at the laundry facilities and the chemicals of concern are volatile, the estimated ambient vapor concentration is calculated as follows:

$$C_{vp} = C_w \times f \times F_w \times ET / V_a \quad (3)$$

where:

C_{vp}	=	Ambient air concentration (mg/m^3)
C_w	=	Concentration of chemical in water (mg/L)
f	=	Fractional volatilization rate (unitless)
F_w	=	Flow rate (L/hr)
ET	=	Exposure time (hr/event)
V_a	=	Room volume (m^3)

The number of steam presses and washing machines located inside specific laundry facilities at Camp Lejeune are determined from reviewing as-built drawings given to ATSDR by Camp Lejeune environmental personnel (C. Delaney, electronic communication, September 16, 2014). The as-built drawings show where the machines are located inside the buildings and also provide building dimensions that are used to determine the room volumes. A conservative fractional volatilization rate of 0.9 is used when calculating ambient air concentrations for washing machines, indicating that around 90% of the contaminants of concern chemical concentration in the water volatizes into the ambient air. A fractional volatilization rate of 1.0 is used for steam presses, indicating that all of the chemical concentration in the water volatizes into the air. Washing machine flow rates for equipment in the existing laundry facilities are used to represent machines used during the study period. Steam press flow rates are assumed to be 0.2 gallons per minute (gpm).

Initial water concentrations used to determine inhalation exposures to laundry facility workers are obtained from calculating 15-year running averages of the modeled water concentrations at the Hadnot Point water treatment plant. The total inhalation exposure per event is calculated using equation (2) discussed above. Inhalation exposures from laundry facilities are estimated over the entire year and are converted to 24-hour air concentrations that can be compared to health guidelines. Other values, such as inhalation rates, that are needed to calculate an individual's exposure come from the Environmental Protection Agency Exposure Factors Handbook (USEPA 2011d).

Laundry Facility Results

Table 10(a) lists calculated exposure concentrations from steam presses and washing machines in the Naval Hospital laundry facility (Building H21). TCE and benzene total inhalation exposures to civilians working in the Naval Hospital laundry facility exceed the chronic inhalation MRLs. Trans-1,2-DCE and VC exposures did not exceed the intermediate MRL and RfC, respectively. Table 10(b) lists calculated exposure concentrations from steam presses and washing machines in the Industrial Area laundry facility (Building 1500). TCE and benzene total inhalation exposures to civilians working in the Industrial Area laundry facility exceed the chronic inhalation MRLs. Trans-1,2-DCE and VC exposures did not exceed the intermediate MRL and RfC, respectively. The TCE exposures exceeded both its points of departure, or LOAELs, for immune effects and heart malformations, as presented in EPA's IRIS website. The exposures to PCE, vinyl chloride, and benzene did not exceed their studies points of departure. For the individuals whose values in the following tables are presented in bold font, they could have experienced noncancer health effects described in this PHA's Potential Health Effects from Exposure section. For instance, a person who worked in either the Naval Hospital or Industrial Area laundry facilities might experience toxicity to the central nervous system, kidney, liver, immune system, male reproductive system, and, if pregnant, a developing fetus.

Table 10a: Inhalation Exposure for Civilians Who Worked in the Naval Hospital Laundry Facility

Chemical	Health Guidelines	Calculated Inhalation Exposure in Air, in µg/m³		
		Steam Press	Washing Machine	Total
PCE	40*	6	25	31
TCE	2Ω	136	612	748
trans-1,2-DCE	790β	71	320	391
Vinyl chloride	100¥	9	40	49
Benzene	9.6*	2	10	12

* Acute, Intermediate, and Chronic MRL
Ω Intermediate and Chronic MRL
β Intermediate MRL
¥ RfC

Table 10b: Inhalation Exposure for Civilians Who Worked in the Industrial Area Laundry Facility

Chemical	Health Guideline	Calculated Inhalation Exposure in Air, in µg/m³		
		Steam Press	Washing Machine	Total
PCE	40*	12	48	60
TCE	2Ω	290	1174	1464
trans-1,2-DCE	790β	151	614	765
Vinyl chloride	100¥	19	76	95
Benzene	9.6*	5	19	24

* Acute, Intermediate, and Chronic MRL
Ω Intermediate and Chronic MRL
β Intermediate MRL
¥ RfC

Industrial Area laundry facility workers were exposed to about twice as much contaminant of concern concentration as were persons working in the Naval Hospital laundry facility. The Industrial Area laundry facility was about 1400 sq. ft. larger than the Naval Hospital facility, which would result in less exposure. But the Industrial Area facility housed about three times as many steam presses and washing machines as did the Naval Hospital laundry facility, resulting in nearly twice as much exposure to contaminants of concern for those who worked there. The calculations used to estimate inhalation exposures from washing machines and steam presses at laundry facilities do not take clean air exchange rates into consideration. This is an accurate analysis of what actually occurred; before 1986 proper ventilation to collect the steam was not installed, and it would build up in the laundry facility rooms (C. Delaney, electronic communication, July 24, 2014). Clean air exchange from one room to another should come into consideration when calculating inhalation exposures and would lower the estimated exposure. Using a model that incorporates clean air exchange rates would lower the calculated inhalation concentrations.

Food Preparation/Dishwasher Operations

Inhalation exposures are estimated for enlisted Marines and civilians who worked in mess hall facilities where commercial conveyor dishwashers and steam tables were used. Because air concentrations were not measured at the mess hall facilities and the chemicals of concern are volatile, the estimated ambient vapor concentration is calculated using equation (3) discussed above.

The approximate dimensions of the mess hall rooms where workers were exposed by prerinsing dishes and operating dishwashers were estimated by Camp Lejeune personnel and given to ATSDR (C. Delaney, electronic communication, July 16, 2014). A conservative fractional volatilization rate of 0.9 is used when calculating ambient air concentrations for dishwashers, indicating that around 90% of the contaminant of concern chemical concentration in the water volatizes into the ambient air. Dishwasher flow rates for equipment in the existing mess hall facilities are around 0.7 gallons per rack. Assuming one rack is run every minute, a flow rate of 159 liters per hour is used to represent a dishwasher used during the study period. Steam tables were located in a different room from the dishwashers and pre-rinsing activities. The dimensions of the room where steam tables were located were determined from floor plans provided by Camp Lejeune personnel (S. Williams, electronic communication, February 4, 2015). A fractional volatilization rate of 1.0 is used for steam tables, indicating that all of the contaminants of concern chemical concentration in the water volatizes into the air. Based on a steam table size of 15 feet long and 3 feet wide, containing 6 inches of water, steam table flow rates were assumed to be 80 liters per hour.

Initial water concentrations used to determine inhalation exposures to enlisted Marine who worked in the mess hall facilities are obtained from calculating 3-year running averages of the modeled water concentrations at the Hadnot Point water treatment plant. Initial water concentrations for civilian mess hall workers are obtained from calculating 15-year running averages of the modeled water concentrations. The total inhalation exposure per event is calculated using equation (2) discussed above. Inhalation exposures from mess hall facilities are estimated over the entire year and are converted to equivalent 24-hour concentrations which can be compared with health guidelines. Other values, such as inhalation rates, that are needed to calculate an individual's exposure are obtained from the Environmental Protection Agency Exposure Factors Handbook (USEPA 2011d).

Food Preparation/Dishwasher Operation Results

Table 11(a) lists calculated exposure concentrations for enlisted Marines who worked in the mess hall facilities. PCE, TCE and benzene inhalation exposures to enlisted Marines who pre-rinsed dishes and operated dishwashers exceed the chronic inhalation MRLs. TCE inhalation exposure to enlisted Marines who worked over steam tables also exceeds the chronic inhalation MRL. VC exposures exceed the RfC for all mess hall activities. Trans-1,2-DCE did not exceed the intermediate MRL for the steam table activity. Table 11(b) lists calculated exposure concentrations for civilians who worked in the mess hall facilities. TCE and benzene inhalation exposures to civilians who pre-rinsed dishes and operated dishwashers exceed the chronic inhalation MRLs. TCE inhalation exposure to civilians who worked over steam tables also exceeds the chronic inhalation MRL. Trans-1,2-DCE and VC exposures only exceed the intermediate MRL and RfC, respectively, for the prerinsing activity. The TCE exposures exceeded both its points of departure, or LOAELs, for immune effects and heart malformations, as presented in EPA's IRIS Web site. The exposures to PCE, vinyl chloride, and benzene did not exceed their studies points of departure.

For persons whose values in the following tables are presented in bold font, they could have experienced noncancer health effects described in "Potential Health Effects from Exposure" section of this PHA. For instance, a Marine or civilian who worked in the mess hall at any of the activities (dishwasher, pre-rinsing, steam table) may experience toxicity to the central nervous system, kidney, liver, immune system, male reproductive system, and developing fetus. Regarding vinyl chloride exposures, the RfC is based on continuous lifetime exposures. The exposures that are evaluated here are based on our conservative assumptions and are for less than lifetime and either don't exceed the RfC or only exceed the RfC by one order of magnitude or so. Therefore, adverse health effects are not expected to occur because of exposure to VC.

Table 11a: Inhalation Exposure for Enlisted Marines Who Worked in the Mess Hall

Chemical	Health Guideline	Calculated Inhalation Exposure in Air, in µg/m³			
		Dishwasher	Pre-Rinsing	Dishwasher and Pre-Rinse	Steam Table
PCE	40*	115	361	476	64
TCE	2Ω	2385	7496	9881	1327
trans-1,2-DCE	790β	1250	3928	5178	696
Vinyl chloride	100¥	188	592	780	105
Benzene	9.6*	37	116	153	20

* Acute, Intermediate, and Chronic MRL
Ω Intermediate and Chronic MRL
β Intermediate MRL
¥ RfC

Table 11b: Inhalation Exposure for Civilians Who Worked in the Mess Hall

Chemical	Health Guideline	Calculated Inhalation Exposure in Air, in µg/m³			
		Dishwasher	Pre-Rinsing	Dishwasher and Pre-Rinse	Steam Table
PCE	40*	54	170	224	30
TCE	2Ω	1311	4119	5430	729
trans-1,2-DCE	790β	685	2153	2838	381
Vinyl chloride	100¥	85	267	352	47
Benzene	9.6*	22	68	90	12

* Acute, Intermediate, and Chronic MRL
Ω Intermediate and Chronic MRL
β Intermediate MRL
¥ RfC

We estimated inhalation exposures for enlisted Marines and civilians who worked at two mess halls. Results in this report are only shown for the smaller mess hall, where exposures were expected to be greater. The calculations used to estimate inhalation exposures from dishwashing and steam table activities in mess hall facilities do not take clean air exchange rates into consideration. This is an accurate analysis of what actually occurred, because before 1986, no fume hoods existed to collect the steam and it would build up in the mess hall facility rooms (C. Delaney, electronic communication, July 24, 2014). Clean air exchange from one room to another should be taken into consideration when calculating inhalation exposures and would lower the estimated exposure.

The equations and inputs chosen to estimate the inhalation exposures from indoor swimming pools, laundry facilities, and mess hall facilities are conservative and over-predict what actual exposures were expected to be. Several of the exposure scenarios for the contaminant of concern estimate that the inhalation exposures exceed the selected health guideline. Using a model that incorporates clean air exchange rates would lower the calculated inhalation concentrations. ATSDR is concerned with estimating exposures to individuals who are breathing air directly at the point at which volatilization occurred. Swimmers are in the water and breathe the air at the interface. Steam press workers and dishwashers stand over machines and breathe the air coming directly from the equipment.

Appendix F. ATSDR Health Studies

ATSDR has conducted several health studies at MCB Camp Lejeune. One of the health studies, completed in 2013, evaluated whether *in utero* and infant (up to 1 year of age) exposures to contaminants of concern in drinking water at MCB Camp Lejeune were associated with specific birth defects (i.e., neural tube defects and oral clefts) and childhood hematopoietic cancers. The study population includes births that occurred during 1968–1985 to women who were pregnant while they lived in family housing at the base. This was a case control study, where the exposure to contaminants of concern was compared between mothers who gave birth to a child with birth defects or developed hematopoietic cancer, and mothers who had a live birth without a major birth defect or childhood cancer. Contaminants of concern of major interest to the epidemiological study include PCE, TCE, trans-1,2-DCE, VC, and benzene. The study findings were limited in statistical precision but suggested associations between drinking water contaminants and neural tube defects (i.e. spina bifida and anaencephaly). A weaker association was found with childhood hematopoietic cancers. This study was published in *Environmental Health* in December 2013 (Ruckart et al., 2013).

The second health study is an evaluation of mortality among Marine and naval personnel stationed at Camp Lejeune. The study, completed in 2014, looked at all causes of death, including cancers and other fatal diseases to determine a possible link between the death and exposure to contaminated drinking water at Camp Lejeune. The study focused on active duty Marines and naval personnel who were stationed at Camp Lejeune anytime between April 1975 and December 1985. The mortality study also included a population of unexposed former active duty Marines and naval personnel from Camp Pendleton, California. The study findings were limited in statistical precision, but elevated rates compared with Camp Pendleton personnel were observed for several causes of death, including cancers of the kidney, liver, esophagus, cervix, multiple myeloma, and Hodgkin lymphoma. This study was published in *Environmental Health* in February 2014 (Bove et. al. 2014a).

The third health study is an evaluation of mortality among civilian workers who were employed at Camp Lejeune during 1973–1985. The study used the same methodology as the mortality study of Marine and Navy personnel, with the objective of determining if an association exists between cause of death and exposure to contaminated drinking water. The mortality rates of Camp Lejeune workers were compared with the rates for workers at Camp Pendleton, who performed similar tasks but were not exposed to contaminated drinking water. As was the case for the active duty personnel, the study findings were limited in statistical precision. However, the results showed elevated mortality hazard ratios for kidney cancer, leukemias, multiple myelomas, rectal cancer, oral cavity cancer, and Parkinson's disease. This study was published in *Environmental Health* in August 2014 (Bove et al., 2014b).

The fourth health study is an evaluation of adverse birth outcomes for children whose mothers resided at Camp Lejeune at the time of delivery during 1968–1985. The objective of the study was to evaluate associations between residential prenatal exposure to contaminated drinking water and preterm birth, small for gestational age (SGA), term low birth weight (TLBW), and mean birth weight (MBW) among term births. The findings suggested associations between exposure during pregnancy to TCE and SGA, TLBW, and reduced MBW. The risk of TLBW increased with increasing level of exposure to TCE, particularly in the second trimester of pregnancy. The risk for TLBW also increased with increasing levels of exposure to benzene, which occurred over the entire duration of pregnancy. An association was also noted between exposure to PCE during pregnancy and risk for preterm birth, particularly during the 2nd trimester. This study was published in *Environmental Health* in November 2014 (Ruckart et al., 2014).

The fifth health study is a case-control study to determine whether male Marines who served at MCB Camp Lejeune during periods of contaminated drinking water have elevated rates of breast cancer. The findings suggested possible associations between exposure to PCE, DCE, and vinyl chloride at Camp Lejeune and male breast cancer. Exposures to TCE, PCE, DCE, and vinyl chloride were also observed to possibly accelerate the onset of male breast cancer. The study did not find evidence suggesting

associations between male breast cancer and exposures to benzene. These findings were based on small numbers of exposed cases, however. ATSDR intends to evaluate male breast cancer in a planned cancer incidence study that will involve state cancer registries nationwide as well as federal cancer registries. *Environmental Health* published this study in its September 2015 issue (Ruckart et al., 2015).

ATSDR is also analyzing data from a health survey of Marines, naval personnel, and civilian workers at MCB Camp Lejeune as well as a sample of Marines, naval personnel, and civilian workers at Camp Pendleton. The survey also included Marine dependents at Camp Lejeune who participated in a 1999–2002 survey conducted to identify birth defects and childhood cancers for the published study of neural tube defects, oral clefts, and childhood hematopoietic cancers.

In addition to the aforementioned studies, ATSDR intends to evaluate specific causes of cancer in a planned cancer incidence study that will involve cancer registries nationwide as well as federal cancer registries.

Appendix G. Modeled Contaminants of Concern in Drinking Water

Reconstructing Contaminant Concentrations in Drinking Water

To get estimates of historical exposures, ATSDR used water-modeling techniques and historical reconstruction to quantify concentrations of particular contaminants in drinking water and to estimate the level and duration of human exposure to contaminated drinking water (Maslia, et al., 2007, 2009, 2013). The specific chemicals detected in the water supply systems for Hadnot Point and Tarawa Terrace were TCE, PCE, t-1,2-DCE, VC, and benzene. Estimates of contaminant concentrations based on modeling were derived for each of these chemicals.

Given the limited number of historical contaminant-specific data measurements during most of the period relevant to this public health assessment, ATSDR used historical reconstruction to estimate the spatial and temporal distributions of contaminant-specific concentrations in groundwater and drinking water serving the Tarawa Terrace, Hadnot Point, and Holcomb Boulevard study area. Characteristically, historical reconstruction includes the application of simulation tools, such as models, to recreate or represent past conditions (Rodenbeck and Maslia 1998; McLaren/Hart-ChemRisk 2000; Costas et al., 2001; Reif et al., 2003; Kopecky et al., 2004; Maslia et al., 2005; Sahmel et al., 2010). To achieve the goal of reconstructing historical drinking water concentrations, ATSDR undertook five tasks:

1. Identify chemical compounds and their sources (contaminants of concern) that contaminated drinking water at Camp Lejeune,
2. Estimate when contaminated groundwater arrived at water-supply wells and the duration of the contamination,
3. Determine the distribution of contaminated drinking water throughout the water-distribution systems serving the study areas,
4. Quantify the spatial and temporal distributions of monthly drinking water contaminant concentrations, and
5. Compute contaminant concentration ranges (about a mean) based on simulation results for a specific historical month.

Groundwater was the sole water supply source for MCB Camp Lejeune.

The ATSDR epidemiological studies needed historical drinking water concentrations at monthly intervals, and hence, the use and application of numerical and computational models to estimate monthly mean drinking water concentrations for contaminants of concern.

Confidence in Uncertainty and Variability of Historical Drinking Water Concentrations

Variability and uncertainty are associated with the data, analyses, models, and calibrated model parameters in the historical reconstruction for the Tarawa Terrace, Hadnot Point, and Holcomb Boulevard areas. All modeling analyses have inherent uncertainties. Uncertainty and variability, however, are not limited solely to the historical reconstruction analyses summarized in ATSDR's historical reconstruction reports (Maslia et al., 2007; Maslia et al., 2013). Uncertainty and variability are inherent features of all models and data, even when useful data are plentiful. Thus, best modeling practice requires that evaluations be conducted to ascertain confidence in models by assessing variances and uncertainties associated with the modeling process and with the outcomes attributed to models (Saltelli et al., 2000). Therefore, the Chapter A reports of ATSDR's historical reconstruction analyses (Maslia et al., 2007, 2013) summarize the characterization of uncertainty of model output (simulated concentrations) due to model input parameter uncertainty and variability.

Researchers frequently use several methods to evaluate and quantify uncertainty. Two such methods are sensitivity and uncertainty analysis. Within the generalized classification of uncertainty analysis, Monte Carlo (MC) simulation is a particularly well known numerical method (USEPA 1997, Tung and Yen 2005). For the ATSDR study, four types of sensitivity analyses and three types of uncertainty analyses,

which included a statistical analysis and MC simulations, were conducted using calibrated Hadnot Point-Holcomb Boulevard models.

For more information on the details of the sensitivity and uncertainty analyses, please refer to ATSDR historical reconstruction report's Chapter A supplemental information sections: Suarez-Soto et al., (2012), Guan et al., (2012), Jones et al., (2010), Jang et al., (2012), and Sautner et al., (2012b), and Chapter I for Tarawa Terrace (Maslia et. al. 2009).

Appendix H. Lead and Copper Rule

EPA United States Environmental Protection Agency

Lead and Copper Rule: A Quick Reference Guide

Overview of the Rule

Title[1]	Lead and Copper Rule (LCR)[2], 56 FR 26460 - 26564, June 7, 1991
Purpose	Protect public health by minimizing lead (Pb) and copper (Cu) levels in drinking water, primarily by reducing water corrosivity. Pb and Cu enter drinking water mainly from corrosion of Pb and Cu containing plumbing materials.
General Description	Establishes action level (AL) of 0.015 mg/L for Pb and 1.3 mg/L for Cu based on 90th percentile level of tap water samples. An AL exceedance is not a violation but can trigger other requirements that include water quality parameter (WQP) monitoring, corrosion control treatment (CCT), source water monitoring/treatment, public education, and lead service line replacement (LSLR).
Utilities Covered	All community water systems (CWSs) and non-transient non-community water systems (NTNCWSs) are subject to the LCR requirements.

Public Health Benefits

Implementation of the LCR has resulted in	▶ Reduction in risk of exposure to Pb that can cause damage to brain, red blood cells, and kidneys, especially for young children and pregnant women. ▶ Reduction in risk of exposure to Cu that can cause stomach and intestinal distress, liver or kidney damage, and complications of Wilson's disease in genetically predisposed people.

Major Monitoring Provisions

Lead and Copper Tap

Applicability	▶ All CWSs and NTNCWSs.
Standard	▶ CWSs and NTNCWSs must collect first-draw samples at taps in homes/buildings that are at high risk of Pb/Cu contamination as identified in 40 CFR 141.86(a). ▶ Number of samples is based on system size (see Table 1). ▶ Systems must conduct monitoring every 6 months unless they qualify for reduced monitoring.
Reduced	▶ See Table 1 for sample number and Table 2 for criteria.

Water Quality Parameter (WQP)

Applicability	▶ Systems serving > 50,000 people. ▶ Systems serving ≤ 50,000 during monitoring periods in which either AL is exceeded.
Standard	▶ WQP samples at taps are collected every 6 months. ▶ WQPs at entry points to distribution system (EPTDS) are collected every 6 months prior to CCT installation, then every 2 weeks.
Reduced	▶ See Table 1 for sample number and page 2 for criteria. Does not apply to EPTDS WQP monitoring.

Table 1: Lead and Copper Tap and WQP Tap Monitoring

Size Category	System Size	Number of Pb/Cu Tap Sample Sites[3]		Number of WQP Tap Sample Sites[4]	
		Standard	Reduced	Standard	Reduced
Large	> 100K	100	50	25	10
	50,001 - 100K	60	30	10	7
Medium	10,001 - 50K	60	30	10	7
	3,301 - 10K	40	20	3	3
Small	501 - 3,300	20	10	2	2
	101 - 500	10	5	1	1
	≤ 100	5	5	1	1

[3] With written State approval, PWSs can collect < 5 samples if all taps used for human consumption are sampled.
[4] Two WQP tap samples are collected at each sampling site.

Table 2: Criteria for Reduced Pb/Cu Tap Monitoring

Annual	1. PWS serves ≤ 50,000 people and is ≤ both ALs for 2 consecutive 6-month monitoring periods; or 2. Any PWS that meets optimal WQPs (OWQPs) and is ≤ Pb AL for 2 consecutive 6-month monitoring periods.
Triennial	1. PWS serves ≤ 50,000 people and is ≤ both ALs for 3 consecutive years of monitoring; or 2. Any PWS that meets OWQP specifications and is ≤ Pb AL for 3 consecutive years of monitoring; or 3. Any PWS with 90th percentile Pb and Cu levels ≤ 0.005 mg/L and ≤ 0.65 mg/L, respectively, for 2 consecutive 6-month monitoring periods (i.e., accelerated reduced Pb/Cu tap monitoring).
Every 9 years	PWS serves ≤ 3,300 people and meets monitoring waiver criteria found at 40 CFR 141.86(g).

Lead Consumer Notice

Within 30 days of learning the results, all systems must provide individual Pb tap results to people who receive water from sites that were sampled, *regardless of whether the results exceed the Pb AL*, as required by 40 CFR 141.85(d).

Consumer Confidence Report (CCR)

All CWSs, irrespective of their lead levels, must provide an educational statement about lead in drinking water in their CCRs as required by 40 CFR 141.154. Must be in 2008 CCR (due July 1, 2009) if EPA is Primacy Agency, State adopts the rule by reference automatically, or adopts during 2008. Otherwise, this statement is required in the 2009 CCR (due July 1, 2010).

[1] This document provides a summary of federal drinking water requirements; to ensure full compliance, please consult the federal regulations at 40 CFR 141 and any approved state requirements.

[2] The June 1991 LCR was revised with the following Technical Amendments: 56 FR 32112, July 15, 1991; 57 FR 28785, June 29, 1992; 59 FR 33860, June 30, 1994.

It was subsequently revised by: the LCR Minor Revisions, 65 FR 1950, January 12, 2000, and the LCR Short-Term Revisions, 72 FR 57782, October 10, 2007.

The object above is an embedded picture. Source: USEPA Safe Drinking Water Act website http://water.epa.gov/lawsregs/rulesregs/sdwa/lcr/upload/LeadandCopperQuickReferenceGuide_2008.pdf

For additional information on the LCR

Call the Safe Drinking Water Hotline at 1-800-426-4791; visit the EPA Web site at http://water.epa.gov/drink; or contact your State drinking water representative.

Treatment Technique and Sampling Requirements if the AL is Exceeded[5]

[5] Based on 90th percentile level. Multiply number of valid samples by 0.9 (e.g., 10 samples x 0.9 = 9; thus, use 9th highest Pb and Cu test result to compare to AL). For 5 samples, average 4th and 5th highest results. For < 5 samples, use highest result.

Water Quality Parameter (WQP)	
Applicability	Refer to page 1.
Parameters	▶ pH, alkalinity, calcium *(initial only, unless calcium carbonate stabilization is used)*, conductivity *(initial monitoring only)*, orthophosphate *(if inhibitor is phosphate-based)*; silica *(if inhibitor is silicate-based)*, and temperature *(initial monitoring only)*.
Frequency	▶ Systems installing CCT, must conduct follow-up monitoring for 2 consecutive 6-month periods. ▶ WQP tap monitoring is conducted every 6 months, EPTDS monitoring increases to every 2 weeks. ▶ After follow-up monitoring, State sets OWQP specifications that define optimal CCT.
Reduced Tap Monitoring	▶ Collect reduced number of sampling sites (see Table 1) if meet OWQPs for 2 consecutive 6-month periods. ▶ Collect reduced number of sampling sites at reduced frequency if meet OWQPs for: – 6 consecutive 6-month monitoring periods can monitor annually; – 3 consecutive years of annual monitoring can monitor triennially.
Public Education (PE)	
Applicability	▶ Systems that exceed the Pb AL (*not required if only the Cu AL is exceeded*).
Purpose	▶ Educates consumers about lead health effects, sources, and steps to minimize exposure.
Delivery Method	▶ CWSs: deliver materials to bill-paying customers and post lead information on water bills, work in concert with local health agencies to reach at-risk populations (children, pregnant woman), deliver to other organizations serving "at-risk" populations, provide press releases, include new outreach activities from list in 40 CFR 141.85(a)(2)(vi), and post to Web site (CWSs serving > 100,000 only). ▶ NTNCWSs: posting and distribution to all consumers (can be electronic with State permission). Can apply to CWSs such as hospitals and prisons where population cannot make improvements.
Timing	▶ Within 60 days *after end of monitoring period* in which Pb AL was exceeded if not already delivering PE.[6] ▶ Repeat annually except: water bill inserts - quarterly; press releases - 2x/year, and Web posting - continuous. ▶ Can discontinue whenever ≤ Pb AL but must recommence if subsequently exceed Pb AL.
[6] State may allow extension in some situations. Also, State may require approval of message content prior to delivery.	
Source Water Monitoring and Source Water Treatment (SOWT)	
Applicability	▶ Systems that exceed Pb or Cu AL.
Purpose	▶ Determine contribution from source water to total tap water Pb and Cu levels and need for SOWT.
Timing	▶ One set of samples at each EPTDS is due within 6 months of first AL exceedance. ▶ System has 24 months to install any required SOWT. ▶ State sets maximum permissible levels (MPLs) for Pb and Cu in source water based on initial and follow-up source water monitoring.
Standard	▶ Ground water PWSs monitor once during 3-year compliance periods; surface water PWSs monitor annually.
Reduced	▶ Monitor every 9 years if MPLs are not exceeded during 3 consecutive compliance periods for ground water PWSs or 3 consecutive years for surface water PWSs.
Corrosion Control Treatment (CCT)	
Applicability	▶ All large systems except those meeting requirements of 40 CFR 141.81(b)(2) or (b)(3). ▶ Medium and small systems that exceed either AL; may stop CCT steps if ≤ both ALs for 2 consecutive 6-month periods but must recommence CCT if subsequently exceed either AL.
Study	▶ All large systems except as noted above. ▶ If State requires study for small or medium systems, it must be completed within 18 months.
Treatment	▶ Once State determines type of CCT to be installed, PWS has 24 months to install. ▶ Systems installing CCT must conduct 2 consecutive 6 months of follow-up tap and WQP monitoring.
OWQPs	▶ After follow-up Pb/Cu tap and WQP monitoring, State sets OWQPs. *Refer to WQP section above.*
Lead Service Line Replacement (LSLR)	
Applicability	▶ Systems that continue to exceed the Pb AL after installing CCT and/or SOWT. ▶ Can discontinue LSLR whenever ≤ Pb AL in tap samples for 2 consecutive 6-month monitoring periods; must recommence if subsequently exceed.
Monitoring	▶ Optional: Sample from LSL to determine if line must be replaced. If all samples are ≤ 0.015 mg/L, line is considered "replaced through testing"; must reconsider these lines if Pb AL is subsequently exceeded. ▶ Required: Sample from any LSLs not completely replaced to determine impact on Pb levels.
Replacement	▶ Must replace at least 7% of LSLs annually; State can require accelerated schedule. ▶ If only portion of LSL is replaced, PWS must: – Notify customers at least 45 days prior to replacement about potential for increased Pb levels. – Collect samples within 72 hours of replacement and provide results within 3 days of receipt.

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Appendix I. Additional Information about Lead

Table 12: Possible Sources of Lead Exposure

Place	Source
Indoors	Paint – Ingesting paint chips primarily found in homes built prior to 1978 and on older toys and furniture.
	Dust – Ingesting dust (from hand-to-mouth activity) found in older homes (built before 1978) or tracked in from contaminated soil.
	Water – Drinking water containing lead that comes from corrosion of older fixtures, from the solder that connects pipes, or from wells where lead contamination has affected the groundwater.
	Tableware – Eating foods from imported, old, handmade, or poorly glazed ceramic dishes and pottery that contains lead. Lead may also be found in leaded crystal, pewter, and brass dishware.
	Candy – Eating consumer candies imported from Mexico. Certain candy ingredients such as chili powder and tamarind may be a source of lead exposure. Candy wrappers have also been shown to contain some lead.
	Toy Jewelry – Swallowing or putting in the mouth toy jewelry that contains lead. This inexpensive children's jewelry is generally sold in vending machines and large volume discount stores across the country.
	Traditional (folk) Medicines – Ingesting some traditional (folk) medicines used by India, Middle Eastern, West Asian, and Hispanic cultures. Lead and other heavy metals are put into certain folk medicines on purpose because these metals are thought to be useful in treating some ailments. Sometimes lead accidentally gets into the folk medicine during grinding, coloring, or other methods of preparation.
Outdoors	Outdoor Air – Breathing lead particles in outdoor air that comes from the residues of leaded gasoline or industrial operations.
	Soil – Ingesting dirt (pica) contaminated with lead that comes from the residues of leaded gasoline, industrial operations, or lead-based paint.
Other	Hobbies – Ingesting lead from hobbies using lead such as welding, auto or boat repair, the making of ceramics, stained glass, bullets, and fishing weights. Other hobbies that might involve lead include furniture refinishing, home remodeling, painting and target shooting at firing ranges.
	Workplace – Ingesting lead found at the workplace. Jobs with the potential for lead exposure include building demolition, painting, remodeling/renovation, construction, battery recycling, radiator repair, and bridge construction. People who work in a lead environment may bring lead dust into their car or home on their clothes and bodies exposing family members.

Sources: CDC 2015b; NYDOH 2010.

Figure 14. Ways to Reduce Lead Uptake

Children and the developing fetus of pregnant women are at higher risk for developing health effects caused by exposure to high levels of lead than adults. When too much lead builds up in a child's body, it can cause learning, hearing, and behavioral problems and can harm your child's brain, kidneys, and other organs. Some of these health effects can last a lifetime. Tests are available to let people know how much lead is in their blood.

Ways to prevent high levels of lead in blood include[38]

✔ **Eating 3 healthy meals a day and at least 2 healthy snacks.**

Eating healthy meals can help lower, but not eliminate, the risk of getting high levels of lead in blood. People with empty stomachs get more lead into their bodies than people with full stomachs.

✔ **Eating a balanced diet.**

People's bodies are less likely to absorb lead when their diet is rich in nutrients and vitamins.

- Eat iron-rich foods like
  - Lean red meats, fish or chicken
  - Cereals high in iron
  - Dried fruits such as raisins or prunes
- Eat calcium-rich foods like
  - Milk, yogurt, cheese
  - Green leafy vegetables (spinach, kale, collard greens)
- Eat foods high in Vitamin C like
  - Oranges or orange juice and grapefruits or grapefruit juice
  - Tomatoes, tomato juice
  - Green peppers

✔ **Eating less high fat and fried foods.**

People's bodies are more likely to absorb lead when they eat high fat and fried foods.

- Avoid foods like hot dogs, French fries, and potato chips

✔ **Washing your hands before fixing food and washing and peeling produce before eating it.**

Lead particles that stick to people's hands after gardening and to the surface of garden produce can be washed away before the lead enters a person's body.

✔ **Using only cold water from the tap for drinking, cooking, and for making baby formula**.

Hot water is more likely to contain lead. Run cold water 1–2 minutes before using it.

[38] Sources: CDC 1991; Mahaffey 1981; Mahaffey and Michaelson 1980; Rabinowitz et al. 1980, USEPA 2001

Figure 15. How to Prevent Lead Exposure

Parents can take simple steps to make their homes more lead-safe (CDC 2014b).

- Talk to your local health department about testing paint and dust in your home for lead if you live in a home built before 1978.
- Common home renovation activities like sanding, cutting, and demolition can create hazardous lead dust and chips by disturbing lead-based paint. These can be harmful to adults and children.
- Renovation activities should be performed by certified renovators who are trained by EPA-approved training providers to follow lead-safe work practices.

Lead can be found in a variety of sources.

These include:

- paint in homes built before 1978
- water pumped through leaded pipes
- imported items, including clay pots
- certain consumer products such as candies, make -up and jewelry
- certain imported home remedies

- Learn more at EPA's Renovation, Repair, and Painting rule Web page: http://www.epa.gov/lead/pubs/renovation.htm.
- If you see paint chips or dust in windowsills or on floors because of peeling paint, clean these areas regularly with a wet mop.
- Wipe your feet on mats before entering the home, especially if you work in occupations where lead is used. Removing your shoes when you are entering the home is a good practice to control lead.
- Use only cold water from the tap for drinking, cooking, and for making baby formula. Hot water is more likely to contain lead. Run cold water 30 to 60 seconds before using.
- Remove recalled toys and toy jewelry from children. Stay up-to-date on current recalls by visiting the Consumer Product Safety Commission's Web site: http://www.cpsc.gov/.

Appendix J. 3Ts for Reducing Lead in School Drinking Water

3Ts for Reducing Lead in Drinking Water in Schools

Nearly 56 million Americans, including 53 million children, spend their days in schools. School officials need to know if the drinking water students, teachers, and staff consume contains elevated levels of lead because exposure to lead can cause serious health problems, particularly for young children. To help schools safeguard their occupants' health, the U.S. Environmental Protection Agency (EPA) developed the *3Ts for Reducing Lead in Drinking Water in Schools: Revised Technical Guidance*. It provides the information schools need to:

- Identify potential sources of lead in their facilities,
- Monitor school drinking water for elevated lead levels,
- Resolve problems if elevated lead levels are found, and
- Communicate about their lead control programs.

Although public water systems that supply water to most schools may meet EPA's lead standards, lead can still get into school drinking water. As water moves through a school's plumbing system, lead can leach into the drinking water from plumbing materials and fixtures that contain lead. Testing is the best way for schools to know if there are elevated levels of lead in a facility's drinking water.

Ensuring that the water provided in your school is safe for children to drink is a fundamental responsibility. In addition to the health advantages, schools that voluntarily test drinking water and make information about their program available to the public will enjoy the following benefits:

- Enhanced credibility
- Positive publicity
- Parental and community support
- Stature as a standard-setting "best practices" facility

Health Effects of Exposure to Lead

Infants and children exposed to lead can experience:

- Delays in physical and mental development
- Lower IQ levels
- Reduced attention span
- Learning disabilities
- Hearing loss
- Hyperactivity
- Poor classroom performance

3Ts of Reducing Lead in Drinking Water in Schools

EPA developed the 3Ts (Training, Testing, and Telling) to help schools implement simple strategies for managing the health risks of lead in school drinking water.

- **Training** school officials to raise awareness of the potential occurrences, causes, and health effects of lead in drinking water; assist school officials in identifying potential areas where elevated lead may occur; and establish a testing plan to identify and prioritize testing sites.
- **Testing** drinking water in schools to identify potential problems and take corrective actions as necessary.
- **Telling** students, parents, staff, and the larger community about monitoring programs, potential risks, the results of testing, and remediation actions.

DOWNLOAD The *3Ts For Reducing Lead In Drinking Water In Schools: Revised Technical Guidance* at no cost by visiting www.epa.gov/safewater/schools or order a free copy by calling the Safe Drinking Water Hotline at 1-800-426-4791.

Sources of Lead Exposure

Lead is distributed in the environment by natural and human-made activity. (Past human activities are the major source of lead in the environment.)

Possible sources of lead include:

- **Lead-based paint** that can flake off into soil, window sills, or floors
- **Lead in the air** from industrial activities
- **Dust and soil** from roadways and streets where automobiles, which used leaded gas, travelled
- **Lead dust** brought home by industrial workers on their clothes and shoes
- **Lead in water** from the corrosion of plumbing products containing lead

Although most lead exposure occurs when people eat paint chips and inhale dust, EPA estimates that 10 to 20 percent of human exposure to lead may come from lead in drinking water.

Potential Sources of Lead In Drinking Water

- Lead solder
- Lead pipe and pipe fittings
- Fixtures, valves, meters and other system components containing brass
- Sediments

Start Your Lead in Drinking Water Control Program Today

The first step to implementing a successful lead control program is to read the recommendations found in the *3Ts for Reducing Lead in Drinking Water in Schools: Revised Technical Guidance*. Schools can follow the straightforward guidance found in the 3Ts to:

- **Collect information on school drinking water and identify assistance to help implement a school lead control program.** The 3Ts provides tips on finding past testing results; asking water utilities for help or financial assistance; reaching out to state drinking water programs for support; and evaluating existing resources.
- **Develop a plumbing profile.** A plumbing profile helps schools identify potential problem areas and assess factors that contribute to lead problems. Lead contamination may not occur uniformly throughout a building and the 3Ts describes various factors that affect the likelihood of lead contamination in order to identify those areas as priorities for testing. Chapter 3 of the guidance provides tips on developing a school plumbing profile.
- **Develop a drinking water testing plan.** The results of a plumbing profile will help schools create their testing plans. Key issues to consider include who will be in charge of the effort; who will collect and analyze the samples and maintain records; and where samples will be taken. Chapter 3 of the guidance helps schools answer these questions and suggests possible sources of assistance for school testing efforts.
- **Test the facilities' drinking water for lead.** EPA recommends a two-step sampling process to test for lead in drinking water. The two-staged process will help schools determine if particular outlets have elevated lead levels ***and*** locate the source of the problem. The recommended testing plan allows schools to determine if the source of lead is at the sampled outlet or within the facility's interior plumbing. Schools will find detailed and easy-to-follow instructions on testing for lead in water in Chapter 4.
- **Correct problems when elevated lead levels are found.** Addressing elevated lead levels in school drinking water typically requires temporary and permanent solutions. Chapter 5 recommends short-term solutions to reduce the risk of exposure to lead in drinking water in schools and provides suggestions for permanent solutions, such as replacing pipes, fixtures, or faucets containing lead with lead-free alternatives.
- **Communicate with the school community about a school lead control program.** Lead is a serious public health risk and monitoring school drinking water for lead is one important way schools can protect their community's health. Schools will benefit if they communicate about their lead monitoring program with students, teachers, staff, parents, and other members of the school community. Chapter 6 of the guidance provides communication strategies and sample materials schools can use.

EPA United States Environmental Protection Agency

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Office of Water (4606)

DOWNLOAD The *3Ts For Reducing Lead In Drinking Water In Schools: Revised Technical Guidance* at no cost by visiting www.epa.gov/safewater/schools or order a free copy by calling the Safe Drinking Water Hotline at 1-800-426-4791.

Appendix K. Peer Reviewer Comments and ATSDR Responses

ATSDR received the following comments from independent peer reviewers on the *Camp Lejeune Drinking Water* public health assessment. For comments that questioned the validity of statements made in the document, ATSDR verified or corrected the statements.

Reviewer	*Reviewer Comment*	*ATSDR Response*
1. Does the public health assessment adequately describe the nature and extent of contamination?		
1	Yes.	Thank you for the confirmation.
2	I think the nature and extent discussion is generally adequate, though it does prompt the more interested reader to consult either an appendix, or other sources for any depth in detail regarding the historic water concentration modeling. I don't see that as a major issue. Despite this, I think it would be helpful for the document to discuss in greater detail the uncertainty associated with the historic modeling. There is a point in the conclusions where an epi study (Ruckart et al. 2014) found an association between PCE and preterm birth, and yet the modeled exposure concentrations did not reach health benchmarks for any health endpoints. While I agree with the statement about attribution to a single chemical and exposure level, I think it would be useful to reiterate the limitations of the historic modeling.	The limitations of this epi study include relying on vital statistics data and Camp Lejeune housing records, only including births occurring in women who lived on base at the time of delivery, lack of detailed information on residential history or other maternal characteristics (e.g., alcohol consumption, weight gain during pregnancy, smoking status) not captured by birth certificates during the study period, and only modeling residential exposures to drinking water contaminants. Since drinking water exposures could occur during daily activities all over the base, some mothers categorized as unexposed may have had some drinking water exposure. This exposure misclassification bias could have distorted exposure-response trends in comparisons involving more than two levels. Regarding the limitations of the historic modeling, in the ATSDR Investigation of Environmental Exposure Section, the reader is referred to • "Analysis of Groundwater Flow, Contaminant Fate and Transport, and Distribution of Drinking Water at Tarawa Terrace and Vicinity, U.S. Marine Corps Base Camp Lejeune, North Carolina: Historical Reconstruction and Present-Day Conditions" (Maslia, et al. 2007)[39] and • "Analysis and Historical Reconstruction of Groundwater Flow, Contaminant Fate and Transport, and Distribution of Drinking Water within the Service Areas of Hadnot Point and Holcomb Blvd Water Treatment Plants and Vicinities – U.S. Marine Corps Base Camp Lejeune, North Carolina" (Maslia, et al. 2013)[40]. Chapter A of both reports provide a detailed discussion of sensitivity and uncertainty of the historical reconstruction process.

[39] Report available at http://www.atsdr.cdc.gov/sites/lejeune/docs/ChapterA_TarawaTerrace.pdf.
[40] Report available at http://www.atsdr.cdc.gov/sites/lejeune/docs/chapter_A_hadnotpoint.pdf.

Reviewer	Reviewer Comment	ATSDR Response
3	The assessment does provide results from elaborate reconstructions of historical water concentrations. This is a definite strength of the assessment. Exposures by several routes were considered. It is obvious that the exposure assessment was a large part of this work. One minor note, was lactational transfer of solvents to infants evaluated in this document? I did not find it.	Lactational transfer was not evaluated as an exposure pathway in this assessment. While transfer of VOCs from maternal blood to breast milk can occur to a limited extent, direct contact with water is the primary source of exposure to these VOCs. For that reason, exposure through breast milk was not included in the assessment.
4	Yes. The assessment adequately describes the nature and extent of contamination.	Thank you for the confirmation.
5	This public health assessment is excellent. Very detailed but organized in a manner for experts to follow. ATSDR excels in public health scenarios and statements so it will be interesting to see how these details will be presented in a manner for non-technical public. This reviewer did have concerns that with this very detailed and carefully conducted risk evaluation that non-quantitative words such as slightly, low, high appeared in the document. These words need to be removed or placed into context. As a reviewer, I feel these additions weaken an excellent document. Please see my specific comments for examples on points 1,2,3,7,8 and 20 on the attached document.	ATSDR agrees. We have reviewed the document to clarify uses of the specified types of qualifiers.
2. Does the PHA adequately incorporate the consideration of uncertainty in the discussion of exposures and associated health impacts?		
1	As incorporated in my track-changes and document comments, the document tends to emphasize uncertainties that are inherent in any/every risk assessment, e.g., detailed listing of the adjustment or uncertainty factors for the MRLs or RfDs used, but fails to adequately discuss some of the important strengths/limitations and uncertainties specific to the site-related work. Particularly, I would like to see more discussion of the strengths and limitations of the epidemiological studies conducted so far. Having these studies is a critical asset for this PHA. There are always limitations in an epi study but it is quite powerful information when the studies find that populations exposed on base are experiencing increased risk.	From the perspective of dose and risk calculations, ATSDR believes the greatest uncertainty/limitation lies with using modeled exposure point concentrations rather than measured data, as detailed in the Limitations section and Appendix F. We understand the value of having epidemiologic data on the same population and will attempt to make effective reference to those results in this document. The epidemiological studies conducted thus far are described in the PHA as background, with the study findings serving to provide perspective on actual health outcomes observed in populations of concern. This document was not intended to be a validation of the findings from the epidemiologic studies. We will expand the discussion about both the concordance and the gaps between the epidemiologic endpoints that were examined and the predicted effects from our toxicological evaluation. However, it is not our intent to conduct an exhaustive review of the strengths/limitations and uncertainties for each of these studies and will refer the reader to those publications for that specific information. A statement regarding the limitations of using epidemiologic data to establish causal relationships has been included in the document.

Reviewer	*Reviewer Comment*	*ATSDR Response*
	The issue of mixture risk is glossed over as an uncertainty (pg 47) (currently pg 31). Given that ATSDR has done so much work on methods for mixture assessment, it deserves further discussion and explanation.	A discussion about exposure to the mixture of chemicals in Camp Lejeune water systems was included in a separate section. The basis for this discussion is contained in the ATSDR Interaction Toxicological Profile, which summarizes mixtures data that includes on TCE, PCE, and Vinyl Chloride. Detailed summaries of those analyses have been inserted into Appendix D. The outcome of that evaluation is that use of the additive approach used in this assessment is the most conservative (health-protective).
2	There is a fair bit of discussion of uncertainty, and this is good/acceptable. It would be better, however, to highlight/spend more time discussing the lack of understanding of interaction between site contaminants. It is currently listed last in the limitations and isn't discussed very much. See also in-text comment.	A discussion about exposure to the mixture of chemicals in Camp Lejeune water systems has been included in a separate section. The basis for this discussion is contained in the ATSDR Interaction Toxicological Profile, which summarizes mixtures data that includes on TCE, PCE, and Vinyl Chloride. Detailed summaries of those analyses have been inserted into Appendix D. The outcome of that evaluation is that use of the additive approach used in this assessment is the most conservative (health-protective).

Reviewer	Reviewer Comment	ATSDR Response
	The assessment rightfully identifies a number of important limitations and uncertainties in the lead section. Given this, more sensitivity analyses are needed to examine whether these uncertainties are important enough to justify further data collection/intervention.	ATSDR does not believe a sensitivity analysis is needed to justify further data collection/intervention because programs are already set up for continued monitoring of lead in tap water and continued monitoring of children's blood lead levels (BLLs). Specifically, 1. As stated in the main text of this document, since 2013, MCB Camp Lejeune has followed its Environmental Standard Operating Procedure which requires increased monitoring frequency of drinking water and an immediate followup sample to be collected following any detection of an inorganic contaminant, including lead (MCB Camp Lejeune 2013). This is a voluntary action undertaken by the base—an action that goes beyond regulatory requirements. In 2014, as its school and daycare sampling strategy, MCB Camp Lejeune began to follow the USEPA 3T guidance (MCB Camp Lejeune 2014). Camp Lejeune also follows the regulatory monitoring requirements set forth in USEPA's Lead and Copper Rule (USEPA 2012c). 2. The Pediatric Lead Poisoning Prevention Program (PLPPP) states that all Military Treatment Facilities must operate a formal pediatric lead screening program that focuses on children aged six months to six years due to their increased susceptibility to high BLLs. Following the draft release of this document in July 2014, the Navy and Marine Corps Public Health Center provided ATSDR with a Camp Lejeune summary report of BLLs in children collected as part of the PLPPP from March 2004 to October 2015 for the Camp Lejeune area. The results of this report have been added to the main text of the document. Overall, although there are limitations stated in Camp Lejeune summary report, only a few elevated BLLs[41] in children (i.e., 5 of 4,354 children tested) were found between March 2004 and October 2015 (NMCPHC 2015).

[41] Elevated BLL is based on the reference level in place at the time of testing. NMCPHC used a BLL reference value of 10 µg/dL for the years 2004 through 2013 and found two children with elevated BLLs. NMCPHC used the current BLL reference value of 5 µg/dL for the years 2014 through 2015 and found 3 children with elevated BLLs (NMCPHC 2015).

Reviewer	*Reviewer Comment*	*ATSDR Response*
3	Uncertainty is mentioned in various places in the document. Because epidemiological studies and a classical style site risk assessment were both conducted for the site, health effect conclusions drawn from the risk assessment need to be placed in context with the epidemiological findings. Drawing conclusions about health risks from the risk assessment numbers, per sec, is uncertain, especially if derived from animal studies. I am not sure what type of uncertainty analyses was conducted with the fate and transport modeling, but is probably important to put bounds on the possible water concentrations.	As noted there are many sources of uncertainty in this assessment. The revised text expands the discussion on those sources. There are also uncertainties in the epidemiologic studies, which have been expanded in the revised document. The estimated water concentrations are mean values, but are subject to uncertainties in the modeling and in the limited amount of actual measured water concentrations.
4	No. The PHA does not adequately incorporate the consideration of uncertainty (or variability) in the discussion of exposures and associated health impacts. Detailed comments are included in the markup as comments. In particular: A. It should be clearly documented the extent to which the exposure estimates are "conservative" or "central tendency." It may make sense to include both estimates.	For the purposes of displaying the comparison of estimated exposure doses to effect levels from experimental or epidemiologic studies, Figures 11-16 will be revised to incorporate both the "Central Tendency" and the "Upper End" exposure doses/concentrations. Those comparisons will be made using Human Equivalent Doses and Concentrations, and will focus on the scenarios that are of greatest impact (i.e. young children, workers, Marines-in-training).
	B. Overall, there needs to be a characterization of the degree of uncertainty & variability. Particularly for variability, it needs to be communicated clearly how relatively small the degree of variability is (e.g., exposure is described as "upper bound," but the exposure at the central tendency is seems like it would only be slightly lower).	For the water ingestion pathway, there is actually only limited variability in the dose estimates between average and upper end exposure levels. The estimated dose from inhalation of chemical vapors from use of contaminated water is subject to a greater level of uncertainty, in part due to a larger number of input parameters with estimated values. The assessment will be revised to reflect both the average and upper end exposure levels.
	C. In several places, noted in the markup, the uncertainty in the cancer slope factor is overstated. In these particular cases – TCE, vinyl chloride, benzene – there is actually fairly high confidence that the slope factors are not unreasonable. They are either based on human data or consistent with human data, so interspecies extrapolation is not (much) a concern. Additionally, these involve less low-dose extrapolation because their consistency with human data, which are closer to the exposures of concern. Furthermore, these are genotoxic, which implies that linear extrapolation provides a reasonable estimate of risk.	The statements regarding cancer slope factors and inhalation unit risk values reflect general uncertainty descriptions for assessment of risk for carcinogens that appear in EPA documents and in ATSDR guidance. The phrasing of the cancer section and Appendix D in this document has been revised to make the characterization of uncertainty more specific to the chemicals that are included in this assessment.

Reviewer	*Reviewer Comment*	*ATSDR Response*
5	In most places, I feel the document does a good job of discussing uncertainty especially for exposures. Please see some specific comments such as point 12 and 16 in the attached file on use of uncertainty factors (document is a bit uneven in providing justifications). Please see also my comments on point 22. (my comment on point 12 in repeated below for emphasis) Point 12 "Starting page 24. When uncertainty factors are given, please provide a brief explanation for the basis of choosing the factors used for each of the endpoints. Some places in document this was very clear in others no details were given."	The basis for each uncertainty factor has been added in the Toxicity Section for those that were lacking.
3. Are all relevant environmental and toxicological data (i.e., hazard identification, exposure assessment) being appropriately used?		
1	See specific comments in the draft report. In general, I found that the environmental and toxicological data have been appropriately described. It is hard to say whether the data are appropriately used without a thorough review of the algorithms and results of the exposure and risk calculations.	The equations used in the risk calculations are shown in Appendix C. A summary of the underlying calculations from the spreadsheet file are also shown in the Appendix section. An independent review of the dose calculations has been conducted to verify the calculated doses and risk.
2	It is not clear to me whether the drinking water intake assumptions supporting the various concentration benchmarks presented in Table 1 account for the active military population. My understanding is that MCLs and other concentration-based metrics make assumptions about intake that reflect typical adult/child residential populations. If these concentration benchmarks are used in consideration of active duty military populations, it would be better to have some assurance that their typical drinking water intake rates used to develop these values are comparable or less than what one would expect to see in the average adult (which, based on other parts of the report, they appear not to be). I would suspect, in a place like SE North Carolina that can have fairly hot summers, active duty personnel may be in the practice of drinking much more water than the average adult. If this is the case, it is likely that exposure assumptions used to make these comparisons are not well suited for this population and thus MCLs and other water standards would not be very meaningful for selected subpopulations. Further – an appendix detailing the calculation of EMEGs and RMEGs should be provided (demonstrating the assumptions employed to derive these values).	ATSDR screening values (EMEGs, RMEGs, CREGs) are based on standard methods described in the Public Health Assessment Guidance Manual (PHAGM; http://www.atsdr.cdc.gov/HAC/PHAManual/appf.htm). These screening values are used to identify Chemicals of Concern in the health assessment. The MCL values are presented for the purpose of providing a regulatory context for the health assessment, and were not used to eliminate chemicals for consideration. All of the chemicals presented in this assessment (benzene, trans-1,2-DCE, PCE, TCE, and vinyl chloride) were further evaluated using the exposure assumptions presented in Tables 3 and 4. These exposure assumptions were selected based on upper end estimates of water use and consumption, which would take into consideration the warmer summer temperatures and also conditions during intensive Marine training.

Reviewer	*Reviewer Comment*	*ATSDR Response*
	The assessment examines persons in contact with site-related contamination prior to the year 2000 (in many cases, decades before) – with that in mind, it probably makes sense to use exposure factors derived based upon population characteristics/behavioral patterns (e.g. body weight, life expectancy, etc.) from the earlier edition of the EPA Exposure Factors Handbook (1987), rather than the current one (2011), which incorporates data from population surveys that occurred years after the end of the period of exposures under study.	ATSDR policy is to use the most current exposure information in the 2011 EPA Exposure Factors Handbook as the most robust data source for our health assessments. It is acknowledged that there may be differences in the adult body weight (71.8 kg vs 80 kg; representing a 11% change) and in life expectancy (70 yrs vs 78 yrs; representing a 11% change) if data from the earlier EPA Exposure Factors Handbook were to be used. However, even if the older exposure values were to be used, there would be very minor differences in the exposure estimates, and would not result in any changes in our conclusions about the health impact.
	Given the magnitude of the hazard indices (HIs), they should be segregated by target organ, which will give a more refined/precise estimate of hazard (see EPA RAGS A, page 8-14).	Target organ hazard indices have been included as an appendix and a summary provided in the text.
	It would be helpful to justify the 3-year averaging time for children, and possibly non-military adults on base (those spending more than 3 years). It makes sense for military personnel and does not require additional justification.	The 3 year averaging time was derived from base housing records and accounts for the Marine and Naval personnel entire base population, including children of military personnel who lived on base in family housing. The worker population (15 year) was also derived from base housing records but through discussions with the CAP, most of the more “permanent” workers lived off-base where their children would not be exposed.
	The characterization of risk via the dermal pathway does not consider GI absorption, as recommended in EPA RAGS E. The current draft just multiplies the dermal exposure dose by the oral slope factor, which is inappropriate.	EPA RAGS Part E recommends that GI absorption rates be used to adjust the oral toxicity criteria from an administered dose to an absorbed dose. In the case of the organic compounds assessed in this document, the default absorption rate is considered to be 100%. Therefore, no adjustment of the toxicity value was made, including the oral slope factor. In that case, the multiplication of the dermal exposure dose by the oral slope factor is the appropriate calculation of dermal risk.
	More clarity is needed for the explanation of how TCE’s mutagenic properties re: kidney cancer were handled vs. other affected organs. It is only mentioned in text, but the specific quantitative treatment is not provided. I have noted in an in-text comment the EPA guidance for completing such calculations.	The text describes the methodology. A screenshot of the revised EPA spreadsheet that was used to calculate the TCE cancer doses for each exposure group is presented in Appendix C with the other dose equations.
	I am perplexed by what is being done for the ingestion pathway calculation mentioned in the cancer risk characterization section and modeled in Appendix C (page 85 at the top) (currently pg 82). No reference for this methodology is provided, the equation doesn’t make sense, and inadequate justification is provided.	It appears that the comment is directed to the ingestion and inhalation equations for vinyl chloride, which includes a time-independent dose term for early life exposure to children. This method of calculating exposure beginning at birth is described in the EPA Toxicological Review of Vinyl Chloride; EPA/635R-00/004; 2002. The methodology is described in Section 5.3.5.1. The text in Appendix D has been modified to include an excerpt from that document that describes the basis for this term and example calculations.

Reviewer	*Reviewer Comment*	*ATSDR Response*
3	Using PBPK models for route-to-route extrapolation is probably ok at the level of how you are using it. However, technically, the toxic endpoints depend on what is tracked, such as metabolites. That is, for cancer the dosimetrics would be metabolites for TCE and for fetal cardiac malformations, maybe the same. I know you used the PBPK model to do route-to-route extrapolation for the parent chemical. Good job, consider including work in an Appendix.	The methodology for the route-to-route extrapolation for TCE from ingestion to inhalation is described in the EPA IRIS file (http://cfpub.epa.gov/ncea/iris/iris_documents/documents/subst/0199_summary.pdf) and in the ATSDR Toxicological Profile (http://www.atsdr.cdc.gov/toxprofiles/tp19.pdf).
4	No. In addition to the comments for question #2, my comments are as follows: A. The methodology for making comparisons between exposure and toxicity in the case that the screening values are exceeded should be laid out – currently, the methodology is virtually absent. My detailed comments are in the markup, but in sum, a table of the PODs should be made, and the PODs themselves should be adjusted to human equivalent doses or concentrations (for TCE, the 50th percentile should be used, since it is most analogous to other human-equivalent PODs).	The screening methodology is presented in Appendix A. ATSDR screening values (EMEGs, RMEGs, CREGs) are based on standard methods described in the Public Health Assessment Guidance Manual (PHAGM; http://www.atsdr.cdc.gov/HAC/PHAManual/appf.htm). These screening values are used to identify Chemicals of Concern in the health assessment. Table 5a and 5b have been inserted to present the Point of Departures (PODs) for all of the chemicals, ingestion and inhalation
	B. I also suggest that ATSDR consider whether, for TCE, the route-to-route extrapolated PODs should also be included.	Tables 5a and 5b have been inserted to present the Point of Departures (PODs) for all of the chemicals, ingestion and inhalation.
	C. These comments apply to Figures 11-16. In these figures, it is also suggested both “central” and “upper bound” exposure estimates be presented.	For the purposes of displaying the comparison of estimated exposure doses to effect levels from experimental or epidemiologic studies, Figures 11-16 will be revised incorporate both the “Central Tendency” and the “Upper End” exposure doses/concentrations. Those comparisons will be made using Human Equivalent Doses and Concentrations, and will focus on the scenarios that are of greatest impact (i.e. young children, workers, Marines-in-training).
5	Yes, the document is extremely well done and logical in flow and presentation. Please see comments on point 13 and 14 in the attached document for specific comments on how mode of action information was included. This was very uneven. See especially lack of information for application of the ADAF.	For those chemicals with a known mode of action, that information will be included. Additional information about the application of the ADAF has been inserted into the Toxicological summary for TCE.
4. Does the public health assessment accurately and clearly communicate the health threat posed by the site?		
1	Yes.	Thank you for the confirmation.
2	It is difficult to judge this, at least until some of the other concerns expressed here are resolved.	Hopefully our revisions allay the concerns you have regarding accuracy and clarity.

Reviewer	*Reviewer Comment*	*ATSDR Response*
3	I am having some trouble with the language used for interpreting the historic exposures to chemicals. In my experience site specific risk assessments are generally used for remediation purposes. In this case, the risk assessment calculations (results) are translated to probable or possible health effects. I do think that if you want to do this you are compelled to compare the site-specific epidemiological data that exists with the risk assessment results.	ATSDR's PHA process is aimed at evaluating whether harmful exposures had, are, or might be occurring based on site-specific conditions in the past, present, or future. While general approaches for calculating exposure doses and estimating cancer and noncancer risks are similar, the PHA process is distinct from EPA's risk assessment process which is aimed at evaluating the need for remediation, as the reviewer notes. As such, as noted in the PHA, quantitative and qualitative descriptions are included to provide public health perspective. Health study data exist for the Camp Lejeune population (with acknowledged strengths/limitations), which is not always the case and ATSDR's intent is to provide a balanced review of the documented and potential health risks in the site community.
	I was wondering if the epidemiological evaluations could be brought to bear in a more meaningful fashion? For example, were there any causative site- specific epidemiologic findings obtained? If only associations were observed, were there any associations between the epidemiological findings and the risk assessment findings (e.g., cancer endpoints, non-cancer, and heart development)? This seems like a special situation exists for you to have both risk assessment and epidemiological work done for this site.	The reader is referred to the various ATSDR health studies. The authors felt a brief mention of their findings was sufficient for the intent of this document. Findings from the studies that mirrored the health effects found in exposure literature were highlighted in the conclusions.
4	Partially. My view is that the conclusions are sound in that it is likely that observable toxicity could have resulted from the exposures being considered. However, these conclusions could be better supported if my recommendations for questions 2 & 3 are followed.	For the purposes of displaying the comparison of estimated exposure doses to effect levels from experimental or epidemiologic studies, Figures 11-16 will be revised incorporate both the "Central Tendency" and the "Upper End" exposure doses/concentrations. Those comparisons will be made using Human Equivalent Doses and Concentrations, and will focus on the scenarios that are of greatest impact (i.e. young children, workers, Marines-in-training).
5	Yes, I would say that this is a thoughtful, detailed discussion of the health threats posed by the site but it is for a technical audience. See my concerns about using qualitative words without definition – very confusing? (See comments on points 1,2,3,7,8 and 20. See also comment on point 18 about other potential Pb impacts in adults.)	The phrases that used undefined qualitative words have been removed and those statements made clearer.

Reviewer	*Reviewer Comment*	*ATSDR Response*
5. Are the conclusions and recommendations appropriate in view of the site's condition as described in the public health assessment?		
1	I think the conclusions and recommendations are appropriate as far as they go but is there something more general to say? Conclusions 1 – 5 are presented piece-meal. Are there any overarching comments/discussion to include? For example, it may be useful to say something about the current environmental health operations on the base. Are systems in place to detect and prevent future contamination events?	The base is actively engaged in detecting and preventing future exposures. The lead portion of this PHA references the bases' 2013 environmental SOP where they outline their sampling strategies that go beyond current regulations. The base also follows EPA's 3T guidance which is intended to reduce lead consumption in schools and daycare facilities. The purpose of the PHA was to evaluate past exposure to contaminants of concern. The PHA does state that the contaminated wells were closed and that current wells are routinely monitored.
2	Each of the "Next Steps" sections concludes with "Concerned persons should discuss any health concerns with their health care providers." This seems inadequate and assumes much in the way of environmental health expertise on the part of health care providers. This is a dangerous assumption and in my opinion is likely to lead to a good deal of frustration among potentially-affected persons. I would suggest that ATSDR establish a hotline to respond to queries related to site exposures (I see that such a hotline is available, but just for lead).	The Next Steps sections have been revised to read, "Concerned persons can discuss any health concerns with their own healthcare providers, who may refer them to an Association of Occupational and Environmental Clinic (AOEC), which has doctors who specialize in occupational and environmental medicine. A list of AOEC locations is available at http://www.aoec.org/."
	Re: conclusion 4 – it is good to do a cancer epi study, but what about other health endpoints? It would be a mistake to ignore the other possible outcomes.	ATSDR has studied other health endpoints (e.g., adverse birth outcomes such as neural tube defects, mortality data), as described in the ATSDR Health Studies section of the PHA.

Reviewer	*Reviewer Comment*	*ATSDR Response*
	The recommendations for lead are not well referenced and do not seem to be very meaningful. I have doubts about their effectiveness in mitigating site-based lead exposure (since they seem to be entirely based around behavioral changes of potentially exposed persons).	Recommendation 1. The appropriate reference was added. Recommendation 2. Refers to a figure, which has been referenced and cited appropriately in Appendix H. Recommendation 3. Refers to a table and figure, which have been referenced and cited appropriately in Appendix H. Recommendation 4. Reference already provided in the document. Recommendation 5. This recommendation was split into two separate recommendations, and appropriate citations to the guidance were added. Note that if lead is present in drinking water at MCB Camp Lejeune, the contamination occurs after the water leaves the treatment plants. Groundwater is not the source of lead in the drinking water. Even so, lead found in tap water can come from the corrosion of older fixtures or from the solder that connects pipes. When water sits in leaded pipes for several hours, lead can leach into the tap water. For MCB Camp Lejeune, routine and regulatory monitoring of lead in tap water occurs that includes resolving problems if elevated lead levels are found (see lead Recommendation 5). In addition to this monitoring, the first four lead recommendations provided by ATSDR give people ways to mitigate potential exposures to lead and are appropriate as good public health practice measures.
3	I think you can state that the site was a historic public health concern. But to use risk assessment endpoints, derived from animal studies, and state, with some certainty that humans are at risk is probably beyond the scope of science. For example, fetal cardiac heart malformations and TCE seem very uncertain since we were unable to reproduce the findings, when we included Paula Johnson in a study and a boarded pathologist and blinded the study. Stronger statements about the strengths and weaknesses of the epidemiological work are needed to better support your human health statements. Perhaps even explanations of what the epidemiological findings mean, not merely stating the findings. If you could do this, and tell a story and combines the findings of the epidemiological and toxicology risk assessment, it would be a much stronger document. You may need to break new ground. For example, in human occupational studies are there any toxicology findings similar to information you report for epidemiological or toxicology risk assessment? I think this is an opportunity to do an innovative health evaluation.	We understand the value of having epidemiologic data on the same population and have attempted to make effective reference to those results in this document. The epidemiological studies conducted thus far are described in the PHA as background, with the study findings serving to provide perspective on actual health outcomes observed in populations of concern. This document was not intended to be a validation of the findings from the epidemiologic studies. We will expand the discussion about both the concordance and the gaps between the epidemiologic endpoints that were examined and the predicted effects from our toxicological evaluation. However, it is not our intent to conduct an exhaustive review of the strengths/limitations and uncertainties for each of these studies and will refer the reader to those publications for that specific information. There is a general acknowledgement about the limitations of using epidemiologic data to establish causal relationships.

Reviewer	Reviewer Comment	ATSDR Response
4	Yes. The conclusions and recommendations are appropriate in view of the site's conditions as described in the public health assessment. However, as noted above, enhancing the discussion of uncertainty and variability will better support the rationale for these conclusions and recommendations.	The discussion regarding uncertainty and variability has been expanded.
5	I agree with the overall conclusions of the assessment with the inclusion of edits that I provide in my written comments attached. Please see also my comments on the actions to be taken based on these conclusions. I feel additional actions are needed.	ATSDR has reviewed and incorporated changes throughout the document. Specific comments on our conclusions and recommended actions are contained later in this appendix (see Reviewer 5 additional comments).
6. Are there any other comments about the public health assessment that you would like to make?		
1	It may be useful to address differences between the 1997 assessment and this PHA explicitly. The current draft discusses the historical reconstruction to some extent and does reference the epidemiological studies completed and ongoing. I notice in this assessment that you have used the 2011 Exposure Factors Handbook for numerous defaults. If risk calculations were done in the 1997 report, different defaults would have been used. A discussion about these differences will be important if you anticipate anyone will be comparing these reports.	The 1997 PHA is no longer available publicly. There is not a lot of expectation that individuals will compare the two reports. Further, this PHA is a more complete analysis of drinking water exposure and includes updated guidance. A meaningful comparison of the two reports would be difficult because the exposure evaluation process has evolved since the 1997 assessment.
-2	There is a general shortcoming in much of the document with regard to provision of references/citations to support methodologies employed in the assessment. I've tried to note some of these in my redline markup. It is especially important when the methods employed deviate from standard risk procedures that some explanation, justification and methodological origin be included/cited. One area that is especially deficient is in the cancer risk estimation section.	The references have been reviewed to ensure that the various guidance documents and other citations are included. We do not consider the methods used in this assessment to be a deviation from standard methods, but rather the application of specialized approaches to evaluate somewhat unique exposure conditions. One methodology that has required additional presentation is the adjustment for estimating cancer risk for young children. The IRIS file for vinyl chloride recommends a 2 fold-adjustment for lifetime exposures that begin at birth. However, a different method for calculating cancer risk is recommended when evaluating less-than-lifetime exposures, which is described in Section 5.3.5.1 of the EPA Toxicological Review of Vinyl Chloride; EPA/635R-00/004; 2002. The methodology uses a time-independent dose term for early life exposure to children that is added to the typical exposure duration term in the risk calculation. Appendix D has been modified to include an excerpt from that document that describes the basis for this term and example calculations.

Reviewer	*Reviewer Comment*	*ATSDR Response*
	The section entitled, "ATSDR Investigations of Environmental Exposures" could be organized more intuitively (and possibly improved simply with the inclusion of clear subheadings). As it stands, the order of presented elements is as follows: Discussion of reconstruction of historic contamination estimates, discussion of environmental guidelines, and then area-specific discussions that seem to haphazardly combine background information about specific chemicals, approaches to the modeling of exposure (with focus on temporality), and discussions of changes in contaminant concentrations over time. No synthesis is provided on a site-by-site basis.	This section was renamed "ATSDR Evaluation of Environmental Exposures" and was made its own main section with the screening process and area evaluations as subsections. Bullets were added to the chemical discussions. The background information about the chemicals was moved to a text box under Table 1.
	It would have been useful to send the spreadsheets used to derive the exposure estimates, to clearly indicate values employed in the models and their rationales.	The spreadsheets are available to anyone who requests them.
	The background section on lead is poorly referenced and does not include adequate citation to the scientific literature needed to support the statements being made.	Where citations are requested in the text by Reviewer #2, the appropriate references were added.
	More detail is needed about the sampling locations for lead. The document notes that samples were taken "for the Hadnot Point, Holcomb Blvd, Rifle Range, and MCAS New River service areas. These four water treatment plants provide drinking water to family housing units, barracks, and other buildings." Were these samples taken at the treatment plants? Or from residences? It would be much more informative to know what residents are experiencing at the tap – this is a better indicator of potential hazard. Regardless of what was done, it needs to be clearly communicated in the document.	Residential samples were taken at the kitchen tap. The samples were taken after water was stagnant in the lines for 8 hours to represent a worst case sample. Table 7 also provides a brief description of sample location for those tap water samples that exceeded 15 ppb. At the start of the *Lead Levels in Camp Lejeune's Drinking Water* section, see the first three sentences, which state "MCB Camp Lejeune tests onbase tap water for lead. Samples are taken from locations where people can be exposed. For example, when MCB Camp Lejeune samples onbase residences, it takes the samples from the kitchen sink." The wording in the bullets following these sentences was modified to clarify the samples were from the tap. Because the confusion may also have come from Table 7, which provides the tap water data by service area, a note was added to the table that states: "Tap water samples were collected from these service areas. These data do not represent samples collected from the distribution facility, but from the exposure point (like a kitchen sink)."

Reviewer	Reviewer Comment	ATSDR Response
	When IEUBK was run, only drinking water lead parameters were site-specific. Given the nature of the site (older military base), is it reasonable to perform some sensitivity analyses looking at lead exposure via other pathways? Soil?	As stated in the main text, ATSDR determined in its 1997 PHA that lead exposure in drinking water at MCB Camp Lejeune was an immediate health concern (ATSDR 1997). The primary focus of the lead evaluation in this PHA is to update the 1997 assessment by evaluating the public health significance of more recent exposure to lead in drinking water. ATSDR notes it also changed the soil default concentration in the IEUBK model. ATSDR set the value of lead in soil to 100 ppm, which is greater than the lead levels found at Camp Lejeune in a wide range of soil types from both developed and undeveloped locations (CH2M HILL 2011). Overall, the report found that background soil levels at the base ranged from 0.5–55 ppm (CH2M HILL 2011). ATSDR notes also that USEPA recommends < 100 ppm lead in soil for gardens (USEPA 2014). ATSDR changed the lead in drinking water levels, the soil level, and the BLL reference level for risk estimation. ATSDR did not have any other site-specific data to justify changing the other parameters from their default IEUBK settings.
	The lead assessment isn't very thorough – it appears that ATSDR has just run IEUBK with a few lead concentrations (some of which seem to be randomly selected). This doesn't seem to go far to describe the risks to the base population. Also, could anything be done to make sense of lead exposures for adults? At least quantify drinking water exposures… do something!	ATSDR updated Table 7 to incorporate the model results for all drinking water results at MCB Camp Lejeune that were over the 15 ppb lead action level. As stated in previous responses to comments, if lead is present in the drinking water at Camp Lejeune, the contamination occurs after the water leaves the treatment plants. Groundwater is not the source of lead in the drinking water; the lead is likely from the corrosion of older fixtures or from the solder that connects pipes. ATSDR does not know what percent of the barracks, housing units, and other drinking water sources on the base have older fixtures or solder that may contain lead. Although routine, regulatory monitoring of tap water occurs, not every drinking water tap is sampled. Thus, ATSDR cannot quantify the risks to the base population overall. ATSDR focuses its lead exposure evaluations on children and the fetuses of pregnant women, both being the most susceptible populations. ATSDR notes that the USEPA developed the Adult Lead Methodology (ALM) to predict the risk of elevated blood lead levels in nonresidential settings, such as the workplace. For adult women's exposures to soil; however, the ultimate receptor is the fetus. More information about USEPA's adult lead methodology can be found at http://www.epa.gov/superfund/lead/products.htm.

Reviewer	*Reviewer Comment*	*ATSDR Response*
	Throughout the entire assessment, I've made numerous comments and suggested minor edits in red-line form in the attached version of the document.	Thank you for the comments and edits. ATSDR has reviewed and incorporated them into the PHA, where appropriate.
3	I do appreciate the incredible efforts of ATSDR and understand some of the difficulties. From a scientific point of view perhaps a case study (lessons learned) can be completed evaluating the results from conducting a risk assessment and epidemiological assessments. It is obvious this population was a highly exposed population. What is required for a site-specific epidemiological study to be robust enough to provide sound results?	ATSDR has conducted five health studies at MCB Camp Lejeune. A brief description of these health studies is provided in the Background section and Appendix F of the PHA. More information about the five completed health studies can be found in the individual studies (see Bove et. al. 2014a, 2014b; Ruckart et al. 2013, 2014, 2015).
4	No.	*No response needed*
5	I have concern about the document stopping with the recommendations in the current public health action plan pages 64 and 65 (currently pgs 60 and 61). I would suggest that more specific health surveillance should be offered for these populations especially for those with modeled and estimated repeated exposures over guideline values. Populations of concern would include those that may have had exposure during pregnancy and for which there have been recent positive epidemiological association with subsequent health impacts. See specific comments in the attached document.	In addition to the five health studies already completed at MCB Camp Lejeune, ATSDR is planning the following: • Analyze data from a health survey of Marines, naval personnel, and civilian workers at MCB Camp Lejeune as well as a sample of Marines, naval personnel, and civilian workers at Camp Pendleton. The survey also included Marine dependents at Camp Lejeune who participated in a 1999–2002 survey conducted to identify birth defects and childhood cancers for the published study of neural tube defects, oral clefts, and childhood hematopoietic cancers. • Evaluate specific causes of cancer in a planned cancer incidence study that will involve cancer registries nationwide as well as federal cancer registries.
7. The toxicological assessment of exposure to vinyl chloride including a methodology that incorporates an additional cancer risk for individuals who are exposed between birth through age 6 years old. This methodology is described in the EPA IRIS Toxicological Review of Vinyl Chloride (2000) and shown as an additional term in the equation in Appendix C. Is the inclusion of this additional cancer risk term appropriate for the assessment of less than lifetime exposure to vinyl chloride?		
1	In the EPA IRIS Toxicological Review of Vinyl Chloride (2000), a 2-fold adjustment is recommended for early-life exposure. This is found in Chapter 6 of the EPA Toxicological Review, page 59. In Appendix C of the draft PHA, an additional bodyweight adjusted intake is added to the ingestion dose equation. I do not think this is the correct way to represent the early-life adjustment for VC. I think it is more appropriate to include this adjustment with Table 3 in the main text (perhaps as a footnote, since you are using the default ADAFs for the other chemicals).	The IRIS file for vinyl chloride recommends a 2 fold-adjustment for lifetime exposures that begin at birth. However, a different method for calculating cancer risk is recommended when evaluating less-than-lifetime exposures, which is described in Section 5.3.5.1 of the EPA Toxicological Review of Vinyl Chloride; EPA/635R-00/004; 2002. The methodology uses a time-independent dose term for early life exposure to children that is added to the typical exposure duration term in the risk calculation. Appendix D has been modified to include an excerpt from that document that describes the basis for this term and example calculations.

Reviewer	*Reviewer Comment*	*ATSDR Response*
2	As noted in my comments in the previous section – I am not opposed to this consideration, but the description and justification provided are wholly inadequate. To consider its appropriateness, I would need to see a thorough explanation of the methodology and at least a reference/citation to its origins.	The IRIS file for vinyl chloride recommends a 2 fold-adjustment for lifetime exposures that begin at birth. However, a different method for calculating cancer risk is recommended when evaluating less-than-lifetime exposures, which is described in Section 5.3.5.1 of the EPA Toxicological Review of Vinyl Chloride; EPA/635R-00/004; 2002. The methodology uses a time-independent dose term for early life exposure to children that is added to the typical exposure duration term in the risk calculation. Appendix D has been modified to include an excerpt from that document that describes the basis for this term and example calculations.
	I did try to dig through the VC tox review for the description of the methodology. I did not find specific quantitative (or qualitative) recommendations for calculating risk estimates that consider early life exposures, but I did find this statement: "In general, the potential for added risk from early-life exposure to VC is accounted for in the quantitative cancer risk estimates by a twofold uncertainty factor. If exposure occurs only during adult life, the twofold factor need not be applied." (page 56 as numbered in the document) (currently pg 91). I am not certain that this is consistent with the methods employed in the Camp Lejeune Assessment – it does not appear to be, at least.	See previous note. The difference in methodology is due to the fact that the Camp Lejeune assessment is assessing less-than-lifetime exposures to vinyl chloride that begin at birth and early childhood. An excerpt from the EPA Toxicological Review document has been inserted into Appendix D to describe the methodology in more detail.
3	I think so. The risk occurs during this age because of cell turnover rates (and mutations), so theoretically this risk continues from early life exposure even if the exposure is discontinued.	Thank you for the confirmation.
4	Yes. The inclusion of the additional cancer risk term is appropriate for the assessment of less-than-lifetime exposures to vinyl chloride.	Thank you for the confirmation.
5	This reviewer is supportive of this approach. The potential for key issues is early exposure, during key developmental windows which may be able to impact later risks for cancer. Please see my specific comments on TCE and how mutagenic mode of action impacted these decisions to apply or not to apply ADAF. This needs to be modified in document either by providing more details on what was done or to apply the ADAF more widely.	As per EPA guidance on the cancer evaluation, ATSDR applied ADAF adjustments to the kidney component for the cancer slope factor and inhalation unit risk values. The approach was based on the determination that the mutagenic mode of action for TCE only applies to the carcinogenic effects on the kidney.
What is your overall recommendation on this report?		
1	Recommend with Required Changes	
2	Recommend with Required Changes	
3	Recommend with Required Changes	

Reviewer	*Reviewer Comment*	*ATSDR Response*
4	Recommend with Required Changes	
5	Recommend with Required Changes	
Recommended Changes		
1	There are many small comments and suggestions embedded in the draft document. Four more significant changes are listed below:	
	1) Expand discussion of the epidemiological studies. Include strengths and limitations, the unique value these studies offer.	The primary objective of this document is to assess the potential health impacts from exposure to chemical contaminants in drinking water. The published findings of the various epidemiological studies were summarized in the document for the purpose of further information about the investigations that ATSDR has conducted at Camp Lejeune. The health assessment was not intended to serve as a validation of the findings of the epidemiological studies. Readers are referred to the published studies for a discussion of their strengths and limitations. However, we understand the value of having epidemiologic data on the same population and have attempted to make effective reference to those results in this document.
	2) Expand discussion of mixture exposures and risks.	A discussion about exposure to the mixture of chemicals in Camp Lejeune water systems was included in a separate section. The basis for this discussion is contained in the ATSDR Interaction Toxicological Profile, which summarizes mixtures data that includes on TCE, PCE, and Vinyl Chloride. Detailed summaries of those analyses have been inserted into Appendix D. The outcome of that evaluation is that the use of the additive approach used in this assessment is the most conservative (health-protective).
	3) Re-structure the toxicity review section (pages 24-29). Reduce text detailing uncertainty factors or move these details into an appendix. It is appropriate to discuss the issues related to the uncertainty adjustments (differences between animals and humans, human variability, lack of chronic study, etc) in narrative.	The Toxicity Review Section has been moved to Appendix D, with additional discussion of uncertainty factors.
	4) In the summary and at the end of the assessment, include an overarching discussion of any topics that cut across the 5 specific questions investigated.	Providing an integrated perspective is an important objective of the document, so we review the summary portions to make sure that integration is clear.
	5) Review Appendix C and remove any equations not used in the PHA, e.g., there are dose estimating equations for inorganic chemicals but none were assessed in the PHA. Lead was evaluated with IEUBK.	The unused equations were removed.
2	See comments in this document and on the attached red-line markup of the assessment.	Thank you for the comments and edits. ATSDR has reviewed and incorporated them into the PHA, where appropriate.

Reviewer	Reviewer Comment	ATSDR Response
3	See comments about integrating site-specific risk assessment outcomes and epidemiological studies in a more meaningful way.	We understand the value of having epidemiologic data on the same population and have attempted to make effective reference to those results in this document. The epidemiological studies conducted thus far are described in the PHA as background, with the study findings serving to provide perspective on actual health outcomes observed in populations of concern. This document was not intended to be a validation of the findings from the epidemiologic studies. We will expand the discussion about both the concordance and the gaps between the epidemiologic endpoints that were examined and the predicted effects from our toxicological evaluation. However, it is not our intent to conduct an exhaustive review of the strengths/limitations and uncertainties for each of these studies and will refer the reader to those publications for that specific information. There will be a general acknowledgement about the limitations of using epidemiologic data to establish causal relationships.
4	A. Adding discussion throughout as to whether an "upper confidence" or "central estimate" is assumed – and discussing how different they would be from each other.	For the purposes of displaying the comparison of estimated exposure doses to effect levels from experimental or epidemiologic studies, Figures 11-16 will be revised incorporate both the "Central Tendency" and the "Upper End" exposure doses/concentrations. Those comparisons will be made using Human Equivalent Doses and Concentrations, and will focus on the scenarios that are of greatest impact (i.e. young children, workers, Marines-in-training). For the water ingestion pathway, there is actually only limited variability in the dose estimates between average and upper end exposure levels. The estimates of dose from inhalation of chemical vapors from use of contaminated water is subject to a greater level of uncertainty, in part due to a larger number of input parameters with estimated values. The assessment will be revised to reflect both the average and upper end exposure levels.
	B. Adding documentation as to the methodology for comparing exposure and hazard when the exposure exceeds to the screening value.	The methodology for conducting a toxicological evaluation for exposures exceeding the screening level is described in the ATSDR Public Health Assessment Guidance Manual, 2005. The text will be revised to make sure that citation is clear.
	C. In characterizing exposures above the screening values, make comparisons with PODs based on human equivalent doses/concentrations.	Tables 5a and 5b have been revised to include Points of Departure, the basis for their derivation, and their Human Equivalent doses/concentrations.
5	See attached detailed comments.	Thank you for the comments and edits. ATSDR has reviewed and incorporated them into the PHA, where appropriate.

Reviewer	*Reviewer Comment*	*ATSDR Response*
Additional General Comments		
3	I have been thinking about the Camp Lejeune Document. If it is impossible to reconcile the epidemiologic and risk assessment outcomes in a meaningful way, the risk assessment could be placed in the following context: Use a human PBPK model for the solvents and calculate steady state serum concentrations associated with the historic model predicted exposures, then simulate a human equivalent dose associated with a RfD, NOAEL, etc from an animal study. This would require animal to human extrapolation of internal dose. Then calculate the margin of internal exposure (MOiE) (plasma concentration for POD/ plasma concentration for historic exposures). If the MOiE is less than 100 or 10 then there was probable undue health risks if the animal studies are a good human health model for toxicity. This way the analyses is more on exposure and less on health risks, per sec. The technology is available to do this type of advanced analysis.	The idea of comparing Margins of Internal Exposure between the predicted human equivalent dose from the animal study to the estimated exposures to the individuals at Camp Lejeune is a very interesting approach and worthy of consideration. However, this is beyond the scope of the public health assessment process.
Additional Document Comments		
1	p.III (currently pg i) Foreword. Currently residing? Or only past residents/workers?	The PHA addresses past and current residents and workers.
1	p.IV (currently pg vii) BMDL. Check this usage in document. EPA defines BMDL as benchmark dose lower bound…signifying the dose at the lower statistical confidence limit on the benchmark dose EPA 2012 Benchmark Dose Technical Guidance EPA/100/R-12/001, June 2012	Benchmark dose lower bound is the correct term. This edit has been made in the PHA.
1	p.X (currently pg xii) Conclusions. Suggest adding a "Data and Methods" section before summarizing the conclusions. Include a summary of major sources of data, e.g., Defense Manpower Data Center, historical reconstruction of chemical concentrations in water, Exposure Factors Handbook, etc. Give an overview of the types of analyses done – chemical risk assessment, evaluation of epidemiological data from surveillance and observational research, etc. and how all the information is considered, i.e., what is your approach to integrating the evidence?	The routine format for PHAs is followed in this document. The Introduction section that precedes the page xii conclusions describes the historical reconstruction concentrations that are used. These are also elaborated upon in the ATSDR Evaluation of Environmental Exposures section. The Exposure Dose Calculations section includes information on the exposure parameters.
1	p.XI (currently pg xiii) Conclusion Basis. I like having this section.	Thank you for the comment.
2	p.XI (currently pg xiii) Conclusion 1 Basis. How about comparability with RfDs?	Comparison to RfDs was part of the noncancer health effects evaluation although not explicitly stated in the Conclusion Basis section.

Reviewer	Reviewer Comment	ATSDR Response
1	p.XII (currently pg xiv) Conclusion 2 Basis. May need more explanation here about the limitations of the study.	The Conclusion section mentions a study about the cardiac effects of TCE exposures. The limitations of this study are discussed in more detail in the Toxicity Section.
1	p.XII (currently pg xv) Conclusion 2 Next Steps. What about those concerned about pre-term birth?	Since the drinking water exposures on base ended in 1985, there is no longer a risk of preterm birth. The last babies conceived or carried on base when the drinking water was contaminated were born in 1986.
1	p.XIV (currently pg xvi) Conclusion 5. This is meant to address current conditions, right?	The sentence in question refers to current and future exposures. The sentence was modified as appropriate to clarify the exposure timeframe.
1	p. XV (currently pg xviii) Conclusion Limitations. I think this is meant to be a discussion of the conclusions overall? A subheader is needed so people don't think this is just for Conclusion 5. This is also an opportunity to make any broader, overarching comments about environmental health at Camp Lejeune or anything that bridges across the 5 separate conclusions. As far as limitations go there are also limitations in the epidemiological studies that were done (specific to each study) and given that this is a historical exposure situation, there are limitations to the types of studies that can be done. That said, having even the suggestive findings from the epidemiological studies is an unusual advantage for a PHA and more can be made of those data, I believe. Including the recent release of the male breast cancer study, 3 published studies (I haven't reviewed the mortality findings so maybe more?) have found associations between Camp Lejeune exposures and numerous health effects cancer and non-cancer. These findings are expanding our understanding of health effects of solvent exposures and justify the continuing work.	The results of the epi studies provide useful information for the PHA, but we recognize that there are limitations in those studies. One limitation common to all the epi studies is that ATSDR only modeled residential exposures to drinking water contaminants. Since drinking water exposures could occur during daily activities all over the base, some people categorized as unexposed may have had some drinking water exposure. This exposure misclassification bias could have distorted exposure-response trends in comparisons involving more than two levels. For that reason, the ATSDR epi studies used a comparison population at Camp Pendleton (CP), assuming that all marines/navy personnel at CL were exposed either residentially and/or during training and other activities and that all marines/navy personnel at CP were unexposed. The same was done for civilian workers.

Reviewer	*Reviewer Comment*	*ATSDR Response*
2	p.1 Site Description and History. It seems relevant to note what prompted the initial 1983 assessment.	What prompted the 1980 distribution system testing was the interim THM standard promulgated by EPA under SDWA in 1979. What prompted the initial site assessments in 1982-1983 were concerns about possible toxic waste source areas on base such as landfills, storage tanks and tank farms, and likely also the discovery of high levels of TCE in the Hadnot Point treatment plant finished water, and high levels of PCE in the Tarawa Terrace treatment plant finished water. Further details are described in Chapter A of the ATSDR's 2013 "Analysis and Historical Reconstruction of Groundwater Flow, Contaminant Fate and Transport, and Distribution of Drinking Water within the Service Areas of Hadnot Point and Holcomb Blvd Water Treatment Plants and Vicinities – U.S. Marine Corps Base Camp Lejeune, North Carolina" (page A17 in the Investigations and Occurrence of Groundwater Contamination section of Chapter A).
2	p.1 Site Description and History. More detail on what types of waste would be helpful.	In response to a previous comment, this sentence has been deleted from the PHA.
2	p.1 Site Description and History. A brief summary of those operations and practices would help build context for the reader.	Faye et al. 2010, 2012b provides more detail on the base's past disposal practices and operations. Respectfully, we do not to add more non-exposure evaluation detail to an already lengthy report. The reference is included at the end of the sentence in question.
1	p.4 ATSDR Health Studies. Are there general strengths/limitations of these studies that should be discussed here, e.g., related to study design?	See above.
1	p.4 ATSDR Health Studies. Why is it limited in statistical precision?	As stated in the cited reference, the limited statistical precision is due to the wide confidence intervals in the odds ratio for the association between exposure and birth outcomes.
2	p.5 ATSDR Health Studies. Brief summary?	The fifth health study is completed. The PHA has been updated to include a summary of the findings of the male breast cancer study and link to the full study.
2	p.6 ATSDR Investigations of Environmental Exposures. Do you mean dose-response metrics? "Health guidelines" isn't very specific.	The sentence was changed (italic section added): Environmental Guidelines are media-specific substance concentrations ATSDR derives from health guidelines (MRLs, RfCs, RfDs), which integrate default exposure assumptions *and dose-response criteria from toxicological studies.*
5	Page 7, 1st paragraph (currently pg 8). Need to add a few more critical points. For example on line #24, the text discusses "low concentrations" of benzene in drinking water for decades. It is important to add values or range of values to ensure understanding of what "low" means.	The intent of the statement was to indicate that benzene contamination did continue beyond 1985. The description of the levels as being low has been removed.

Reviewer	Reviewer Comment	ATSDR Response
5	Page 7, 1st bullet point (currently pg 8, 2nd bullet). Why was 85% used rather than 90-95% as is frequently used in risk assessment?	To avoid confusion, the text was shortened to explain that 3 years was used for consistency with the ATSDR health studies' exposure duration. The reason for selecting this exposure period is described later in the Health Effects Evaluation – Exposure Dose Calculations section: The tour-of-duty data from base housing records show the mean tour of duty time as 21.3 months and the median time spent at the base as 18 months. ATSDR determined that 85% of the active duty Marines and their families lived onbase for 3 or fewer years (Bove 2013). Using this information, a 3-year exposure duration is considered a conservative onbase-time estimate for most Marine personnel and their families.
	The text says "presence of benzene at low concentrations in the drinking water supply is estimated to have continued until 1996". However, on page 10, Figure 3 shows values for benzene until 1946 over the CREG cancer risk guide. How is low defined? Needs to be modified.	To clarify "low", the range of estimated concentrations was added to the PHA.
1	p.7 Table 1. Why are some chemical names in bold and others not?	This was corrected so that none of the chemical names are bold.
1	p.7 (currently pg 8) Hadnot Point Water Supply Area. Not sure what is meant by "followed by"? Is that the timing of the first estimated exceedence? This is not clear.	The text was clarified to say that the first estimated detections of the other chemicals occurred later.
2	p.7 (currently pg 8) Hadnot Point Water Supply Area. This isn't presented very clearly, and this is an important detail of the exposure assessment. What does the distribution of time spent on base look like? Some descriptive statistics would help me react to this. What did the tails look like? Without knowing more, 3 years sounds reasonable as an assumption for most active duty personnel, but not for the "more highly exposed population". ** I've come back to this section, now that I've read more about this below – I'm not sure why this discussion is even included in this section – it is explained more clearly below in the exposure assessment section. **	To avoid confusion, the text was shortened to explain that 3 years was used for consistency with the ATSDR health studies' exposure duration.

Reviewer	*Reviewer Comment*	*ATSDR Response*
5	Page 8, 1st paragraph. Good choice to use monthly averages versus 3yr averages. I probably would have also done peak values to see how high these values might have been. Unclear about maximum concentration plotted on Figure 3 – please clarify calculation. Relate to this and subsequent figures. Perhaps foot note is needed for these figure legends or reference to specific section of the document where this is discussed?	The modeling of the water concentrations had outputs of monthly estimates, so those represent the peaks. The maximum concentration shown with the dot is the highest reading for any 1-month period.
2	p.8 Hadnot Point Water Supply Area. Unclear. What do you mean by this? If this is a reference to an approach presented more clearly elsewhere in text, direct the reader to that passage.	The term water supply area refers to the area that received drinking water from the Hadnot Point water treatment plant.
2	p.8 (currently pg 7) Benzene. Do the background bits on each of the chemicals belong here? Seems like the text could be streamlined and this could be presented earlier (not in a site-specific section) or in an appendix.	The chemical background information was moved to a text box below Table 1.
2	p.8 Benzene. How often? Half of the time? Once? The whole time? On average? It would help to know more about the variability, especially since you are talking about a 33 year period.	As shown in Figure 3, the estimated concentrations of benzene consistently exceeded the CREG from 1963 to 1996.
1	p.8 Benzene. Reported by whom? It seems you do not believe the 2500 ppb report is valid? Why?	Maslia et al. (2013) discusses sampling issues with this specific reported benzene value and with all historical water-quality sampling data at USMC's Camp Lejeune. The laboratory analysis noted that the 2,500 µg/L benzene sample "appears to have been contaminated with benzene, toluene, and methyl chloride" (JTC Environmental Consultants 1985). Further, it was noted that this data point is "not representative" (U.S. Marine Corp Base Camp Lejeune Water Document CLW #1356). It should be noted that this measurement was recorded at a time (November 1985) when it was reported that all contaminated water supply wells had been shut down for the past year.
2	p.8 Benzene. I'd be concerned about the validity of this, too. Is there recordkeeping that would support the notion that odor and taste thresholds were never exceeded (i.e. people never reported unusual odors/tastes)? That event happened 30 years ago – how can we be sure nothing like this happened? I'd want to be certain this is an unreliable measurement before fully dismissing – it could be indicative of substantial temporal variability in contamination.	We have no information about taste or odor complaints. We are just comparing ATSDR's historical reconstruction concentrations to odor thresholds that are reported in the literature.

Reviewer	*Reviewer Comment*	*ATSDR Response*
1	p.8 (currently pg 9) Benzene. How do we know? Need more explanation here.	As discussed earlier in the paragraph and shown in Figure 3, the maximum estimated benzene level was 12 ppb, which is well below the taste/odor threshold of 500 ppb.
5	Page 8, benzene section. Use of words such as "slightly exceeded" are concerning and are not useful and undermine the detailed assessment that was included. If used, clear definitions are needed for these definitions and how a "slightly exceeded" comment differs from an "exceeded" comment (see additional comments on #7 and #8).	The text was edited to remove "only slightly".
2	p.8 (currently pg 9) TCE. Like what? And were these conditions observed here? If you're going to make mention of this, it seems relevant to follow through with a judgment on whether it applies in the situation under consideration.	The text was edited to remove "under specific conditions".
5	Page 8 (currently pg 9), last paragraph. Document switches back and forth between ppb and ug/L should be avoided, keep all units same to the extent possible.	Changed all instances of µg/L to ppb.
5	Page 9 (currently pg 7), (VC) section. Can the review state further information? Something like: "By reviewing processes and site activities we can document state that no other source for VC is known at site than microbial degradation of TCE and PCE? If true, would be important to add.	We cannot state that with certainty. The intent of this document is not to debate the source of the contaminants but to evaluate exposures. To clarify, the text was edited to read "The detection of VC in groundwater can be the result of the microbial-degraded TCE and PCE."
2	p.10 Figure 3. Great figure – very helpful.	Thank you for the comment.
5	Page 11. Please modify wording such as "barely exceeded" the MCC in paragraph 2. Again this paragraph has a mixture of ppb and ug/L. See earlier comment.	To clarify, the estimated concentration range from 4–9 ppb was added to the text. All instances of µg/L were changed to ppb.
5	Page 11, 4th paragraph. Again use of words such as "slightly below" should be replaced with facts. Exceeding values by X fold could be helpful or comparisons to other values but do not use non quantified words.	The text was edited to remove "slightly".
2	p.12. Figure 4. Would be good to include a vertical line indicating when most highly contaminated Tarawa Terrace wells were taken offline.	The highly contaminated wells were taken offline February 1985 and is mentioned throughout the document.

1	p.13 (currently pgs 13 and 14) Exposure Pathway Analysis. Explain Table 2. What is meant by "Past completed pathway" and "Future Potential Pathway"	Per ATSDR's established PHA exposure assessment process, ATSDR evaluated possible exposure situations as a critical step in evaluating health hazards. "Completed" exposure pathways represent those where all five "elements" of exposure exist (a population who could be exposed, the existence of contaminated media, a contaminant source, and an exposure point and route). Table 2 lays out these elements. In the case of past situations, the pathway has been labeled complete because contamination was detected in well water that we know people were using for drinking and bathing purposes. ATSDR has designated future exposures as "potential" because it is possible that groundwater contamination plumes could migrate to active wells.
2	p.14 Table 2. Incidental water ingestion can occur during showering and swimming. Same comment below.	This is true, but it is a minor contribution compared to inhalation.
2	p.15 (currently pg 17) Additional Exposure Scenarios. Why?	These are specific scenarios different and separate from what we evaluated for the drinking water pathway. The community assistance panel expressed concern that these scenarios contributed to exposure and we felt it prudent to evaluate these pathways. This evaluation is provided in Appendix E.
1	p.15 (currently pg 17) Additional Exposure Scenarios. Where? Is it available?	Appendix E provides details of the additional scenarios evaluation
2	p.15 (currently pg 17) Additional Exposure Scenarios. What about dermal contact?	We would consider healthcare workers to fall under the worker scenario, where their exposure to contaminants is mainly through ingestion of drinking water and showering on-base. The dermal dose estimations based on modeling of dermal absorption of chemicals from water are generally low for VOCs. This is based on the fact that these chemicals have a prolonged lag time before beginning to cross the skin surface, estimated to be between 0.24-0.9 hrs for the VOCs detected in the water at Camp Lejeune. Handwashing would be of such a short duration that it would not contribute significantly to exposure. In the case of an individual putting on gloves, they would generally dry their hands first, therefore removing any residual water from the surface. Therefore, occultation is not a relevant contribution to exposure. The important point is that the most significant pathways of exposure to healthcare workers are included in the assessment.Dermal was evaluated and found to have a minor contribution to overall exposure.
5	Page 15. (currently pg 17) In an effort to be transparent – this hand washing scenario could be calculated and shown compared to shower exposure model. This scenario calculation would support or not the need for further evaluation of health care workers putting on gloves after washing hands and where occultation could have taken place.	See previous response.

Reviewer	Reviewer Comment	ATSDR Response
2	p.16 (currently pg 18) Exposure Dose Calculations. What did the right side of the distribution look like?	ATSDR concluded that the 3-year exposure duration is appropriate based on data found within the Defense Manpower Data Center. The majority of Marines and their families were not on base more than 3 years. To be consistent with the previously published health studies, the same data set was used for this evaluation.
2	p.16 (currently pg 18) Exposure Dose Calculations. Would water ingestion rates for active duty military personnel in North Carolina be different from those of the general population? I would assume so. Also, frequency of showering events would likely differ, too.	Tables 3 and 4 list the exposure parameters used in the assessment. The 95th percentile reasonable maximum exposure (RME) ingestion rate was used for adult residents and civilian workers. The Marine-in-training was assumed to consume 6 L/day for 3 times per week and 3.1 L/day for 4 times per week, which was based on information gathered from former Marines at the community assistance panel meetings and recommended military fluid replacement guidelines (Kolka et al. 2003).
2	p.16 (currently pg 18) Exposure Dose Calculations. Since the mean tour of duty time was less than 2 years (as stated above), it seems sensible to use a 2-year running average). I understand it is possibly conservative to assume 3 years of exposure (as the exposure duration), but if the intent is for the modeled exposure concentration to closely reflect actual concentrations, 2 years seems to make more sense.	ATSDR used an upper end exposure duration in the public health assessment. Further, a 3-year exposure duration is consistent with the ATSDR health studies that were previously published. ATSDR does not believe that using a 2-year exposure duration would substantially change the results.
2	p.16 (currently pg 18) Exposure Dose Calculations. It is mentioned above that the second term of pregnancy was relevant for PCE and preterm birth risk.	ATSDR's fourth health study (Ruckart et al. 2014) found an association between exposure to PCE during pregnancy and risk of preterm birth, particularly during the 2nd trimester. The sentence referenced by the reviewer is discussing fetal heart effects and other potential birth outcomes that might occur from TCE exposures during the first trimester of pregnancy. To evaluate pregnant women's exposure, ATSDR used the historical reconstructed concentrations for each month of pregnancy.
5	Page 16 (currently pg 18), bullet point 5. If Children's Exposure Factor Handbook was used as well I would specifically reference this here.	The 2011 Exposure Factors Handbook provided all the information on the childhood age groups.

Reviewer	*Reviewer Comment*	*ATSDR Response*
4	p.19 (currently starting on pg 38). It is not clear whether these are "mean" or "upper percentile" estimates of exposure. My recommendation would be to pick one of two options: (a) Show the results of an "upper percentile," but also to note that a "central estimate" would only be "X-fold" smaller – for this exposure assessment, I think the difference is 2~3 fold. (b) Show both "central tendency" and "upper percentile" results. The upper percentile could be thought of as a "screening" value. For Hazard Quotient / Hazard Index calculations, the upper percentile is probably most appropriate.	For the purposes of displaying the comparison of estimated exposure doses to effect levels from experimental or epidemiologic studies, Figures 11-16 will be revised incorporate both the "Central Tendency" and the "Upper End" exposure doses/concentrations. Those comparisons will be made using Human Equivalent Doses and Concentrations, and will focus on the scenarios that are of greatest impact (i.e. young children, workers, Marines-in-training).
2	p.19 (currently pgs 15 and 16). Yes, the equations are there, but there is not much detail in the way of the assumptions. Also, some annotation of the assumptions with support for why specific values were employed should be included.	The exposure assumptions, along with their sources, are provided in Tables 3 and 4.
1	p.19 (currently pg 18). What program? Please specify.	For ingestion, the Contaminated Media (Risk) calculator at the Risk Assessment Information System (RAIS), available on the Oak Ridge National Laboratory site was used (see Health Effects Evaluation section).
4	p.20/21 (currently pgs 15 and 16) Tables 3/4. This appears to be a mix of "central tendency" and "upper percentile" measurements. It is not clear whether the overall methodology is to simulate an "upper percentile" or not. See recommendation in previous comment.	It is correct that the overall methodology uses a mix of mean values (e.g. body weight) and higher percentile (e.g. water ingestion rate, showering frequency, bathroom time) exposure estimates to generate a scenario that reflects upper end level of exposure.
4	p.20/21 (currently pgs 15 and 16) Tables 3/4. The Exposure Factors Handbook has recommendations for IR/BW directly – why weren't those used? That would obviate the need to mix central tendencies and upper percentiles.	The ingestion rates and body weights used in ATSDR's assessment are from EPA's Exposure Factors Handbook (USEPA 2011d). Only the ingestion rate for Marines-in-training was modified to account for their increased activity level (Kolka et al. 2003).
2	p.20/21 (currently pgs 15 and 16) Tables 3/4. What is the basis for a 78 year lifetime? 70 is a much more commonly-employed value.	Tables 3 and 4 cite the EPA's 2011 Exposure Factors Handbook's recommended life expectancy, which is 78 years (USEPA 2011d).
5	Section 22 through 37. Good clear explanations.	Thank you for the comment.

Reviewer	Reviewer Comment	
4	p.22 (currently pg 23) Discussion of Noncancer and Cancer Health Effects. On page 77, it states that if the exposure is greater than the guideline, then the exposure is compared "to known toxicologic values for that chemical… ("see Discussion section"). However, this discussion only describes the guideline ("screening") levels, and does not describe the methodology for comparing exposure to toxicity when the "screening" levels are exceeded. There should be a table of those values as well. In particular, I recommend a table of the HED50 and HEC50, values, if they are available. If not, then the NOAEL or LOAEL or BMD should be adjusted to a human equivalent either by BW^3/4 (EPA 2011) or by the RfC dosimetry methodology (EPA 1994). Such a table should also include the endpoint and magnitude of effect (e.g., BMR level, or if it is a LOAEL or NOAEL). Much of the information is already contained on pages 26-29, or in the documents therein. Alternatively, this table could be placed on page 38 (currently pg 35), "Summary of Potential Health Effects …" – since the Figures in that section appear to be where the comparison with "known toxicologic values" is	Tables 5a and 5b have been inserted to summarize the Points of Departure for the specific toxicity values used in the screening, and the basis for their derivation. In addition, the exposure doses are also compared to other cancer and noncancer endpoints, as shown in Figures 11-16. The objective of this display is to provide context to the estimated exposure levels.
1	p.22 (currently pg 23) RfD. NRC (2009) Science and Decisions: Advancing Risk Assessment suggests calling these "adjustment" factors since not all of the adjustments related to uncertainty, some address variability.	Current guidance by ATSDR and EPA refer to these as uncertainty factors, although it is acknowledged that some of the factors are applied to reflect variability in various parameters.
5	Starting page 24 (currently pg 23 and Appendix D). When uncertainty factors are given, please provide a brief explanation for the basis of choosing the factors used for each of the endpoints. Some places in document this was very clear in others no details were given.	Descriptions of uncertainty factors have been revised to include the basis for each (see Appendix D).
2	p.24 (currently Appendix D, pg 85) TCE Toxicity. These chemical specific sections seem unnecessary – this information is readily available in IRIS/ToxFAQs. If the intent was to modify the dose-response assessment based on a re-interpretation of the evidence, I could see that necessitating this level of discussion. It doesn't appear that this is the case, though. That said, it doesn't seem worthwhile to include these chemical-specific treatments in the main document. If anything, I'd make this an appendix.	The text describing the derivation of the health guidelines was moved to Appendix D.

Reviewer	*Reviewer Comment*	*ATSDR Response*
1	p.24 (currently Appendix D, pg 85) TCE Toxicity. In general I think you have too much detail in these sections reviewing toxicity for the chemicals of concern. I suggest a streamlined presentation here along these lines: -Summary of health effects from human and animal studies -Present the RfD/RfD – discuss relevant data issues considered in deriving these and cut details out for an appendix. -Present CSF/IUR - discuss relevant data issues considered in deriving these and cut details out for an appendix.	ATSDR moved the detailed discussion to Appendix D.
1	p.24 (currently Appendix D, pg 85) TCE Toxicity. Too much information for the main body of the report. This can be presented as supplemental information in an appendix for those interested in further detail.	ATSDR moved the detailed discussion to Appendix D
5	Page 25. (currently Appendix D, pg 86) TCE Cancer. The discussion of mutagenic mode of action proposed only for kidney tumors needs additional explanation here and on pages 34 and 35. Nothing is stated that says how TCE caused non-Hodgkin lymphoma and liver cancers. If they are not by a mutagenic mechanisms state this and provide details and justification. See my comments on page 34 for ADAF.	The most recent EPA Toxicological Review for TCE (p.5-130) states that: "When there is sufficient weight of evidence to conclude that a carcinogen operates through a mutagenic mode of action, and in the absence of chemical-specific data on age-specific susceptibility, EPA's Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens (U.S. EPA, 2005e) advises that increased early-life susceptibility be assumed and recommends that default ADAFs be applied to adjust for this potential increased susceptibility from early-life exposure. As discussed in Section 4.4, there is sufficient evidence to conclude that a mutagenic mode of action is operative for TCE-induced kidney tumors." TCE is clearly immunotoxic, however, the mode of action for the induction of non-Hodgkins lymphoma is unclear.
5	Page 29. (currently Appendix D, pg 92) Note that section on Benzene Cancer is "silent" on mode of action. See earlier point about action for TCE mode of action for kidney tumors. If ATSDR considers Benzene associated cancers are possible by mutagenic mode of action then ADAF should be added. Did I miss this discussion? Especially clarify on page 24.	Induction of cancer by exposure to benzene has been associated with multiple modes of action. Based on the current weight of evidence, the list of chemicals where application of ADAF adjustments for children's exposure does not include benzene. Therefore, an ADAF is not applied in the cancer calculations for benzene.
1	p.30 (currently pg 26) deleted text. This is not consistent with EPA interpretation of HI. It is not an estimate of risk and not likely to be proportional to risk. See RAGS Part A, Ch. 8, Risk Characterization Risk Assessment Guidance for Superfund, Volume I: Human Health Evaluation Manual (Part A) EPA/540/1-89/002 December 1989 http://www.epa.gov/oswer/riskassessment/ragsa/ http://www.epa.gov/oswer/riskassessment/ragsa/pdf/ch8.pdf	ATSDR's PHA process is similar but has distinct differences from EPA's risk assessment process. ATSDR uses estimated HI values to assess the likelihood of adverse health outcomes. When toxicity values such as an MRL, RfD, or RfC are exceeded (i.e., HI>1), ATSDR PHA process does call for additional evaluation and that risk context be provided. An additional evaluation is to determine the effects on specific target organs, as described in the text. ATSDR stands by the statement as phrased.

Reviewer	Reviewer Comment	ATSDR Response
4	p.30 (currently pg 26) Calculation of Hazard Quotient/Hazard Index. See previous comments – need to delineate more how the "further evaluation" is done.	See previous
1	p.34 (currently pg 30) Calculation of Cancer Risk. Include the footnote about why a risk from dermal absorption can be calculated using an oral slope factor.	Because of the absence of any dermal-specific cancer slope factors for the chemicals of concern, ATSDR used the oral values to calculate HQs for the dermal pathway. That said, however, oral toxicity values are based on administered dose, while the dermal exposure dose is based on absorbed dose. For organic compounds, the default assumption is that the 100% of the chemical is absorbed from the gastrointestinal tract into the blood. In these cases, no adjustment is needed. But for inorganic compounds with a lower gastrointestinal absorption, an adjustment of the MRL or RfD is needed. All of the chemicals evaluated in this assessment are organic compounds, therefore no adjustment was applied.
2	p.34 (currently pg 30) Calculation of Cancer Risk. Provide a link to the determination of this. Also, how is it handled (quantitatively)? Guidance is provided by EPA here: http://www.epa.gov/reg3hwmd/risk/human/rb-concentration_table/faq.htm#FAQ19	EPA concluded "by a weight of evidence evaluation, that TCE is carcinogenic by a mutagenic mode of action for induction of kidney tumors. As a result, increased early-life susceptibility is assumed for kidney cancer and the age-dependent adjustment factors (ADAFs) should be used for the kidney cancer component of the total cancer risk when estimating age-specific cancer risks." http://cfpub.epa.gov/ncea/iris/index.cfm?fuseaction=iris.showQuickView&substance_nmbr=0199#carc
2	p.34 (currently pg 30) Calculation of Cancer Risk. What is this?	Vinyl chloride also has a mutagenic mode of action, but the methodology for the calculation of cancer risk is distinguished by the age at onset of exposure. The methodology for assessing less than lifetime exposure beginning during early life is presented in Section 5.3.5.1 of the EPA Toxicological Review of Vinyl Chloride; EPA/635R-00/004; 2002. The methodology uses a time-independent dose term for early life exposure to children that is added to the typical exposure duration term in the risk calculation. Appendix D has been modified to include an excerpt from that document that describes the basis for this term and example calculations.

Reviewer	*Reviewer Comment*	*ATSDR Response*
4	p.34 (currently pg 30) Calculation of Cancer Risk. While this might be true in the generic case, in the specific case of TCE, benzene, and vinyl chloride, the case that the risk "might be zero" is not as strong. First, these are genotoxic (for TCE, at least kidney cancer is). Second, they are based on human data, or consistent with human data (in the case of Vinyl Chloride). Recommend softening this assertion, and acknowledging strengths of the cancer risk estimates in this case.	The statements regarding cancer slope factors and inhalation unit risk values reflect general uncertainty descriptions for assessment of risk for carcinogens that appear in EPA documents and in ATSDR guidance. The phrasing of the cancer section and Appendix D in this document has been revised to make the characterization of uncertainty more specific to the chemicals that are included in this assessment.

Reviewer	Reviewer Comment	ATSDR Response
5	Page 34, lines 14-16 (currently Appendix D, pgs 86 and 87). Need to add further explanation on why TCE is only considered as a mutagen in kidney. See early request for clarification for page 25. The other points made about calculation of cancer risks and application of cancer risks and application of ADAF are consistent with current practice in risk assessment. This reviewer would apply ADAF to other non-kidney tumors for TCE unless additional explanation is provided. Further clarification for use/not use of ADAF for Benzene is needed in this same section. Perhaps a table of carcinogens and application context for ADAF would make this more transparent! Some of this is in the current Tables 3 &4 but make sure text supports Table.	As of June 2012, U.S. EPA identified 19 chemicals with a mutagenic mode of action. ATSDR suggests using ADAFs for the following 18 chemicals: Acrylamide (79-06-1),Benzidine (92-87-5),Benzo[a]pyrene (50-32-8),Coke oven emissions (8007-45-2),Dibenz[a,h]anthracene (53-70-3),1,2-dibromo-3-chloropropane (96-12-8),Dichloromethane (75-09-2),Diethylnitrosamine (55-18-5),Dimethylbenz[a]anthracene (57-97-6),Dimethylnitrosamine (62-75-9), Ethylnitrosourea (759-73-9),3-methylcholanthrene (56-49-5),4,4'-methylenebis (2-chloroaniline) (101-14-4),Methylnitrosourea (684-93-5),Safrole (94-59-7),Trichloroethylene (79-01-6),1,2,3-trichloropropane (96-18-4),Urethane (51-79-6) Per EPA guidance, for chemicals with a mutagenic mode of action, each age-specific cancer risk is multiplied by an age-dependent adjustment factor (ADAF), based on ADAFs recommended by the U.S. EPA (2008): • Children 0 < 2 years 10 • Children 2 to < 16 years 3 • Children and adults 16 and older 1 TCE has been determined to be carcinogenic for kidney, liver, and non-Hodgkins lymphoma. However, the mode of action is only mutagenic for kidney tumors. Therefore, the ADAF only applies to the kidney component of the cancer slope factor. See IRIS file for details at http://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=199 Vinyl chloride also has a mutagenic mode of action, but the methodology for the calculation of cancer risk is distinguished by the age at onset of exposure. The methodology for assessing less than lifetime exposure beginning during early life is presented in Section 5.3.5.1 of the EPA Toxicological Review of Vinyl Chloride; EPA/635R-00/004; 2002. The methodology uses a time-independent dose term for early life exposure to children that is added to the typical exposure duration term in the risk calculation. Appendix D has been modified to include an excerpt from that document that describes the basis for this term and example calculations.

Reviewer	*Reviewer Comment*	*ATSDR Response*
4	p.38 (currently pg 35) Summary of Potential Health Effects from Contaminated Water Supplies. This section needs to describe the methodology for comparing with PODs. In particular, as previously noted, I recommend a table with the PODs – and that they all be human equivalents or converted to human equivalents by standard methods. For TCE, they should be 50th percentile human equivalents (e.g., HED50), though in the comments, though you might include the 99th percentiles as well. The 50th is most comparable to the (human equivalent) PODs for the non-TCE studies, so that is why I suggest using it instead of the HED/C99. Another thing to consider for TCE is whether to include the route-to-route extrapolated HEDs/HECs. That is, for the ingestion graph, whether the HEDs extrapolated from inhalation studies should be included. They might be informative as to characterizing risk. Furthermore, in the Figures, it may be useful to have both the "conservative" as well as the "central estimate" exposure measures. If the "central estimate" exposure measures exceed the PODs (adjusted to human equivalents), then that implies that exposures reached levels where toxicity would be expected to be observed in the "typical" individual. If the "upper end" exposure estimate exceeded, but not the "central" estimate, then that still implies that some individuals will have been expected to have observable toxicity. Moreover, my sense is that in these exposure scenarios, the difference between the "central" and "upper end" estimate is not very large (2~3 fold?).	Table 5a and 5b have been added that list the Point of Departure, the Human Equivalent Doses and Concentrations, and the basis for the extrapolation. For the purposes of displaying the comparison of estimated exposure doses to effect levels from experimental or epidemiologic studies, Figures 11-16 will be revised incorporate both the "Central Tendency" and the "Upper End" exposure doses/concentrations. Those comparisons will be made using Human Equivalent Doses and Concentrations, and will focus on the scenarios that are of greatest impact (i.e. young children, workers, Marines-in-training).
2	p.38 (currently pg 35) Summary of Potential Health Effects from Contaminated Water Supplies. For those unfamiliar with Camp Pendleton (like me), this comparison isn't helpful without some description of the people and chemical exposures occurring at that base.	Details of that study are described in the published Bove et al. 2014. Morality Study Fact Sheet states "The Camp Pendleton workers were not exposed to contaminated drinking water."
2	p.38 (currently pgs 35 and 36) Hadnot Point Water Supply Users. Consider reversing the order of presentation to display risk estimates first, followed by epi evidence that does not have the same level of quantitative estimation.	The ordering has been adjusted.
1	p.38 (currently pgs 35 and 36) Hadnot Point Water Supply Users. Has ATSDR looked at immune outcomes in the studies it has conducted? If yes, is there any corroborating human evidence? If ATSDR has not looked at this, explain why not.	Multiple Sclerosis (MS) was evaluated as an immune outcome in the marine mortality study and a slight effect was found. MS, scleroderma and lupus are being evaluated in the health survey. There is no registry of immune effects and characterization of the full range of potential immune impacts would be a very challenging study design.

Reviewer	Reviewer Comment	ATSDR Response
1	p.39 (currently pg 36) Hadnot Point Water Supply Users. Could add here or in next sentence that risk management undertaken at MCB Camp Lejeune has included taking contamination wells off-line, etc.	ATSDR agrees that acknowledging and encouraging ongoing risk prevention/management at MCB Camp Lejeune is an important point. However, we do not believe the point necessarily fits into this particular section that is focused on describing health effects for one of several water supplies. Other sections of the document highlight ongoing monitoring practices for inorganic and organic contamination aimed at ensuring compliance with federal drinking water standards.
1	p.40 (currently pg 37) Holcomb Blvd Water Supply Users. Also reference Ruckart et al 2013 here? Did that study separate groups by water supply?	Yes. We modeled each study participant's individual exposure history, taking into account where and when they lived on base to assign exposure.
4	p.41 (currently pg 38) Figure 11. Animal studies should be converted to human equivalent doses.	Doses from animal studies have been converted to human equivalent doses and concentrations.
2	p.41 (currently pg 38) Figure 11. It would be helpful for RfDs and other health benchmarks to be colored differently from the exposure doses. Also, rather than naming them "RfDs from scientific evidence", they should be named what they actually are (e.g. "EPA IRIS RfD for TCE", etc. The same comments apply to similar figures.	The term reference doses from scientific evidence in the footnotes will be edited to avoid confusion between the health guidelines, the exposure doses/concentrations and the levels of observed effects.
4	p.42 (currently pg 39) Figure 12. Convert to human equivalent concentrations (if not already done)	Doses from animal studies have been converted to human equivalent doses and concentrations.
2	p.43 (currently pg 40) Figure 13. I'm not a fan of the top dot in the cancer figure which almost seems to imply a threshold by stating a concentration needed to elicit liver cancer in animals. Unless of course, you are intending to imply a threshold – though I am assuming you are not. To provide clarity, either footnote and explain that this is a study dose, or provide an explanation in the figure. Same comment for the next figure.	That point on the chart was not intended to imply a threshold cancer effect. It was included to reflect the dose level associated with an effect in the animal study. The label for the study will be revised to explain that this was a high dose study and is not considered to be a threshold for cancer effects.
4	p.43-46 (currently pg 40) Figures 13-16. See previous comments. Can use "default" methods to derive the HED or HEC.	All animal exposures have been converted to HEDs and HECs.
5	Tables 11-16 (currently pgs 38 to 40). These tables were very useful. Please clarify text that uncertainty factors considered appropriate for comparing exposures in animals to humans and across studies were not added in these figures.	These figures show the health guideline values, the estimated exposure doses/concentrations, and the human equivalent exposure levels associated with health effects. Only the guideline values incorporate uncertainty factors.

Reviewer	*Reviewer Comment*	*ATSDR Response*
4	p.47 (currently pg 41) Data Limitations. If the exposure concentrations are intended to be "accurate" (not biased higher or lower), then why is it "health protective?" That makes it sounds like this is conservative, while it is actually a "central estimate" (however uncertain).	For the purposes of displaying the comparison of estimated exposure doses to effect levels from experimental or epidemiologic studies, Figures 11-16 will be revised incorporate both the "Central Tendency" and the "Upper End" exposure doses/concentrations. Those comparisons will be made using Human Equivalent Doses and Concentrations, and will focus on the scenarios that are of greatest impact (i.e. young children, workers, Marines-in-training).
4	p.47 (currently pg 41) Data Limitations. This is not "very" conservative – less than 2-fold different than a "central" estimate.	The parameter of exposure duration is based on how long Marines where in training. Information provided to ATSDR indicated that the use of a 3 year on-base duration would cover 85% of those individuals. We believe that to be a conservative (health-protective) exposure assumption. We also included longer term workers at the base to ensure that the potential impacts to individuals who were exposed for a longer duration were considered.
2	p.47 (currently pg 41) Data Limitations. This is good and reasonable – but the detail that it is the 85th percentile should have been mentioned above in the earlier discussions of that assumption.	That fact is mentioned earlier in the section describing the Exposure Dose Calculations.
2	p.47 (currently pg 41) Data Limitations. I recall mention above that guidance on water consumption and bathing frequency was provided by base leadership/military personnel…?	Individual exposures may vary. ATSDR used a combination of site-specific parameters, such as bathing frequency and water ingestion rate for Marines-in-training, and upper end exposure parameters from reliable sources such as EPA's Exposure Factors Handbook.
4	p.47 (currently pg 41) Data Limitations. In many of these cases, however, the "upper end" is not too far different than a central estimate.	For the water ingestion pathway, there is actually only limited variability in the dose estimates between average and upper end exposure levels. The estimated of dose from inhalation of chemical vapors from use of contaminated water is subject to a greater level of uncertainty, in part due to a larger number of input parameters with estimated values. The assessment will be revised to reflect both the average and upper end exposure levels.
2	p.47 (currently pg 41) Data Limitations. You should discuss this more – and explain the possibilities for its impact. Perhaps even recommend this be a subject of a future ATSDR mixture assessment…?	A discussion about exposure to the mixture of chemicals in Camp Lejeune water systems has been included in a separate section. The basis for this discussion is contained in the ATSDR Interaction Toxicological Profile, which summarizes mixtures data that includes on TCE, PCE, and Vinyl Chloride. Detailed summaries of those analyses have been inserted into Appendix D. The outcome of that evaluation is that the use of the additive approach used in this assessment is the most conservative (health-protective).

Reviewer	Reviewer Comment	ATSDR Response
1	p.47 (currently pg 41) Data Limitations. There are approaches for assessing chemical mixtures so at a minimum more explanation is needed. ATSDR has an Interaction Profile that includes some of these chemicals. I think there needs to be acknowledgement that risk estimates would be higher based on additive assumptions used for mixtures. Because risks were found to be high on the basis of the individual chemical assessments, risk management activities were completed. The risk management actions reduced exposure to all the chemicals of concern.	A discussion about exposure to the mixture of chemicals in Camp Lejeune water systems has been included in a separate section. The basis for this discussion is contained in the ATSDR Interaction Toxicological Profile, which summarizes mixtures data that includes on TCE, PCE, and Vinyl Chloride. Detailed summaries of those analyses have been inserted into Appendix D. The outcome of that evaluation is that the use of the additive approach used in this assessment is the most conservative (health-protective).
4	p.47 (currently pg 41) Data Limitations. This point needs to be made earlier in the document	The text has been revised (see the ATSDR Evaluation of Environmental Exposures section).
5	Page 47 (currently pg 41). Excellent discussions on how data limitations were handled.	Thank you for the comment.
1	p.49 (currently pg 43) Conclusion 1 Basis. Also discuss any relevant epidemiology studies	The findings of the epidemiological studies at Camp Lejeune are discussed in the Background section of the document.
1	p.50 (currently pg 45) Conclusions 2 Next Steps. What about the noncancer effects?	Individuals concerned about other health concerns, including noncancer effects, should consult with their healthcare provider.
2	p.51 (currently pg 45) Conclusion 3 Basis. How is it suggested? Does this mean statistically significant? Also, provide a citation.	We say suggested because the study results were based on small numbers of cases and the odds ratios had wide confidence intervals.
2	p.53 (currently pg 47) Sources of Lead in the Environment. What does this mean? What are the parts of the environment?	The parts of the environment are the land, air, and water. The sentence has been modified to include this information.
2	p.53 (currently pg 47) Lead Exposure Risk Factors. Just Mexico?	Yes, based on the references reviewed for these bullets (Dixon et al. 2009; USEPA 2013a).
2	p.53 (currently pg 47) footnote. IS THIS THE BEST CITATION?	The Mayo Clinic (2015) reference is appropriate. ATSDR has also added a citation to the Centers for Disease Control and Prevention (2013c) in further support of the footnote.
2	p.54 (currently pg 48) Blood Lead Levels and Health Effects. (explain…?)	The sentence about chelation therapy was modified and further explanation provided.
2	p.56 (currently pg 50) Lead Levels in Camp Lejeune's Drinking Water. Big range – is there any spatial pattern?	ATSDR did not notice a spatial pattern.

Reviewer	*Reviewer Comment*	*ATSDR Response*
2	p.56 (currently pg 50) Lead Levels in Camp Lejeune's Drinking Water. Summarize the most important points in text.	The most important points related to Table 7 are already summarized in the bullets and text of this section. A few clarifying statements were added to the text on page 50 (see second paragraph below the bulleted items).
2	p.56 (currently pgs 50 and 51) Lead Levels in Camp Lejeune's Drinking Water. So, what does this mean? Synthesis would strengthen this section.	The database indicated that major repairs were completed in 2007 at MCAS New River location 545 G 521 (a small building at Camp Geiger), and Table 7 shows the lead level decreased to below the USEPA action level upon further sampling (i.e., lead was not detected). Partial renovations were completed in 2014 at MCAS New River location 541 G 560 (a recreation center at Camp Geiger), but Table 7 shows the lead tap water level had dropped to be below the USEPA action level before the renovation. Interior and exterior repairs were completed in 2011 at MCAS New River location 458 AS 4025 (barracks). ATSDR notes that sampling of tap water at these barracks showed lead was not detected in June 2007 and June 2010, which was before repairs were completed in 2011. However, in September 2013, at this same location, lead was detected above the 15 ppb action level. ATSDR recommended this tap water location be retested. For the remaining 11 locations where no repairs/renovations took place, the lead levels decreased to be below the USEPA action level upon further sampling, but in some instances the levels fluctuated. It is not known why the lead levels fluctuated. This information was added to the section.
2	p.57 (currently pg 52) Table 7 (two places). Why did sampling not continue here?	ATSDR only reports the sampling data; the agency does not determine when and from where samples are collected. Note that one sample found 10 ppb, which is below the EPA action level of 15 ppb; guidance does not indicate followup sampling is needed at this location. ATSDR notes that the other sample found 17 ppb, which is above the EPA action level of 15 ppb. According to MCB Camp Lejeune operating procedures instituted in 2013, followup sampling would be indicated (MCB Camp Lejeune 2013). In addition, as stated previously in response to another comment, sampling of tap water at this location (barracks) showed lead was not detected in June 2007 and June 2010, which was before repairs were completed in 2011. However, in September 2013, at this same location, lead was detected at 17 ppb. ATSDR recommended this tap water location be retested.

Reviewer	Reviewer Comment	ATSDR Response
5	Page 58-61(currently pgs 48 and 49). This reviewer would suggest an additional look at efforts of lead. There have been discussions on non-neuro endpoints. Please re-review. Also see comments about biomarker surveillance (i.e. blood level) to confirm lead exposure values in your populations of interest. I would support this rather than additional environmental exposures.	ATSDR describes many health endpoints, including non-neuro endpoints such as hearing, delays in puberty, and kidney problems (see *Blood Lead Levels and Health Effects* section). After the draft was released for external peer review, the Navy provided a site-specific pediatric BLL data summary report. As stated in response to previous comments, ATSDR has added the summary data to the document.
2	p.59 (currently pg 54) Table 8. Is this for all ages <7?	Yes, as described in the text, the IEUBK model predicts the risk of elevated blood lead levels in children 6 months to 7 years of age. This was added as a note to the table.
2	p.60 (currently pg 56). More detail is needed here. Yes, I know the factsheet is in the appendix, but the appendix is better suited for details beyond what is needed to understand the paragraph at hand. There is not enough presented here to understand what 3T guidance will require/do.	Clarification was added to the previous sentence that provides details about the USEPA 3T program.
2	p.60 (currently pg 56). What? Please provide a scientific rationale for this assertion.	Nutrients like calcium and iron reduce lead uptake. This clarification was added to the sentence.
2	p.64 (currently pg 60). Recommended Public Health Actions. What is expected to come of this?	Concerned persons can discuss any health concerns with their own healthcare providers, who may refer them to an Association of Occupational and Environmental Clinic (AOEC), which has doctors who specialize in occupational and environmental medicine. A list of AOEC locations is available at http://www.aoec.org/.
1	p.64 (currently pg 60) Recommended Public Health Actions. Again, what about noncancer risks?	ATSDR edited the text to read: "…persons concerned about increased cancer or noncancer risk…"
5	Page 64, bottom of page (currently pg 60). Do MDs have clear talking points for concerned resident/workers? I would add this to plan.	ATSDR will keep this suggestion in mind when developing the final communication and outreach plan.

Reviewer	*Reviewer Comment*	*ATSDR Response*
5	Pages 64-65 (currently pgs 60 and 61). Excellent, very well done articulated Public Health Action Plan. a. For "Public Health Actions Undertaken" add year actions taken. b. For action #6, link with web link to 3T sampling guidance or to document citation/reference. c. This reviewer applauds the ongoing surveillance studies. However this reviewer was surprised that there wasn't more emphasis on biomonitoring in the action plan. As mentioned, recent publications showing positive associations with several endpoints including cancer and adverse birth outcomes should trigger next level of monitoring. Shouldn't health monitoring studies be indicated for the populations most at risk identified from their modeled exposure profiles? Yes, this reviewer would extend these long term evaluations. Wouldn't a centralized and probability based Pb sampling program be as or more informative for Pb concerns than additional environmental sample data suggested in the document? The recently published epidemiology studies on Camp Lejeune site suggest other potential targets for surveillance and monitoring. The potential for TCE exposure in utero to be associated with cardiac defects is of concern and supports the need to examine more carefully this cohort for developing adverse public health impacts for exposed individuals as they develop and age.	a. ATSDR added years where appropriate. Some actions are ongoing. b. ATSDR added the requested web link. c. Regarding a lead sampling program, yes, there has been ongoing monitoring of BLL levels in children. ATSDR was provided a summary report of those data after the agency had provided the draft document to the external peer reviewers. The summary BLL data has been included in the updated document.
5	Appendix A. Excellent, very clear explanations of Screening Analysis and reference values for health assessments. This clarity stand in contrast with the use of non-quantitative comparisons seen in document e.g. "slightly exceeding" or high or low. See earlier comments.	The qualitative, undefined terms have been deleted and replaced with more direct statements.
1	p.77 (currently pg 76) RfD. Since all of these noncancer dose-response metrics include adjustment factors, why call it out for RfD?	The definitions have been revised based on phrasing on IRIS, without reference to the safety or uncertainty factors.

Reviewer	Reviewer Comment	ATSDR Response
4	p.78 (currently pg 77) Cancer Health Effects. Not necessarily "worst-case" – these are based on lower 95% confidence of the BMD. Additionally, in these specific cases, they are mostly based on human data, so the uncertainty is much less than being based on animal data. Even for Vinyl Chloride, which is based on animal data, it is documented that the animal-based estimates are very consistent with estimates based on human epidemiology. Furthermore, for the genotoxic carcinogenic endpoints, linear extrapolation may be a reasonable choice, and not "worst-case" by any means. Finally, recent work has indicated that, taking model uncertainty into account, linear extrapolation may not be "conservative" (Chiu and Slob, 2015, in press DOI:10.1289/ehp.1409385 ; Slob et al., 2014 DOI: 10.1111/risa.12194)	The statements regarding cancer slope factors and inhalation unit risk values reflect general uncertainty descriptions for assessment of risk for carcinogens that appear in EPA documents and in ATSDR guidance. The phrasing of the cancer section in this document has been revised to make the characterization of uncertainty more specific to the chemicals that are included in this assessment.
5	Page 78. This reviewer does not agree with the recommendation to use undefined qualitative terms. See comments for points 1,2,3,7,8 and 20. In most cases when quantitative or semi-quantitative terms are used their definitions are provided that help guide the reader.	The qualitative, undefined terms have been deleted and replaced with more direct statements.
1	p.82 (currently pg 80) Appendix C. Exposure doses were calculated only for organics, right? Lead was evaluated with IEUBK. Delete equations that were not used.	The unused equations were deleted.
1	p.85 (currently pg 80) Appendix C. In regard to question 7 of the peer review: I don't get how an additional intake term as shown here relates to the EPA recommended 2-fold cancer risk adjustment for early life exposure.	Vinyl chloride also has a mutagenic mode of action, but the methodology for the calculation of cancer risk is distinguished by the age at onset of exposure. The methodology for assessing less than lifetime exposure beginning during early life is presented in Section 5.3.5.1 of the EPA Toxicological Review of Vinyl Chloride; EPA/635R-00/004; 2002. The methodology uses a time-independent dose term for early life exposure to children that is added to the typical exposure duration term in the risk calculation. Appendix D has been modified to include an excerpt from that document that describes the basis for this term and example calculations.
1	p.99 (currently pg 113) Appendix F. How limited? How many samples were there? Taken when? I realize this has been documented elsewhere but it would be helpful to have at least a brief review of some key details here.	The intent of this PHA was to evaluate past exposures to contaminants of concern. The authors tried to keep the document concise and provide references in areas where we felt the reader may want more detail on pertinent studies. Including too much of their information in our document may make an already lengthy document unwieldy.

Reviewer	*Reviewer Comment*	*ATSDR Response*
5	Page 100 (currently pg 116). Four methods for sensitivity and 3 uncertainty analysis are identified. This section missed a link back to document where methods are used and results described. Only reference to methodological approaches are given in this appendix. Briefly describe each of these methods and types of output. This would help the user of the document.	The Modeled Contaminants of Concern in Drinking Water appendix has been updated to refer the reader to the specific sections and page numbers in Chapter A of the "Analysis and Historical Reconstruction of Groundwater Flow, Contaminant Fate and Transport, and Distribution of Drinking Water within the Service Areas of Hadnot Point and Holcomb Blvd Water Treatment Plants and Vicinities – U.S. Marine Corps Base Camp Lejeune, North Carolina" that elaborate on sensitivity and uncertainty analysis. (Sensitivity Analysis section begins on page A70 and the Uncertainty Analysis section begins on page A92.

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Completing the survey should take less than 5 minutes of your time. If possible, please provide your responses within the next two weeks. All information that you provide will remain confidential.

The responses to the survey will help ATSDR determine if we are providing useful and meaningful information to you. ATSDR greatly appreciates your assistance as it is vital to our ability to provide optimal public health information.

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