Exhibit 103

General Causation Expert Report of

Steven B. Bird, MD

Hematopoietic Cancers:
Leukemia & Non-Hodgkin's Lymphoma

Prepared by:
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December 9, 2024

Contents

I. QUALIFICATIONS

I earned my Bachelor of Science degree in biology cum laude in 1991 from Yale University, where I was named a Yale University Richter Fellow. I worked in the laboratory of Professor Sidney Altman, Dean of Yale College and winner of the 1989 Nobel Prize in Chemistry. I was awarded my Doctor of Medicine degree by Northwestern University in 1995 and was also elected to the Alpha Omega Alpha national medical honor society (generally awarded to the top 10% of medical students nationally). Following medical school, I gained post-graduate training through residencies with the Naval Hospital San Diego (surgery) and the University of Massachusetts Medical School (emergency medicine). In addition, I completed a two-year fellowship in medical toxicology at the University of Massachusetts Medical School in 2004.

I began my independent clinical career in the Department of Emergency Medicine at the University of Massachusetts Medical School in 2002. I was promoted to Assistant Professor of Emergency Medicine in 2004, to Associate Professor in 2010, and to full Professor in 2016. In addition, I served as Program Director of the Emergency Medicine Residency Program and as Vice Chair of Education for the Department of Emergency Medicine at the University of Massachusetts Medical School from 2011 to 2019. I am currently the Division Chief of Medical Toxicology at the UMass Chan Medical School and UMass Memorial Health. I work as an Attending Emergency Physician at UMass Memorial Medical Center and Clinton Hospital. I am actively involved with numerous professional committees within the UMass Chan Medical School and its Department of Emergency Medicine and Division of Medical Toxicology, and in national and international scientific organizations, such as the Society for Academic Emergency Medicine, the American College of Medical Toxicology, and the American College of Emergency Physicians. I served on the Board of Directors of the Society for Academic Emergency Medicine from 2014-2020 and was President of the Society from 2018-2019. Additionally, I was formerly President of the Medical Staff of UMass Memorial Healthcare.

During my professional career, I have received several awards, including the Navy and Marine Corp Achievement Medal, the Outstanding Contribution to Medical Toxicology Research by the American College of Medical Toxicology; the Society for Academic Emergency Medicine ("SAEM") Best Resident Basic Science Presentation Award, the SAEM New England Regional Research Directors Excellence in Research Award, the teaching award (twice) from the UMass Emergency Medicine Residency, and a Young Investigator Award from the Society for Academic Emergency Medicine.

I am a reviewer for several scientific journals, including the Journal of Medical Toxicology; Clinical Toxicology; Annals of Emergency Medicine; Academic Emergency Medicine; Toxicology; the New England Journal of Medicine; and JAMA. I currently serve on the Editorial Board of Academic Emergency Medicine and was a founding editorial board member of the Journal of Medical Toxicology. I am certified by the American Board of Emergency Medicine and the American Board of Medical Toxicology. I currently hold a license to practice medicine in Massachusetts. In my practice of emergency medicine medical toxicology, I evaluate people exposed or potentially exposed to a variety of substances on a daily basis.

Attached as exhibits are my CV, a list of publications from the past 10 years, a list of cases in which I testified in the past four years, and my fee schedule for this case.

II. METHODOLOGY

In my review of this case, I utilized scientifically valid and reliable methods to perform my research, followed by a consideration of the weight of the evidence and the Bradford Hill viewpoints.

In my search of the medical and scientific literature, I conducted many searches of the PubMed database using terms including (but not limited to):

(TCE OR PCE OR benzene OR vinyl chloride OR trichloroethylene OR tetrachloroethylene OR perchloroethylene) AND leukemia

(TCE OR PCE OR benzene OR vinyl chloride OR trichloroethylene OR tetrachloroethylene OR perchloroethylene) AND (non-Hodgkin lymphoma OR NHL OR chronic lymphocytic leukemia OR CLL OR multiple myeloma OR MM OR acute lymphocytic leukemia OR ALL OR follicular lymphoma OR B-cell lymphoma)

I also performed numerous searches using Google Scholar, which provides quick access to full-text articles as well as an immediate list of citing articles for that manuscript. In order to identify even more articles, I reviewed the articles cited in the manuscripts I reviewed. I also reviewed toxicology and medical toxicology textbooks, as well as chemical toxicity databases such as the Hazardous Substances Data Bank, United States Environmental Protection Agency's (EPA) Integrated Risk Information System (IRIS), and Agency for Toxic Substances and Disease Registry (ATSDR). In addition, I reviewed the records and other materials that counsel for Plaintiffs sent to me.

My methodology for reviewing literature in this case is identical to my methodology when seeing a patient and that which I teach residents and fellows.

After exposure to a toxin, people will often present at the emergency department. In my practice of emergency medicine and medical toxicology, I evaluate people exposed or potentially exposed to a variety of substances on a daily basis. In my review of this case, I utilized scientifically valid and reliable methods to perform my research, followed by consideration of the weight of the evidence and the Bradford-Hill viewpoints.

Even though some of the epidemiological results presented in this report are not statistically significant under traditional methods, they are important and relevant information with regards to causation where the standard is equipoise because the concept of equipoise refers to genuine uncertainty within the expert medical community. Many of the results are very nearly statistically significant and are clearly not directed towards a decrease in occurrence or risk of the cancers. Furthermore, the use of traditional statistical significance does not capture or account for biological plausibility of cancer causation. Likewise, relying on traditional statistical significance ignores known carcinogenic properties of a substance. Lastly, biostatisticians have largely abandoned the dichotomous interpretation of statistical significance (i.e., significant vs. non-significant) and instead focus on the estimation of effect sizes.

I am being compensated at a rate of $600 per hour for review and report writing and $1,000 per hour for deposition or trial testimony.

This report reflects my opinions formed to a reasonable degree of medical and scientific certainty. I reserve the right to supplement this report.

III. "AT LEAST AS LIKELY AS NOT" STANDARD

The statute at issue in this case, the Camp Lejeune Justice Act (CLJA), states:

(2) Standards – To meet the burden of proof described in paragraph (1), a party shall produce evidence showing that the relationship between exposure to the water at Camp Lejeune and the harm is –

> (A) Sufficient to conclude a causal relationship exists; or
>
> (B) sufficient to conclude a causal relationship is at least as likely as not.

This standard has significant implications for the analysis at issue in this report. The standard and its language have application in the field of toxicology, epidemiology, and other similar sciences. The determination of a causal relationship is naturally different under a standard that requires a proof "more likely than not," as compared to a standard that requires a proof "as likely as not."

To this point, ATSDR (2017) in its assessment of the evidence, utilized differing causality standards in the context of assessing the causal relationship between the toxins in the drinking water at Camp Lejeune and different diseases. Specifically, ATSDR utilized the following causality standards:

> Sufficient evidence for causation: the evidence is sufficient to conclude a causal relationship exists. This category would be met, for example, if:
>
> 1. There is sufficient evidence from human studies in which chance and biases (including confounding) can be ruled out with reasonable confidence, or
>
> 2. There is less than sufficient evidence from human studies but sufficient evidence in animal studies and strong evidence that the agent acts through a relevant mechanism in humans.
>
> Equipoise and above evidence for causation: The evidence is sufficient to conclude that a causal relationship is at least as likely as not, but not sufficient to conclude that a causal relationship exists. This category would be met, for example, if:
>
> 1. The degree of evidence from human studies is less than sufficient but there

is supplementary evidence from animal studies and/or mechanistic studies that supports causality, or

2. A meta-analysis does not provide convincing evidence (e.g., the summary risk estimate is close to the null value of 1.0, i.e., < 1.1), or if the meta-analysis observes a non-monotonic exposure-response relationship) but there is at least one epidemiological study considered to be of high utility occurring after the meta-analysis has been conducted, in which an association between the exposure and increased risk of the disease of interest has been found and in which chance and bias can be ruled out with reasonable confidence.

3. A meta-analysis has not been conducted, but there is at least one epidemiological study considered to be of high utility in which an association between the exposure and increased risk of the disease of interest has been found and in which chance and biases can be ruled out with reasonable confidence.

Similar standards have been used in other areas of toxicology, epidemiology and by other governmental bodies. For example, as ATSDR notes, the classification scheme used in the 2017 assessment of the evidence is one "recommended by an IOM panel that reviewed the VA's presumptive disability decision-making process for veterans (IOM 2008)."

This classification scheme is consistent with my many years of experience in these fields of science and also based on sound scientific and methodological grounds. It therefore informs an analysis of causality that is necessarily based upon toxicology, epidemiology and other similar sciences. Even though some of the epidemiological results presented in this report are not statically significant under traditional methods, they are important and relevant information with regards to causation where the standard is equipoise because the concept of equipoise refers to genuine uncertainty within the expert medical community. Many of the results are very nearly statistically significant and are clearly *not* directed towards a decrease in occurrence or risk of cancers.

Opinions in this report are provided under a "more likely than not" standard, which necessarily exceeds the "at least as likely as not" threshold established in the Camp Lejeune Justice Act. This conclusion is supported by the Act's language, the ATSDR classification system, and scientific literature regarding "equipoise" which I am familiar with as part of my scientific and medical training and expertise.

IV. SUMMARY OF OPINIONS

In my opinion, the water at Camp Lejeune, which was contaminated with significant levels of benzene, trichloroethylene (TCE), perchloroethylene (PCE), and vinyl chloride, posed a clear risk of causing hematopoietic cancer, specifically NHL and leukemia to those exposed to it. Each of these chemicals has been strongly linked to cancer in general, with benzene and TCE in particular being associated with leukemia and NHL. Benzene is widely acknowledged as a carcinogen, classified by the International Agency for Research on Cancer (IARC) and other regulatory bodies that have evaluated its risks. This substance is identified as a leukemogen, which means it directly causes leukemia, and it has also been linked to NHL. IARC has identified benzene as a substance that can lead to acute myeloid leukemia (AML), in addition to other types of leukemia, and "positive associations have been observed for non-Hodgkin lymphoma." [IARC Monograph 120, 2018]. Moreover, ATSDR has concluded that there is "sufficient evidence for causation for benzene and all leukemia types, i.e., ALL, CLL, AML, and CML" as well as for benzene exposure with NHL. [ATSDR Assessment of the Evidence for the Drinking Water Contaminants, 2017; ATSDR Public Health Assessment, 2017].

Similarly, TCE is also classified as a human carcinogen by IARC and every other regulatory body that has evaluated it, and it has been directly linked to hematopoietic cancers, including leukemia and NHL. ATSDR has concluded that there is "equipoise and above evidence for causation for TCE and all adult leukemias, including AML, ALL, CML, and CLL," while epidemiologic studies suggest "a causal relation between TCE exposure and NHL." [EPA Toxicological Review of Trichloroethylene, 2011]. "It has been demonstrated that TCE increases the risk of non-Hodgkin's lymphoma (NHL) and its subtypes" specifically. [Rosenfeld PE. Water Air Soil Pollut 2024;235:124]. IARC "recognized positive associations between trichloroethylene [TCE] and non-Hodgkin lymphoma." [IARC Monograph 106, 2014]. "Based on the meta-analyses, the study of NHL subtypes [Cocco P. Occup Environ Med 2013;70:795-802], and the mechanistic evidence that TCE causes immunosuppression, which is a risk factor for NHL," ATSDR concluded sufficient evidence shows NHL causation for TCE. [ATSDR PHA, 2017].

PCE is classified as a likely human carcinogen by the EPA and other regulatory bodies. Multiple epidemiological studies support a causal association between PCE and non-Hodgkin lymphoma specifically. The EPA believes that "results from the collection of studies pertaining to non-Hodgkin lymphoma indicate an elevated risk associated with tetrachloroethylene exposure." [U.S. EPA Toxicological Review of Tetrachloroethylene, 2012]. ATSDR concluded that the epidemiological evidence for PCE and NHL "was sufficient to classify the causal association as at least equipoise." [ATSDR 2017].

Vinyl chloride carcinogenicity has been evaluated by IARC, and IARC found "There is sufficient evidence in humans for the carcinogenicity of vinyl chloride. Vinyl chloride causes angiosarcoma of the liver, and hepatocellular carcinoma. There is sufficient evidence in experimental animals for the carcinogenicity of vinyl chloride." [IARC Monograph 100F, 2012 at 451]. Similarly, the EPA has classified vinyl chloride as Group A "carcinogenic to humans." [EPA Hazard Assessment for Vinyl Chloride, report 75-01-4, January 2000]. The National Toxicology Program has also found that vinyl chloride "is known to be a human carcinogen based on sufficient evidence of carcinogenicity from studies in humans." [NTP 15th Report on Carcinogens, 2021].

The evaluation of lymphoma risks, particularly for NHL, presents challenges due to the diversity of the disease. NHL consists of more than 60 major subtypes with some distinct genetic, morphologic, and clinical features. As a result, "[i]nterpretation of the results from case–control studies on non-Hodgkin lymphoma [is] complicated by the variety of systems used to classify the lymphomas." [IARC 2014]. Additionally, the use of different ICD codes in studies, as well as evolving understandings of lymphoma biology, further complicates analysis. For instance, lymphomas in the past may have been misclassified as multiple myeloma or leukemia. [Scott SC and Chiu WA. Environ Health Perspect 2006;114:1471-8]. These complexities, however, would generally underestimate the associations between exposure to the chemicals of concern and NHL.

Many studies have also "lacked the statistical power necessary to detect differences in risk factors by NHL subtype. [Chihara D. Expert Rev Anticancer Ther 2015;15:531-44], often because many NHL subtypes are rare cancers. A specific risk factor may be strongly associated with a particular subtype but not others, leading to an overall underestimation of association. For example, an adult with BMI greater than 25 has a higher risk of developing mycosis fungoides (MF) (RR: 1.95 [95% CI 1.10–3.46]) but a significantly lower chance of developing lymphoplasmacytic lymphoma (LPL) (RR 0.40 [95% CI 0.23–0.69]). [Chihara 2015].

In addition, I have been asked to evaluate the levels of exposure to these chemicals that have been identified in scientific literature to be hazardous to human beings generally. Numerous studies provide evidence of specific levels of exposure—some of which align with the contamination observed at Camp Lejeune—that are associated with increased risks for leukemia and NHL. The literature demonstrates several levels of exposure to these chemicals (and to the water at Camp Lejeune generally) that are hazardous to humans, specifically levels of exposure that can cause hematopoietic cancer, including NHL and leukemia:

1. **Water containing 20 ppb of total volatile organic compounds (TVOCs)**: Cohn P, Klotz J, Bove F, Berkowitz M, Fagliano J. Drinking water contamination and the incidence of leukemia and non-Hodgkin's lymphoma. *Environ Health Perspect*. 1994;102(6-7):556-561.

2. **Water containing 5 ppb of TCE**: Cohn et al., *Environ Health Perspect*, 1994.

3. **Water containing 5 ppb of PCE**: Cohn et al., *Environ Health Perspect*, 1994.

4. **1–6 quarters of residence on base from 1975–1985**: Bove FJ, Greek A, Gatiba R, et al. Cancer Incidence among Marines and Navy Personnel and Civilian Workers Exposed to Industrial Solvents in Drinking Water at US Marine Corps Base Camp Lejeune: A Cohort Study. *Environ Health Perspect*. 2024;132(10):107008. doi:10.1289/EHP14966

5. **Cumulative exposure between 10,868 to 50,563 ppb-months of TCE**: Agency for Toxic Substances and Disease Registry (ATSDR). *Morbidity Study of Former Marines, Employees, and Dependents Potentially Exposed to Contaminated Drinking Water at U.S. Marine Corps Base Camp Lejeune*. April 2018.

6. **Cumulative exposure between 457 to 2,118 ppb-months of PCE**: ATSDR Mortality, 2018.

7. **Over 10,868 ppb-months of TCE**: ATSDR Morbidity, 2018

8. **Over 457 ppb-months of PCE**: ATSDR Morbidity, 2018

Exposure Levels *Specific to Leukemia:*

9. **Cumulative exposure to 27–44 mg of PCE**: Aschengrau A, Ozonoff D, Paulu C, et al. Cancer risk and tetrachloroethylene-contaminated drinking water in Massachusetts. *Arch Environ Health.* 1993;48(5):284-292. doi:10.1080/00039896.1993.9936715.

10. **Employment on base for 2.5 years**: Bove FJ et al. Mortality study of civilian employees exposed to contaminated drinking water at USMC Base Camp Lejeune: a retrospective cohort study. *Environ Health*. 2014;13:68. Published 2014 Aug 13. doi:10.1186/1476-069X-13-68

11. **18 months of residence on base from 1975 to 1985**: Bove FJ, Ruckart PZ, Maslia M, Larson TC. Evaluation of mortality among Marines and Navy personnel exposed to contaminated drinking water at USMC Base Camp Lejeune: a retrospective cohort study. *Environ Health*. 2014;13:10.

12. **Cumulative exposure of > 1-3,100 µg/L-month of TCE**: Bove et al, 2014a.

13. **Cumulative exposure of > 1-155 µg/L-month of PCE**: Bove et al, 2014a.

14. **Cumulative exposure of 2-45 µg/L-month of benzene**: Bove et al, 2014a.

15. **Cumulative exposure of > 1- 4,600 µg/L-month of TVOCs**: Bove et al, 2014a.

16. **Water containing 267 ppb of TCE**: Lagakos et al., J Am Stat Assoc. 1986;81:583-596; Parker et al., Woburn: Cancer Incidence and Environmental Hazards 1969–1978, 1981; Cutler et al., Public Health Rep. 1986;101:201-205; Costas et al., Sci Total Environ. 2002;300:23–35.

17. **Water containing 21 ppb of PCE**: Lagakos et al., J Am Stat Assoc. 1986; Parker et al., 1981; Cutler et al., Public Health Rep. 1986; Costas et al., Sci Total Environ. 2002.

18. **Water containing 37–72 ppb of TVOCs**: Fagliano J, Berry M, Bove F, Burke T. Drinking water contamination and the incidence of leukemia: an ecologic study. *Am J Public Health*. 1990;80(10):1209-1212.

It is also worth noting that the ATSDR, in its 2017 Assessment, stated that the "evidence from the epidemiological studies included in this assessment is not sufficeint to contradict this minimum duration," i.e., 30 days on base. My understanding of the Justice Act is that all Plaintiffs in this case were on the Camp Lejeune base for at least 30 days.

The report continued, "Moreover the results from the Camp Lejeune mortality studies suggest that a 30-day minimum duration requirement may be appropriate since elevated risks for some of the diseases evaluated were observed for exposure durations of 1-3 months. These results should not be surprising given that the levels of TCE, PCE and vinyl chloride measured or estimated in the water systems at Camp Lejeune considerably exceeded their respective MCLs."

The significant evidence from the above valid and methodologically sound studies establishes that exposure to the levels of the toxins in the water at Camp Lejeune were hazardous to human beings generally and are known causes of leukemia and NHL. Much of the evidence related to Camp Lejeune stems from sophisticated natural experiment designs, particularly research comparing leukemia and NHL incidence rates in regions with higher and lower or negligible exposure. Some studies specifically examined leukemia and NHL among personnel stationed at Camp Lejeune compared to those at bases with uncontaminated water supplies.

This body of evidence provides a foundation for analyzing the levels of chemical exposure generally harmful to humans. Numerous studies document elevated leukemia and NHL risks associated with varying levels of exposure to these chemicals. Observing increased hazards and risks at these levels demonstrates that such exposures are clearly capable of causing leukemia and NHL, even though it is likley that lower levels of exposure are also hazardous and pose these same risks.

A limitation in defining hazardous levels of exposure to TCE, PCE, benzene, or vinyl chloride is the absence of randomized controlled trials. Determining precise thresholds would require unethical and impractical long-term studies exposing human participants to these chemicals and monitoring their health outcomes over decades. Instead, there are data from observational studies that give real exposure levels and assess whether affected populations show higher-than-expected leukemia and NHL rates.

It is uncommon for humans to be exposed to environmental chemicals in a way that allows for a precise assessment of negative effects. Epidemiological evidence often reflects gaps in toxicological prevention or regulatory oversight. However, research into TCE, PCE, benzene, and vinyl chloride—especially federal investigations into Camp Lejeune—offers robust data on the consequences of exposure to these chemicals at various concentrations and durations. These data provide compelling evidence that the water contamination at Camp Lejeune was at concentrations known to cause leukemia and NHL.

While epidemiological data often focuses on specific dose ranges where elevated risks have been observed, these should not be interpreted as minimum thresholds below which no hazard exists. Rather, these ranges reflect only the levels studied. The mechanism of action of these chemicals supports the likelihood that lower concentrations also contribute to leukemia and NHL risk. For carcinogens such as TCE, PCE, benzene, and vinyl chloride, even minimal exposure is known to be sufficient to trigger genetic mutations or other biological changes that can lead to cancer. This is consistent with the generally accepted scientific understanding that some carcinogens may not have a threshold below which exposure is entirely safe.

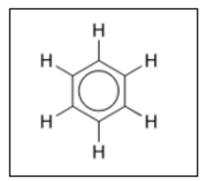
The available data indicates that the levels of chemical exposure at Camp Lejeune were hazardous to humans and are known to cause leukemia and NHL. Epidemiological findings clearly demonstrate increased leukemia and NHL risks at these levels and provides strong support that levels lower than those found specifically in the epidemiology literature are also hazardous to humans generally and are known to cause leukemia and NHL. Mechanistic studies provide evidence of the profound effects that these chemicals have on the DNA and other homeostatic mechanisms of cells, animals, and humans. Decades of mechanistic studies provide a basis for understanding how even low exposure to the Camp Lejeune water contamination chemicals can increase the risk of cancer, including leukemia and NHL. Furthermore, as discussed later in this report, the toxicity of chlorinated hydrocarbons and benzene work in concert (with additive or greater joint effects) to exert their carcinogenicity.

In my opinion, the water at Camp Lejeune more likely than not causes leukemia and NHL—comfortably exceeding the at least as likely standard set forth by Congress. Furthermore, I believe that the quantitative risk of leukemia and NHL from exposure to the combination of TCE, PCE, benzene, and vinyl chloride is more likely than not additive or even higher.

V. EXPOSURE TO THE CHEMICALS FOUND AT CAMP LEJEUNE CAN LEAD TO AN INCREASED RISK OF DEVELOPING LEUKEMIA AND NHL.

A. BENZENE

Benzene has historically been used as a degreaser of metals, a solvent for organic materials, in the chemical industry as an intermediate, and as an additive to gasoline. However, as the carcinogenicity of benzene became more widely recognized, its use has decreased. Benzene in the Camp Lejeune water is thought to have been present as a result of fuel leakage from storage tanks on base.



Benzene is widely recognized as a contributing factor to leukemia. IARC has concluded that benzene contributes to the onset of acute myeloid leukemia and acute nonlymphocytic leukemia. Studies have established a connection between benzene exposure and a heightened risk of acute lymphocytic leukemia, chronic lymphocytic leukemia, multiple myeloma, and non-Hodgkin lymphoma, as noted in the IARC Monograph on Benzene. According to IARC, "a positive association has been observed between exposure to benzene" and "non-Hodgkin lymphoma." [IARC Monograph 120 on Benzene 2018].

“The epidemiological evidence from the meta-analyses (Khalade 2010, Vlaanderen 2011, 2012) indicates that benzene causes all types of leukemia.” [ATSDR Assessment of the Evidence for the Drinking Water Contaminants Causality Assessment, 2017 at 55]. Additionally, ATSDR concludes "there to be sufficient evidence for causation for benzene exposure with non-Hodgkin lymphoma." [ATSDR PHA at 9].

The association between benzene exposure and leukemia has been posited for nearly 100 years.

Building on the early evidence, in 1987, Rinsky et al published a study of leukemia occurrence in people with occupational exposure to benzene [Rinsky RA. NEJM 1987;316:1044-50]. They found an overall standardized mortality ratio (SMR) for leukemia of 3.37 (95% CI 1.54-6.41) and for multiple myeloma of 4.09 (95% CI 1.10-10.47). Furthermore, they identified a monotonic dose-response between benzene exposure and leukemia.

In another key meta-analysis, Steinmaus et al. (2008) identified significant associations between benzene exposure and NHL. Their findings included a summary relative risk (RR) of 1.22 (95% CI 1.02-1.47) for individuals exposed to benzene. Notably, when studies with possible misclassification of exposure groups were excluded, the RR increased to 1.49 (95% CI 1.12-1.97). Further adjustments that excluded studies relying on self-reported occupational histories strengthened the RR even more, to 2.12 (95% CI 1.11-4.02). [Steinmaus C. Occup Environ Med 2008;65:371-8]

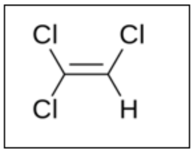
Furthermore, a meta-analysis demonstrates "a causal link between benzene exposure and non-Hodgkin lymphoma, especially for diffuse large B-cell lymphoma." [Rana L. Lancet Planet Health 2021;5:e633–43].

Numerous studies have thoroughly investigated the relationship between benzene exposure and the development of leukemias. The evidence demonstrating the causal relationship between benzene exposure and different types of leukemias is considered some of the strongest in the field of medicine. Similarly, benzene exposure has been linked to lymphomas, including NHL, with the National Toxicology Program proclaiming that "benzene is known to be a human carcinogen based on sufficient evidence of carcinogenicity from studies in humans." [NTP 15th Report on Carcinogens, 2021]. The EPA also characterizes benzene as "a known human carcinogen for all routes of exposure based upon convincing human evidence as well as supporting evidence from animal studies." [EPA Toxicological Review of Benzene (CASRN 71-43-2), 2000].

The link between benzene exposure and non-Hodgkin lymphoma (NHL) has been supported by multiple reviews and meta-analyses. The International Agency for Research on Cancer (IARC) has noted evidence of a "positive association" between benzene exposure and NHL. [IARC Monograph 120 on Benzene 2018]. Similarly, the Agency for Toxic Substances and Disease Registry (ATSDR) has concluded that sufficient evidence exists to establish causation between benzene exposure and NHL. [ATSDR PHA at 9].

Meta-analytical studies have further strengthened the understanding of benzene's role in the development of NHL. Rana et al. conducted an extensive review, suggesting a causal relationship between benzene exposure and NHL, with particularly strong evidence for diffuse large B-cell lymphoma (DLBCL). [Rana L. Lancet Planet Health 2021;5:e633–43].

B. TCE



TCE is a human-made, colorless, volatile liquid chemical that is used as a solvent and in many other applications. TCE is used as a solvent to remove grease from metal, as a paint stripper, and in the production of other chemicals. It can also be found in some household products, such as cleaning wipes, paint removers, and adhesives. TCE is a volatile organic compound (VOC) that is highly persistent in the environment, contaminating soil and groundwater, as occurred at Camp Lejeune.

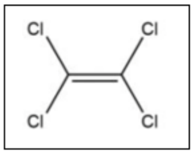
The scientific community agrees that TCE is carcinogenic. IARC classifies it as a known human carcinogen, citing "sufficient evidence in humans for the carcinogenicity of trichloroethylene" [IARC 2014 at 189]. The EPA concurs, describing TCE as carcinogenic to humans through all exposure routes. Furthermore, ATSDR found that the evidence for TCE and leukemia indicates a risk of about 1.10, which was "sufficient to at least reach equipoise." [ATSDR Assessment of the Evidence 2017]. Evidence indicates that TCE specifically contributes to leukemia. These conclusions are drawn from extensive human and animal research. Positive findings for TCE and leukemia have been observed for each type of leukemia. Elevated risks have been found for TCE and AML with HR of 1.12 in medium and high-exposure groups [Talibov M. Scand J Work Environ Health 2014;40:511-7]. Furthermore, a study by Cohn *et al.* demonstrated an increased risk of ALL and CML in residents of New Jersey who had water contaminated with TCE and other chemicals [Cohn P. Environ Health Perspect 1994;102:556-61].

Trichloroethylene (TCE) has been specifically linked to an increased risk of non-Hodgkin lymphoma (NHL). As noted by Rosenfeld, research has demonstrated that "TCE increases the risk of non-Hodgkin's lymphoma (NHL) and its subtypes." [Rosenfeld 2024].

A meta-analysis conducted by Mandel *et al.* in 2006 examined the relationship between TCE exposure and NHL through an analysis of 14 occupational cohort studies and four case-control studies. The meta-analysis focused on workers exposed to TCE and revealed a summary relative risk of 1.29 (95% CI 1.00-1.66) for the total cohort. When isolating data from the seven studies that specifically identified a TCE-exposed sub-cohort, the relative risk increased to 1.59 (95% CI 1.21-2.08). [Mandel JH. Occup Environ Med 2006;63:597–607].

In a review of the literature, Scott and Jinot analyzed findings on TCE exposure and NHL risk. Their report, conducted under the auspices of the U.S. Environmental Protection Agency (EPA), calculated a summary risk estimate of 1.23 (95% CI 1.07-1.42) for overall TCE exposure. For the highest exposure group, the relative risk rose to 1.43 (95% CI 1.13-1.82). [Int J Environ Res Public Health 2011;8:4238-72].

C. PCE



Perchloroethylene (also known as tetrachloroethylene) is widely known for its wide use in the dry-cleaning industry, but it has had other uses in industry. In the 1950s, roughly 80% of PCE was used for dry-cleaning; today, PCE use has been phased out in some states, and much less is used in dry-cleaning. Other industrial uses of PCE include as a degreaser and chemical synthesis intermediate.

PCE is classified by every regulatory body as a probable human carcinogen. In 2014, IARC classified PCE as probably carcinogenic to humans (Group 2A) based upon sufficient evidence in animals and limited evidence in humans [IARC 2014 at 329]. Similarly, in 2012 the EPA declared that PCE is "Likely to be Carcinogenic to Humans" by all routes of exposure. [EPA. Toxicological Review of Tetrachloroethylene (Perchloroethylene) (CAS No. 127-18-4), 2012]. Furthermore, the National Toxicology Program (NTP) has opined that PCE "is reasonably anticipated to be a human carcinogen." [NTP 15th Report on Carcinogens, 2021].

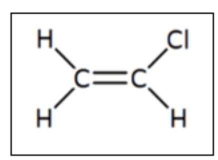
Some epidemiological studies have found an association between PCE exposure and leukemia. For instance, Cohn *et al*. examined water contamination in New Jersey and found an increased incidence of leukemia among females exposed to high levels of PCE, with a relative risk of 1.43 (95% CI 1.97-1.90) and a RR in males of 1.10 (95% CI 0.84-1.43). Similarly, elevated risks were also identified for ALL. Cohn P. Environ Health Perspect 1994;102:556-61]

Similarly, in 2012 the EPA declared PCE exposure is associated with an "elevated risk" of NHL specifically. [EPA. Toxicological Review of Tetrachloroethylene (Perchloroethylene) (CAS No. 127-18-4), 2012]. Furthermore, the National Toxicology Program has opined that PCE "is reasonably anticipated to be a human carcinogen." [NTP 15th Report on Carcinogens, 2021]. ATSDR concluded that, based upon the epidemiological evidence, there is equipoise and above evidence for causation for PCE and NHL. [ATSDR 2017].

Selden and Ahlborg published findings from a cohort of more than 10,000 dry-cleaning and laundry workers that had occupational exposure to PCE and were followed from 1985 to 2006. They found elevated rates of NHL (SIR 2.05; 95% CI 1.30–3.07). [Selden AI and Ahlborg G. Int Arch Occup Environ Health 2011;84:435–43].

A 2016 study by 't Mannetje et al. examined occupations and the development of NHL by conducting a pooled analysis of 10,046 cases and 12,025 controls from 10 NHL studies participating in a consortium of lymphoma researchers. ['t Mannetje A. Environ Health Perspect 2016;124:396–405]. They found an elevated risk of NHL with an OR of 1.29 (95% CI 0.74–2.23) for those with greater than 10 years of employment as a dry-cleaning worker.

D. VINYL CHLORIDE



Vinyl chloride is a volatile compound used almost exclusively by the plastics industry to produce polyvinyl chloride (PVC). Vinyl chloride has been detected at low concentrations in the air in the vicinity of vinyl chloride and PVC manufacturing plants and hazardous waste sites. Vinyl chloride has also contaminated groundwater from spills, landfills, and industrial sources. Vinyl chloride can also enter groundwater after being produced as a byproduct during the degradation of TCE and PCE.

According to IARC, "There is sufficient evidence in humans for the carcinogenicity of vinyl chloride. Vinyl chloride causes angiosarcoma of the liver, and hepatocellular carcinoma. There is sufficient evidence in experimental animals for the carcinogenicity of vinyl chloride." [IARC

Monograph 100F, 2012 at 451]. Similarly, the EPA has classified vinyl chloride as Group A "carcinogenic to humans." [EPA Hazard Assessment for Vinyl Chloride, report 75-01-4, January 2000]. The NTP has also found that vinyl chloride "is known to be a human carcinogen based on sufficient evidence of carcinogenicity from studies in humans." [NTP 15th Report on Carcinogens, 2021].

There are studies demonstrating increased mortality due to leukemias with occupational exposure to vinyl chloride. Hsieh *et al.* studied polyvinyl chloride workers in Taiwan and found significantly increased standardized mortality ratios for leukemia which increased during 1984-1989 (SMR 6.06; 95% CI 1.24-17.53), reached a peak during 1985-1990 (SMR 7.56; 95% CI 2.06-19.35), and then decreased after vinyl chloride exposure was mitigated in the factories. [Hsieh HI. Occup Environ Med 2011;68:120-5]

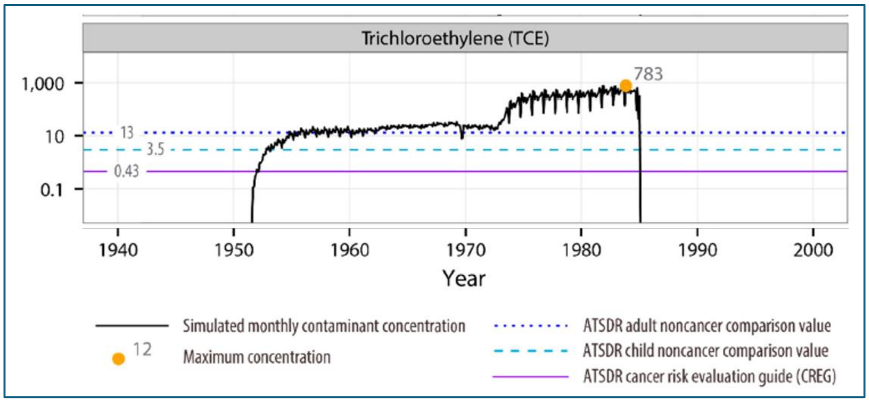
VI. CHEMICAL CONTAMINATION IN THE WATER AT CAMP LEJEUNE SPANNED DECADES

The ATSDR conducted mathematical modeling to simulate the contaminants in the water supplied to base housing and other facilities at Camp Lejeune. The modeling results revealed that water provided by the Tarawa Terrace and Hadnot Point Water Treatment Plants was contaminated with various levels of PCE, TCE, 1,2-tDCE (trans-1,2-dichloroethylene), vinyl chloride, and benzene between 1953 and 1987. Detailed monthly mean contaminant concentrations over time for Tarawa Terrace, Hadnot Point, and Holcomb Boulevard are documented in the ATSDR tables and were also provided to me in Appendices H1, J, and K of the October 25, 2024, Expert Report by Morris L. Maslia.

At the Tarawa Terrace Water Treatment Plant, simulated PCE levels peaked at an average of 183 µg/L per month, with a single measured high of 215 µg/L, both far above the EPA's current limit of 5 µg/L. These levels exceeded the limit between November 1957 and February 1987. At Hadnot Point, simulated TCE levels averaged a maximum of 783 µg/L per month, with a one-time high of 1,400 µg/L, during the period from August 1953 to December 1984. Hadnot Point also supplied contaminated water to the Holcomb Boulevard housing area continuously until June 1972, when the Holcomb Boulevard Water Treatment Plant began operations. After that, Hadnot Point intermittently provided water with TCE levels peaking at 32 µg/L before June 1972 and 66 µg/L between June 1972 and February 1985.

A. HADNOT POINT: TCE CONTAMINATION

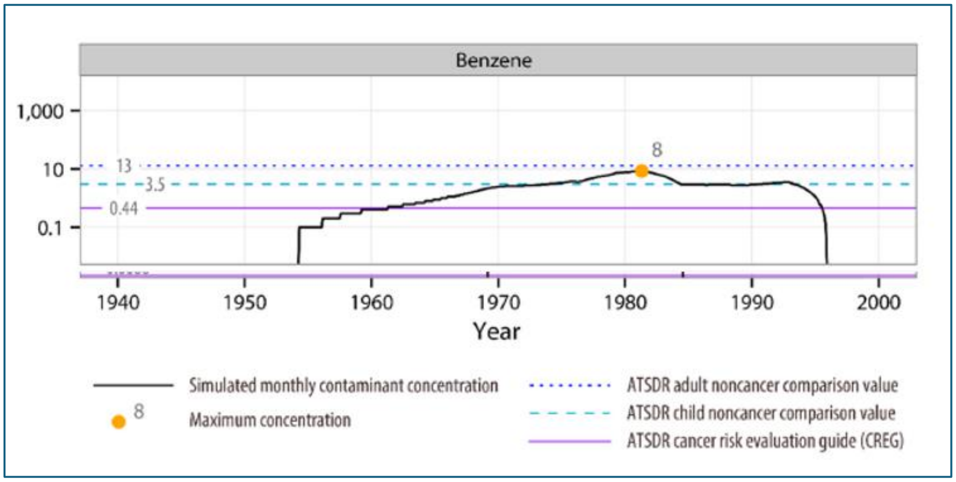
At Hadnot Point, TCE concentrations ranged from 0 to 783 micrograms per liter, with a median level of 366 micrograms per liter. [Bove 2014a at 3]. The reconstructed concentrations in the water are illustrated in the graph below.



The graph illustrates that TCE concentrations at Hadnot Point consistently exceeded CREG level,[1] defined as the "concentrations of cancer-causing substance [that are] unlikely to result in an increase of cancer risk in an exposed population." [ATSDR PHA at 7]. For TCE, the CREG limit is 0.43 ppb. With a maximum concentration of 783 ppb at Camp Lejeune, TCE levels exceeded the CREG limit by a factor of 1,820.

B. HADNOT POINT: BENZENE CONTAMINATION

The reconstructed benzene concentrations in the water at Hadnot Point are illustrated in the graph below.



The graph shows that benzene levels consistently surpassed the CREG level of 0.45 ppb. The maximum benzene concentration recorded at Camp Lejeune was 8 ppb, exceeding the CREG limit by a factor of 17.

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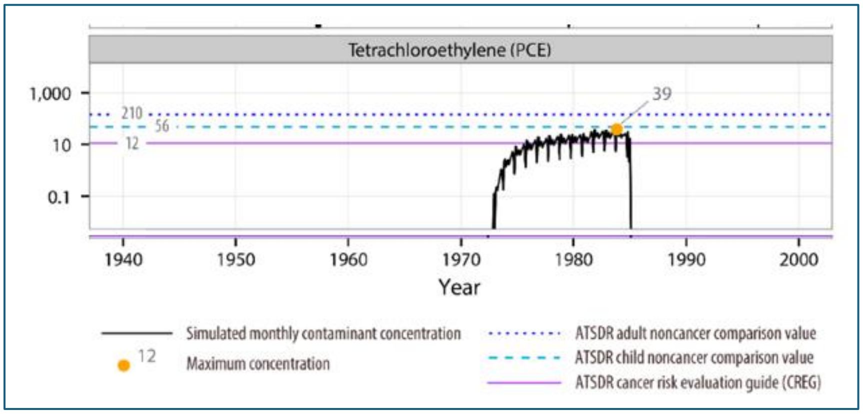
[1] CREG refers to the Cancer Risk Evaluation Guide level developed by the ATSDR. [ATSDR PHA at 7].

C. HADNOT POINT: PCE CONTAMINATION

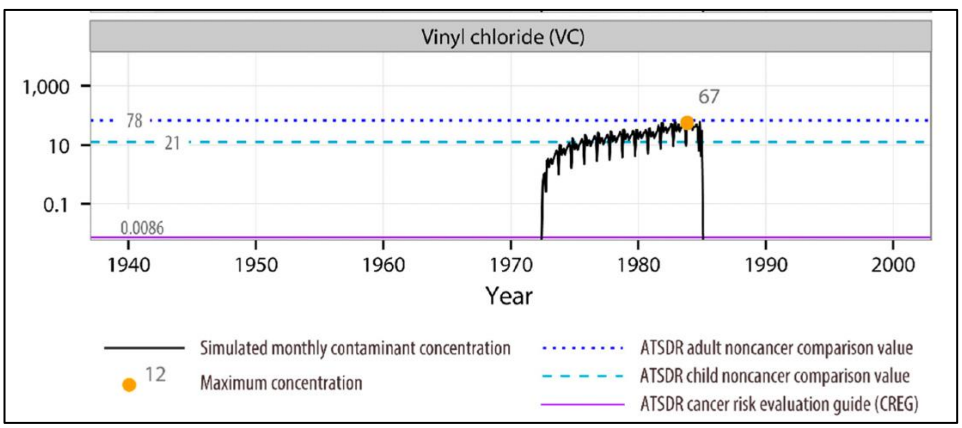
At Hadnot Point, the median monthly PCE contamination was 15 micrograms per liter. [Bove 2014a at 3]. The reconstructed concentrations in the water are illustrated in the graph below.



As shown, PCE concentrations at Hadnot Point regularly exceeded the CREG limit of 12 ppb. The maximum concentration of 39 ppb recorded at Camp Lejeune was more than three times the CREG limit.

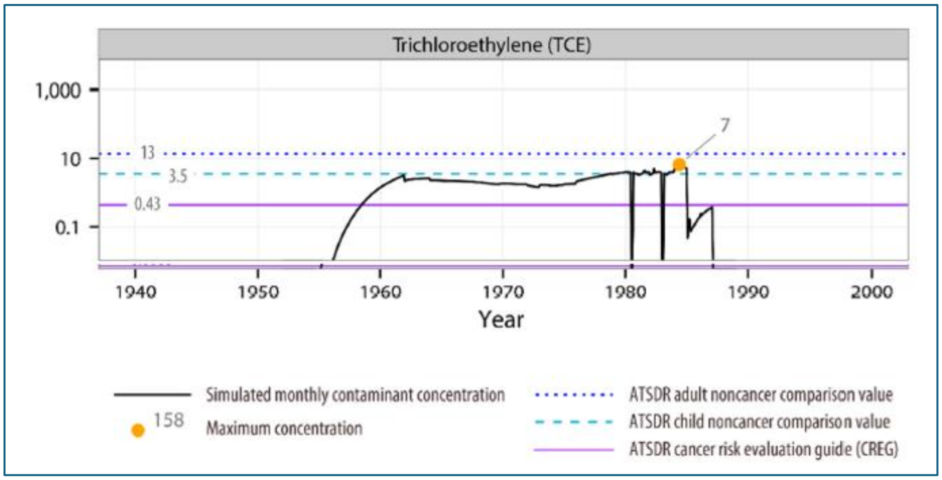
D. HADNOT POINT: VINYL CHLORIDE CONTAMINATION

The reconstructed vinyl chloride concentrations from the water at Hadnot Point are shown below. The graph shows that vinyl chloride concentrations were above the CREG limit of 0.0086 ppb for the entire time concentrations of vinyl chloride were calculated at Hadnot Point (from early 1970s until 1985), with a maximum concentration of 67 ppb.



E. TARAWA TERRACE: TCE CONTAMINATION

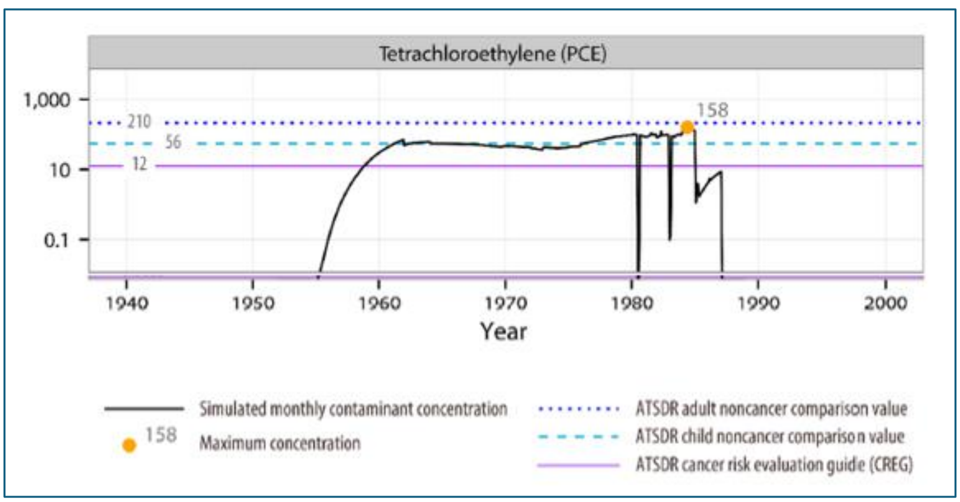
The reconstructed TCE concentrations in the water at Tarawa Terrace are shown below.



The graph reveals that TCE levels at Tarawa Terrace regularly exceeded the CREG limit of 0.43 ppb. The highest reconstructed concentration of 7 ppb at Camp Lejeune was more than 16 times the CREG limit.

F. TARAWA TERRACE: PCE CONTAMINATION

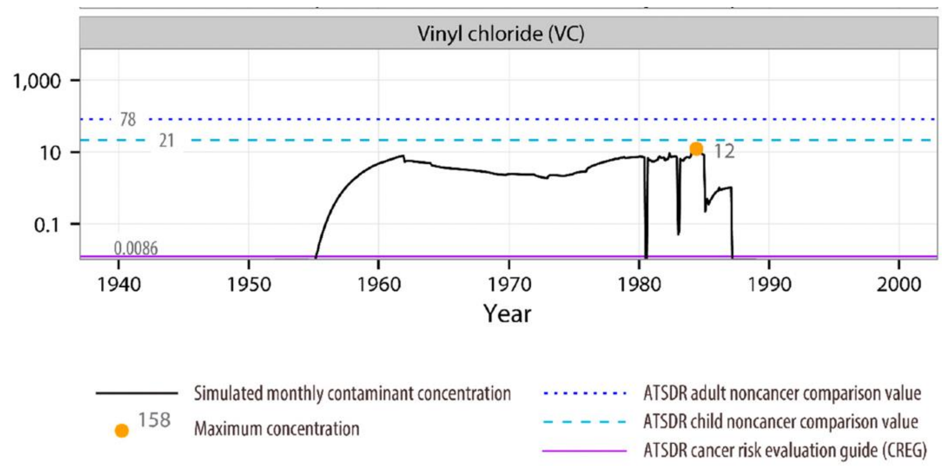
At Tarawa Terrace, concentrations of PCE ranged from 0 to 158 µg/liter, with a median of 85 µg/liter [Bove 2014a at 3]. The reconstructed concentrations in the water are illustrated in the graph below.



The graph indicates that PCE concentrations at Tarawa Terrace routinely surpassed the CREG limit of 12 ppb. The maximum concentration of 158 ppb was more than ten times the CREG limit, exceeding it by an order of magnitude.

G. TARAWA TERRACE: VINYL CHLORIDE CONTAMINATION

The reconstructed vinyl chloride concentrations from the water at Tarawa Terrace are shown below. The maximum reconstructed vinyl chloride concentration at Tarawa Terrace was 12 ppb, which occurred around 1985. From 1958 to early 1985 the estimated vinyl chloride concentrations levels exceeded the current 2-ppb maximum contaminant level. In addition, from early 1955 to early 1987, the 0.0086-ppb ATSDR CREG value was continuously exceeded.



H. HOLCOMB BOULEVARD

Holcomb Boulevard was also affected by the contamination. Before 1972, its water supply came from Hadnot Point water system, meaning the exposure analysis for Holcomb Boulevard aligns with that of those in Hadnot Point [ATSDR PHA at 14].

Even after 1972, Holcomb Boulevard intermittently received water from Hadnot Point, with TCE concentrations ranging from 38 ppb to 1,148 ppb. These concentrations exceeded CREG limits of 0.43 ppb by factors ranging from over 80 to more than 2,500.

I. RISK ASSESSMENTS

1. Risks based on CREG limits underrepresent actual cancer risk

The Cancer Risk Evaluation Guide (CREG) limits are established to achieve a "target risk level" of 1 x 10^{-6}, equivalent to a theoretical risk of one additional cancer case per million exposed individuals. These limits are intended to be conservative, and focus on public health by minimizing the potential for cancer cases resulting from chemical exposure. However, CREG limits have notable limitations. Regulatory assessments, including those used to establish CREG levels, are not designed to estimate individual cancer risk; their primary focus is on identifying population-level hazards.

A limitation is that CREG levels are not cancer specific. They define the general risk of cancer within a population without distinguishing between cancer types, such as leukemia or NHL. This stems from their regulatory purpose—agencies are tasked with identifying and mitigating unacceptable risks without the need to classify risks by cancer type. Whether a contaminant increases the likelihood of breast cancer or lung cancer is irrelevant to the decision to remediate the site; the focus is on addressing the hazard to public health as a whole. This approach avoids unnecessary delays for cleanup efforts.

Another limitation is that CREG levels are not designed to assess individual risk. The process of regulatory risk assessment is distinct from determining causation. While both rely on similar toxicological and epidemiological data, the goals are different. CREG levels seek to identify environmental conditions that warrant intervention, not to evaluate the likelihood of cancer causation for any particular person. This distinction is important when considering the limitations of dose-response models used in regulatory settings.

For example, cancer dose-response models do not account for inter-individual variability. Factors such as genetics, developmental stage, dietary habits, and behavior influence the way a person responds to chemical exposure. [Li L. Front Sustain. 2021;2:648138]. Because CREG levels are derived based on population medians, they may underestimate risks to individuals who are more vulnerable to toxic effects. Studies have documented these limitations, highlighting the potential for CREG levels to understate risk in sensitive individuals. [Varshavsky JR. Environ Health. 2023;21:133].

Despite these limitations, CREG levels remain effective for identifying hazards that necessitate intervention. Once a risk greater than 1×10^{-6} is demonstrated, site remediation is justified, regardless of whether the true risk is 1×10^{-6}, 1×10^{-4}, or even 1 in 10. The purpose of CREG limits is to highlight unacceptable risks, not to differentiate different degrees of high risk.

2. Theoretical risks are grounded in conservative assumptions

It is also important to understand that CREG limits are based on theoretical risks derived from animal studies rather than observed cancer rates in humans. Ethical constraints prevent exposing humans to carcinogens like TCE and PCE in controlled experiments, so scientists rely on animal data to extrapolate human risk. This process involves assumptions about dose-response relationships and cross-species equivalencies. [NTP 15th Report on Carcinogens Monographs on TCE and PCE, 2015].

These extrapolations are subject to uncertainty. The applicability of dose-response curves in animal studies to human physiology leads to necessary uncertainty. Adding to this uncertainty is the fact that interspecies variation is well-documented. For example, the lethal dose of dioxin in guinea pigs is 0.1 micrograms per kilogram of body weight, while in hamsters, it is over 10,000 times greater. [EFSA Journal. 2018;16:5333]. This variability illustrates the challenges of translating animal study findings into human risk assessments.

Uncertainty increases at lower doses, where direct measurements are often unavailable. Scientists must make assumptions about how chemicals behave at these levels, leading to significant uncertainty that can span several orders of magnitude. [Slob W. Risk Analysis. 2014;34:1401-22].

3. Human epidemiology evidence

Although CREG limits are useful for identifying environmental hazards, human epidemiological data are valuable for assessing cancer risk, particularly for populations like those at Camp Lejeune. Epidemiological studies evaluate real-world exposures and outcomes, providing critical insights into the actual risk posed by contaminants. Unlike CREG levels, these studies can sometimes account for the combined effects of multiple chemicals and the synergistic interactions between them. [Vandenberg LN. Environ Health. 2022;21:121].

For instance, research specific to Camp Lejeune has consistently demonstrated elevated risks for cancers such as leukemia and NHL among those exposed to the contaminated water.

4. Contaminant levels far exceeded CREG limits

Finally, while CREG limits suggest a theoretical risk of 1×10^{-6}, the contaminant concentrations at Camp Lejeune vastly exceeded these levels. As detailed above, TCE and PCE concentrations at the base were often several orders of magnitude higher than the CREG limits. For example, the highest TCE concentration at Hadnot Point reached 1,400 ppb—more than 3,000 times the CREG limit for TCE.

Given these levels of contamination and the epidemiological evidence linking Camp Lejeune exposures to increased cancer risks, the theoretical 1×10^{-6} risk associated with CREG limits significantly understates the actual hazard posed to individuals exposed to the water at Camp Lejeune.

VII. ROUTES OF EXPOSURE TO THESE CHEMICALS

The topic of routes of exposure for the relevant identified chemicals naturally relates to the issue of the sources and concentrations of the subject chemicals in the potable water at the base during the statutorily delimited pertinent time period (1950s-1980s). With regard to background of the chemicals and data on their concentrations in the water, I have considered the work of the ATSDR for general background, however I do not opine on issues such as reliability of historical evidence for TCE or PCE water concentrations at the base or of ATSDR water modeling reconstruction of past contaminant levels in the water, and I defer to others with appropriate areas of expertise. With regard to historical factual background regarding the base during the time period at issue, I have in addition to ATSDR publications reviewed and considered the expert report of Dr. Kyle Longley prepared for this case. His report compiles information regarding historical facts of life and work at Camp Lejeune. I have not sought to independently verify Dr. Longley's report, however, I note that if the facts cited by Dr. Longley's report are accurate, they identify a variety of discrete VOC exposure settings at Camp Lejeune through the routes of ingestion, inhalation, and dermal exposure which are of potential significance to the present matter.

A. IN GENERAL

When evaluating the health effects of chemicals, it is important to understand how the chemicals enter and are distributed throughout the body. It is also important to understand how the body metabolizes and excretes the parent chemicals and their metabolites.

Chemicals such as PCE, TCE, benzene, and vinyl chloride are VOCs. People are exposed to VOCs in water by three major routes: inhalation, ingestion, and via dermal contact.

A number of studies have looked at the relative importance of those several routes. For example, over 25 years ago, Weisel and Jo determined estimates of internal doses of TCE due to showering [Weisel CP. and Jo WK. Environ Health Perspect 1996;104:48-51]. They concluded that inhalation and dermal exposure resulted in an internal dose of TCE comparable to the dose ingested in 2 liters of water. More recently, Gordon et al. investigated the contribution of household water use to internal doses of chloroform and other trihalomethanes [Gordon SM. Environ Health Perspect 2006;114:514-21]. They found that showering and bathing resulted in the highest blood and exhaled-breath concentrations of chloroform with both inhalation and dermal absorption being important routes of exposure.

Demonstrating the importance of water temperature, Giardino and Andelman found that the volatilization of TCE during showering was most dependent on the temperature of water [Giardino NJ and Andelman JB. J Expo Anal Environ Epidemiol 1996;6:413-23]. Adding insight to the role that all three forms of exposure play in contributing to the internal dose of TCE, Haddad et al. used assessed different home exposure scenarios and concluded that ingestion contributed less than 50% of the total absorbed dose of TCE [Haddad S. J Toxicol Environ Health A 2006;69:2095-136]. Thus, absorption from the lungs, and the gastrointestinal tract, as well as from intact and broken skin dermal contact, must be taken into account when determining the internal dose that results from use of water contaminated with VOCs.

Whatever the route of exposure to a chemical, ultimately the portion of the chemical that enters the body from the lungs, gastrointestinal tract, or skin (sometimes termed the internal dose) is the portion that exerts biological effects. Pharmacokinetics (or toxicokinetics) and physiologically based toxicokinetic ("PBTK") models are important in addressing uncertainties inherently present in health risk assessments of the water contaminants at Camp Lejeune. Toxicokinetics can be defined as the absorption, distribution, metabolism, and elimination of chemicals. The kinetic processes determine how much of an external dose is absorbed into the blood, reaches systemic circulation; binds to proteins or other sites; enters specific organs; is biotransformed (if relevant) to toxicologically active and inactive forms; interacts with target molecules, cells, and tissues; and is eliminated from the target tissue and the body [Bruckner JV. Toxic effects of solvents and vapors. In Casarett and Doull's Toxicology: The Basic Science of Poisons, 9th Ed]. One or more of those processes can vary widely from one route of exposure to another, from high to low doses, from one species to another, and from one individual to another. Furthermore, as discussed below, in a multi-chemical setting, chemicals mix. "Our knowledge of the toxicity of solvent mixtures is rudimentary relative to the toxicology of individual solvents. While the assumption is frequently made that the toxic effects of solvents are additive, the chemicals may also interact synergistically or antagonistically." [Bruckner JV. Toxic effects of solvents and vapors. In Casarett and Doull's Toxicology: The Basic Science of Poisons, 9th Ed., Chapter 24 (Toxic Effects of Solvents and Vapors), p. 2 of 157].

Various scientific studies published regarding the relevant chemicals such as PCE and TCE have assessed exposure scenarios that involved potable water use and therefore implicitly the potable water exposure routes (ingestion, inhalation of vapor, and dermal). These have included studies reflecting comparable levels of VOC concentrations. See, e.g., Cohn P. Environ Health Perspect. 1994 Jun;102(6-7):556-61, at 557, which was a study of TCE and PCE drinking water contamination and leukemia and non-Hodgkin's lymphoma incidence in a 75-town area. "The highest assigned TCE level was 67 ppb, the highest assigned PCE level was 14 ppb…. The population-weighted concentrations of TCE and PCE in the highest categories were 23.4 ppb and 7.7 ppb, respectively. Four of the six municipalities in the highest TCE category were also in the highest PCE stratum. The population-weighted concentrations of TCE and PCE in the highest strata of the 48 municipalities added for this expanded study are 8.7 and 10.5 in 2 and 4 added towns, respectively."). Also see Fagliano J. Drinking Water Contamination and the Incidence of Leukemia: An Ecologic Study. Am J Public Health 1990;80:1209-12. That study examined the relation between the incidence of leukemias and the occurrence of VOC contamination (TCE and related solvents) of drinking water supplies within a study area. The study described the data including the mean total VOC values assigned to each town or group of towns for the analysis. TCE, PCE, TCA, and dichloroethylenes (DCE) comprised nearly all of the non-THM VOCs involved. Based on inspection of the average values for each town, three categories of total VOCs were set: 1) 37 to 72 ppb, 2) 5 to 12 ppb, and 3) down to less than 1 ppb. Among other things the authors reported that "[t]he sum concentration of all non-THM VOCs was a statistically significant predictor of total leukemia incidence, adjusted for age." Id. at p. 1211.

As another example of a study involving VOCs in drinking water, see Aschengrau A. Cancer risk and tetrachloroethylene-contaminated drinking water in Massachusetts. Arch Environ Health 1993;48:284-92, evaluating an exposure scenario involving PCE that leached from pipe liners into the public water supply. The abstract relates in part: "A population-based case-control study was used to evaluate the relationship between cases of bladder cancer (n = 61), kidney cancer (n = 35), and leukemia (n = 34) and exposure to tetrachloroethylene from public drinking water. Subjects were exposed to tetrachloroethylene when it leached from the plastic lining of drinking water distribution pipes. Relative delivered dose of tetrachloroethylene was estimated, using an algorithm that accounted for (1) residential history and duration, (2) whether lined pipe served the neighborhood, (3) distribution system flow characteristics, and (4) pipe age and dimensions. Whether or not latency was considered, an elevated relative risk of leukemia was observed among ever exposed subjects (adjusted OR = 1.96, 95% CI = 0.71-5.37, with latency; adjusted OR = 2.13, 95% CI = 0.88-5.19, without latency) that increased further among subjects whose exposure level was over the 90th percentile (adjusted OR = 5.84, 95% CI = 1.37-24.91, with latency; adjusted OR = 8.33, 95% CI = 1.53-45.29, without latency). When latency was ignored, there was also an increased relative risk of bladder cancer among subjects whose exposure level was over the 90th percentile (adjusted OR = 4.03, 95% CI = 0.65-25.10)." See id. A later publication regarding the same site described that "[t]ypical levels [of PCE slowly leaching from vinyl pipe liners] in affected towns ranged from 1,600 to 7,750 µg/L in low-flow locations, and from 1.5 to 80 µg/L in medium- and high-flow locations." [Aschengrau A. Environ Health Perspect, 2003 Feb;111(2):167-73 at 167.]

B. ABSORPTION VIA INGESTION

1. TCE

The evidence for oral ingestion absorption of TCE from water contamination is well-documented.

Studies have shown that TCE is absorbed through the gastrointestinal tract when ingested. With regard to animal studies, Liu *et al.* demonstrated that TCE exhibits linear kinetics in rats over a dosage range of 0.1 to 5.0 mg/kg, with bioavailability ranging from 12.5% to 16.4%. [Liu Y. Drug Metab Dispo: Biol Fate Chem. 2009;37:1994-8]. This indicates that a significant portion of ingested TCE from water is absorbed into the bloodstream.

In volunteer studies in humans, Weisel and Jo found that ingestion of TCE from tap water leads to its complete metabolism before entering the bloodstream, suggesting that the absorbed dose is metabolized primarily in the liver. [Weisel CP and Jo WK. Environ Health Perspect. 1996;104:48-51] This presystemic metabolism reduces the amount of TCE reaching systemic circulation, but does not negate the fact that absorption occurs. Furthermore, as discussed in the mechanism of toxicity section of this report, TCE and the other halogenated hydrocarbons undergo metabolism to more toxic chemicals that damage DNA and cause cancer. [See Bruckner JV. Toxic effects of solvents and vapors. In Casarett and Doull's Toxicology: The Basic Science of Poisons, 9th Ed., at Chapter 24 (Toxic Effects of Solvents and Vapors), p. 25 of 157, stating that "[t]he adverse effects of TCE … are generally believed to be associated with TCE's metabolites."]. Publications since Weisel and Jo 1996 provide further insight on the mechanism of TCE absorption via ingestion. [*E.g.*, Lash LH, Fisher JW, Lipscomb JC, Parker JC. Metabolism of trichloroethylene. Environ Health Perspect. 2000 May;108 Suppl 2(Suppl 2):177-200. doi: 10.1289/ehp.00108s2177. PMID: 10807551; PMCID: PMC1637769.]

Additionally, Mortuza *et al.* reported that TCE exhibits nonlinear toxicokinetics with a disproportionate increase in area under the curve and a decrease in clearance with increasing doses, in rats further supporting the absorption and systemic distribution of TCE following oral ingestion. [Mortuza T. Toxicol Appl Pharmacol 2018;360:185-92].

2. PCE

Studies of controlled dosing of PCE in humans are lacking. In one case report, PCE was detected in blood at a concentration of 21.5 µg/mL approximately 1 hour after ingestion by a 6-year-old boy who had ingested between 12 to 16 g of PCE, demonstrating that PCE is absorbed following oral exposure in humans [Koppel C. Clin Toxicol 1985;23:103-15]. The evidence for oral ingestion absorption of PCE from water contamination is also supported by several studies. In a rat study by Frantz and Watanabe, they found after drinking-water administration, the elimination kinetics of PCE were not substantially different from the disposition resulting from inhalation [Frantz SW and Watanabe PG. Toxicol Appl Pharmacol 1983;69:66-72]. Pegg et al.

also found that absorption of inhaled or oral PCE were essentially identical in rats [Pegg DG. Toxicol Appl Pharmacol 1979;51:465-74]. Similarly, PCE is nearly completely absorbed in dogs given a single dose by gavage [Dallas CE. Environ Res 1994;67:54-67].

In addition, a study by Wittlingerová *et al.* provides evidence of PCE contamination in surface water and its subsequent bioaccumulation in fish, indicating that PCE is indeed absorbed by organisms in contaminated water environments. [Wittlingerová Z. Environ Sci Poll Res Int 2016;23:5676-92].

The US EPA in 2012 completed a comprehensive toxicological review of PCE, which included an assessment of its toxicokinetics and metabolism. This review indicated that PCE is absorbed through the gastrointestinal tract when ingested, leading to systemic exposure. [Guyton KZ. Environ Health Perspect 2014;122:325-34].

3. Benzene

The evidence for oral absorption of benzene from water contamination is supported by several studies. In 1996, Beavers *et al.* assessed household exposure from gasoline-contaminated drinking water and found that ingestion of contaminated water contributed significantly to the total benzene dose, although inhalation during activities such as showering also played a major role. [Beavers JD. J Occup Environ Med 1996;38:35-8].

Santos et al. conducted a risk assessment following a gasoline station fuel leak and found that the population exposed to benzene-contaminated water had a significant intake of benzene through ingestion, with estimated benzene intake from water and food reaching up to 0.0091 µg/kg /day. [Santos M dos A. Rev Saúde Pública 2013;47(2):335-44]. The facts reflected that "the community was exposed to benzene from water consumption for 195 days and from water dermal contact and water vapor inhalation for 315 days. The mean concentration of benzene in the water estimated by the model during the oral exposure period (range of 5.1 to 235.5 µg/) was 72.6 µg/L (95%CI 40.9;104.2)."

See also generally Harrison R, Delgado Saborit JM, Dor F, et al. Benzene. In: WHO Guidelines for Indoor Air Quality: Selected Pollutants. Geneva: World Health Organization; 2010 ("Absorption of benzene is also rapid via the oral and dermal routes. Rats absorb and rapidly metabolize oral doses of benzene up to approximately 50 mg/kg.").

4. Vinyl chloride

The evidence for absorption of vinyl chloride after oral ingestion from water contamination is primarily derived from animal studies. Research indicates that vinyl chloride is absorbed and metabolized following oral administration. For instance, Green and Hathway demonstrated that after oral administration of C^{14} vinyl chloride to rats, the compound is primarily eliminated via the pulmonary route, with both unchanged vinyl chloride and its metabolites being excreted through the lungs and kidneys. This study also showed that the biotransformation of vinyl chloride involves several metabolic pathways, leading to the formation of various metabolites, including S-(2-chloroethyl) cysteine and N-acetyl-S-(2-chloroethyl) cysteine. [Green T and

Hathway DE. Chem-Bio Interact 1975;11:545-62].

Additionally, Watanabe and Gehring found that the disposition of vinyl chloride in the body is dose-dependent, with higher doses saturating metabolic or detoxifying pathways, which could correlate with its oncogenic potential. [Watanabe PG and Gehring PJ. Environ Health Perspect 1976;17:145-52] This suggests that vinyl chloride is absorbed and metabolized in a manner that is influenced by the dose ingested.

See also generally World Health Organization 2004. Vinyl Chloride in Drinking-water. WHO/SDE/WSH/03.04/119, at 4 ("Animal studies show absorption of more than 95% after oral exposure.").

C. ABSORPTION VIA INHALATION

1. TCE

Weisel and Jo's research highlighted that individuals are exposed to volatile compounds like TCE from tap water not only through ingestion but also via inhalation and dermal absorption during activities such as showering. Their study found that inhalation exposure during showering can significantly increase the body burden of TCE, indicating that inhalation is a critical route of exposure from contaminated water. [Weisel CP and Jo WK. Environ Health Perspect 1996;104:48-51]. The investigators concluded that "[t]he internal dose derived from inhalation can be calculated from the air concentration, breathing rate, duration of the shower, and adsorption efficiency across the lung barrier." Furthermore, Weisel and Jo found that "approximately equivalent amounts of volatile contaminants from water can enter the body by three different exposure routes, inhalation, dermal absorption, and ingestion, for typical daily activities of drinking and bathing. However, the exposure route affects the rates of metabolism and therefore the compound's potential toxicity. The ingested VOCs were metabolized during the first pass through the liver, thus the parent compound was not measurable in the exhaled breath and would not be present in the bloodstream. However, chloroform and trichloroethene concentrations were measurable in the breath after inhalation and dermal exposure, indicating dispersion throughout the body."

Furthermore, Liu *et al.* assessed the health risks associated with different exposure pathways of volatile chlorinated hydrocarbons, including TCE, in contaminated drinking groundwater. They found that inhalation during showering posed a higher risk compared to oral ingestion, underscoring the importance of inhalational exposure in the overall risk assessment. [Liu W. Environ Pollut 2009;255:113339].

See also ATSDR Public Health Statement for Trichloroethylene (TCE), CAS#: 79-01-6 ("When trichloroethylene is found in water, it can enter your body when you drink or touch the water or when you breathe in steam from the water. Most of the trichloroethylene that you breathe in or drink will move from your stomach or lungs into your bloodstream.").

2. PCE

The evidence for inhalational absorption of PCE from water contamination is supported by several studies that demonstrate the presence of PCE in indoor air and exhaled breath following exposure to contaminated water sources.

Garnier *et al.* described the case of a boy who died in a room in which the curtains had been dry cleaned with PCE. He was asymptomatic when the door and windows were opened (thus providing ventilation), but when the door and windows were closed and he was put to bed for a nap, he died due to PCE exposure. On post-mortem examination he was found to have PCE in his blood at a concentration of 66 μ/mL [Garnier R. Clin Toxicol 1996;34:191-7].

One study conducted in Martinsville, Indiana, found that PCE was detected in all exhaled breath samples from residents living in areas with groundwater contamination, as well as in tap water samples from their homes. This indicates that PCE can volatilize from contaminated water into indoor air, leading to inhalational exposure. [Liu S. Environ Pollut 2022;297:118756]

Another study measured chlorinated hydrocarbons, including PCE, in indoor air and exhaled air samples from individuals exposed to soil contamination. The study found significant levels of PCE in both indoor air and exhaled breath, demonstrating that PCE can intrude into indoor environments from contaminated sources and be absorbed through inhalation. [Scheepers PTJ. Sci Total Environ 2019;653:223-230].

3. Benzene

The evidence for inhalational absorption of benzene from water contamination is well-documented in the literature. Because benzene is also a volatile organic compound, it can be released into the air from contaminated water, particularly during activities that increase water agitation and temperature, such as showering or bathing.

A study by Beavers *et al.* assessed household exposure to benzene from gasoline-contaminated drinking water and found that inhalation exposure during showering contributed significantly to the total benzene dose. The estimated inhaled doses of benzene were similar to the ingested doses, with over half of the inhaled dose associated with shower activities. [Beavers JD. J Occup Environ Med 1996;38:35-8].

Similarly, Santos *et al.* conducted a risk assessment following a gasoline station fuel leak and found that benzene levels in water vapor during showering reached significant concentrations, posing a potential health risk. The study highlighted that inhalation during showering was a critical route of exposure, contributing to the overall benzene intake. [Santos M dos A. Rev Saúde Pública 2013;47(2):335-44].

4. Vinyl chloride

Pleil and Lindstrom demonstrated that vinyl chloride can be absorbed through inhalation during activities such as showering with contaminated water. They used the “single breath canister” technique to measure volatile organic compounds in exhaled breath, showing that vinyl chloride is detectable in breath samples post-exposure, indicating absorption through the respiratory route. [Pleil JD and Lindstrom AB. ClinChem 1997;43:723-30].

Additionally, studies on the pharmacokinetics of vinyl chloride in animal models, such as those by Buchter *et al.* and Hefner *et al.*, provide further evidence of rapid absorption and metabolism of vinyl chloride following inhalation. These studies showed that vinyl chloride equilibrates quickly and is extensively metabolized, supporting that inhalation is a significant route of exposure. [Buchter A. Toxicol Lett 1980;6:33-36; Hefner RE. Environ Health Perspect1975;11:85-95].

D. ABSORPTION VIA DERMAL EXPOSURE.

1. TCE

For 60 years the measurement of skin absorption of organic solvents such as TCE has been determined experimentally via their rates of decay in alveolar air [Stewart RD and Dodd HC. Am Industr Hyg Assoc J 1964;25:439-46]. However, it is unclear whether breath concentrations alone are a reliable measure of skin absorption. One reason for that is that significant differences in pharmacokinetics of chemicals can occur depending on the method of absorption. [Dollery CT. Ann NY Acad Sci 1971;179:108-14].

The evidence for dermal absorption of TCE from water contamination is supported by several studies. [Poet TS. Toxicol Sci 2000;56:61-72]. Poet *et al.* demonstrated that TCE can be absorbed through the skin in both rats and humans, with human skin showing a lower permeability coefficient (K(P) compared to rat skin. Specifically, the K(P) for TCE in a water matrix was 0.015 cm/h in humans, indicating that dermal absorption is a significant route of exposure. Nakai *et al.* also measured the permeability coefficient of TCE through human skin *in vitro*, finding a value of 0.12 cm/h, which supports the opinion that TCE can penetrate human skin from aqueous solutions. [Nakai JS. J Toxicol Environ Health 1999;58:157-70]

Weisel and Jo further corroborated these findings by showing that dermal absorption, along with inhalation, contributes to the total body burden of TCE from tap water exposure. [Weisel CP, Jo WK. Environmental Health Perspectives. 1996;104(1):48-51].

2. PCE

The evidence for dermal absorption of PCE from water contamination is supported by several studies. Nakai *et al.* also demonstrated that the permeability coefficient of PCE through human skin is 0.018 cm/h [Nakai JS. J Toxicol Environ Health 1999;58:157-70]. Dermal absorption of PCE occurs with exposure to the vapor form as well as the liquid form. When volunteers' forearms and hands were exposed to tetrachloroethylene vapor at a concentration of 6.68 mmol/L for 20 minutes, the absorption rate of PCE was 0.054 cm/h (3 times greater than the estimate of Nakai *et al.*), with a peak exhaled air concentration occurring 45 minutes after exposure began [Kezic S. Int Arch Occup Environ Health. 2000;73:415-22].

Citing a study by Bogen, the ATSDR has written that "a 70-kg human with a surface area of 18,000 cm^2, 80% immersed, would take up the [PCE] in 1L of water (of the total amount of water in which the person was immersed) in 20 minutes" [ATSDR Toxicological Profile for Tetrachloroethylene, 1997]. Studies such as these conclusively demonstrate that dermal absorption of PCE does occur and relevant and clinically important rates.

Hake and Stewart reviewed human exposure to PCE and noted that skin absorption can add to the overall exposure burden, particularly in occupational settings where both inhalation and dermal contact occur. [Hake CL and Stewart RD. Environ Health Perspect. 1977;21:231-8]. The authors stated, "Though absorption through the skin is usually not of as great consequence as through the lungs, it should not be overlooked as a contributory factor to the [PCE] body burden. . . ."

3. Benzene

The evidence for dermal absorption of benzene from water contamination is supported by several studies that have investigated the percutaneous absorption of benzene in various settings. Williams *et al.* reviewed and analyzed data from multiple studies and found that the steady-state dermal flux for benzene-saturated aqueous solutions ranges from 0.2 to 0.4 mg/(cm^2·h). [Williams PR. Crit Rev Toxicol 2011;41:111-42] This indicates that benzene can penetrate the skin at measurable rates when present in water.

Modjtahedi and Maibach conducted an *in vivo* study on human subjects and found that the total absorption of benzene through the skin was nominal, with forearm exposure showing an average total absorption of 0.07±0.04% and palmar exposure an average total absorption of 0.13±0.04% of the applied dose. [Modjtahedi BS and Maibach HI. Food Chem Toxicol. 2008;46:1171-4]. These findings suggest that while dermal absorption of benzene from water is possible, the overall absorption rates are relatively low under controlled conditions.

4. Vinyl chloride

Data regarding the dermal absorption of vinyl chloride are mixed. According to a review on the systemic absorption of chemical vapors, the dermal contribution ratio (DCR) for vinyl chloride is approximately 0.0002, indicating that the amount absorbed through the skin relative to total intake (skin and inhalation) is low. This suggests that vinyl chloride is primarily absorbed through inhalation rather than through the skin. The low DCR is largely explained by the chemical properties of vinyl chloride, such as its octanol:water partition coefficient and vapor pressure. [Rauma M. Adv Drug Deliv Rev 2013;65:306-14].

VIII. LITERATURE REVIEW

A. OCCUPATIONAL STUDIES

The body of occupational literature provides compelling evidence that TCE, PCE, and benzene are associated with an increased risk of leukemia and NHL. Although some occupational studies rely on qualitative assessments of exposure, their findings remain significant. A few of the occupational studies are worth discussing in more detail, as they provide insight into the levels of TCE, benzene, and PCE exposure that can cause leukemia and NHL.

1. TCE

Although some occupational studies involved high levels of exposure, "the levels of TCE in the Hadnot Point distribution system were sufficiently high to result in exposures comparable to those that may occur in some occupational settings" [Bove 2014a at 11]. A Marine stationed at Camp Lejeune's daily exposure could be "as high as 3.6 mg/day" [Bove 2014a at 11]. This rate of exposure is entirely comparable to that seen in occupational exposure literature.

Talibov *et al.* investigated elevated risks of AML with solvent exposures (including TCE) in a case-control study from Scandinavia [Talibov M. Scand J Work Environ Health 2014;40:511-7]. They found an elevated HR of 1.12 (95% CI 0.83-1.49) in medium and high-exposure groups. They also found that the HR for TCE remained elevated when examining a 10-year lag time.

A 2014 study by Silver *et al.* investigated the occurrence of cancer (including leukemias) in a cohort of people with occupational exposure to TCE in a microelectronics industry [Silver SR. Am J Ind Med 2014;57:412-24]. Exposure to TCE was determined by use of a job exposure matrix. They found a cumulative risk of non-CLL of 1.31 (95% CI 0.98-1.75).

A cohort study of occupational exposure by Hansen [Hansen J. J Natl Cancer Inst 2013:105:869-77] found elevated standardized incidence ratio of NHL and occupational exposure to TCE of 1.26 (95% CI 0.89-1.73). Furthermore, a pooled case-control study observed exposure-response trends for exposure duration and exposure intensity among workers with high probability of TCE exposure, with elevated risks of follicular lymphoma and CLL [Cocco P. Occup Environ Med 2013;70:795-802].

A 2016 study by 't Mannetje *et al.* examined occupations and the develop NHL by conducting a pooled analysis of 10,046 cases and 12,025 controls from 10 NHL studies participating in a consortium of lymphoma researchers. ['t Mannetje A. Environ Health Perspect 2016;124:396–405]. They found an elevated risk of NHL with an OR of 1.29 (95% CI 0.74-2.23) for those with greater than 10 years of employment as a dry-cleaning worker.

2. Benzene

Occupational studies have consistently demonstrated a link between benzene exposure and an increased risk of leukemia, particularly acute myeloid leukemia (AML). A retrospective cohort study of Chinese benzene-exposed workers found significantly elevated risks for myeloid disorders, including AML and chronic myeloid leukemia (CML), as well as lymphoid disorders such as non-Hodgkin lymphoma [Linet MS. Int J Cancer 2015;137:184-97].

Another study from the Shanghai Men's Health Study reported that high levels of benzene exposure (>550 mg/m^3) were associated with an increased risk of leukemia, with a hazard ratio (HR) of 2.3 (95% CI 1.1-4.5) [DeMoulin D. Cancer Epidemiol Biomarkers Prev 2024;33:1465-74].

A meta-analysis examining parental, in utero, and early-life exposure to benzene also found a significant association with childhood leukemia, particularly acute myeloid leukemia (AML) [Carlos-Wallace FM. Am J Epidemiol 2016;183:1-14]. Additionally, a study on benzene-exposed workers in Brazil reported higher leukemia mortality rates among those exposed to benzene compared to non-exposed workers [Moura-Corrêa MJ. Int J Environ Res Public Health 2023;20:6314].

Regarding NHL, the Bassig *et al.* 2015 study used a comprehensive exposure assessment using an industry job exposure matrix and an occupation job exposure matrix calibrated to air benzene measurements [Basig BA. Environ Health Perspect 2015;123:971–7]. They found that women ever exposed to benzene had a significantly higher risk of NHL (HR 1.87; 95% CI 1.19-2.96). And compared with unexposed women, significant trends in NHL risk were observed for increasing years of benzene exposure and increasing cumulative benzene exposure, with the highest duration (HR 2.07;95% CI 1.07-4.01) and cumulative exposure (HR 2.16; 95% CI 1.17-3.98) tertiles having a significantly increased risk of NHL .

Furthermore, in a systematic review of occupational benzene exposure and the occurrence of NHL, Smith *et al.* reported that of the 43 case-control studies of NHL with occupational exposure to benzene, 40 of the studies showed some elevation of NHL risk, despite the presence of a healthy-worker effect [Smith MT. Cancer Epidemiol Biomarkers Prev 2007;16:385-91].

3. PCE

PCE has long been known to induce cancers, including leukemias, in rodent exposure models, thus providing mechanistic evidence for the carcinogenic potential of PCE [Guyton KZ. Environ Health Perspect 2014;122:325-34].

Occupational evidence of PCE exposure and leukemia comes from Callahan *et al.*, who performed a mortality study of dry cleaners to investigate solvent-related risks [Callahan CL. Epidemiol 2019;30:285–90]. They observed exposure-response relationships for lymphatic/hematopoietic malignancies, including leukemia, with high exposure to solvents, including PCE (HR 4.3; 95% CI 1.4-13.6).

Regarding PCE exposure and NHL, a study conducted in four Nordic countries found that high exposure to PCE was associated with an elevated hazard ratios for NHL of 1.23 (95% CI 1.00-1.52), indicating a increased risk of NHL [Vlaanderen J. Occup Environ Med 2013;70:393–401]. Furthermore, in a long-term mortality study of aircraft manufacturing workers, Boice *et al.* found an increased standardized mortality rate of 1.70 (95% CI 0.73-3.34) for those workers exposed to PCE. [Boice JD. Occup Environ Med 1999;56:581–97] Thus, the scientific literature supports an association between occupational PCE exposure and NHL.

B. WATER-CONTAMINATION STUDIES

The studies discussed above demonstrate that TCE, benzene, and PCE are capable of causing leukemia and NHL. While the concentrations of these chemicals in the studies were often higher than those at Camp Lejeune, this does not imply that lower exposure levels are not capable of causing leukemia and NHL. These studies focused on higher levels of exposure and, by design, did not address the impact of lower levels. What they do confirm with a high degree of certainty is that the elevated exposure levels observed in occupational studies are sufficient to cause leukemia and NHL.

However, occupational studies represent only one part of the body of research on TCE, PCE, benzene, and leukemia and NHL. Beyond occupational literature, multiple studies have shown that these chemicals can also cause leukemia and NHL at lower levels of exposure. Specifically, studies on other water contamination incidents in the U.S. provide relevant evidence that chemical exposures similar to those at Camp Lejeune are sufficient to increase the risk of leukemia and NHL, as detailed below.

As noted earlier, randomized controlled trials are not feasible in this context due to ethical considerations, and incidents like the contamination at Camp Lejeune are rare. Most public water supplies in the U.S. do not contain significant levels of these chemicals, either individually or in combination. [Bexfield LM. Sci Tot Environ 2022;827:154313] As a result, there are fewer human epidemiological studies addressing the effects of these chemicals at lower exposure levels compared to the occupational literature. Nonetheless, existing studies have shown an increased risk of NHL and leukemia among individuals exposed to lower levels of TCE, PCE, and benzene.

1. Fagliano et al., 1990

In 1990, Fagliano et al. conducted an ecological study to investigate the relationship between volatile organic compounds (VOCs), including TCE and PCE, and leukemia incidence. [Fagliano J. Am J Public Health 1990;80:1209-12]. The authors classified towns in New Jersey into categories based on VOC contamination levels: 37-72 ppb (high), 5-12 ppb (medium), and less than 1-3 ppb (low). Their analysis revealed that females in towns with high VOC contamination (37-72 ppb) had a leukemia relative risk of 1.53 (95% CI: 1.02-2.21), corresponding to a statistically significant 53% increased risk.

The study noted that the observed contamination levels were comparable to, and in many cases lower than, those detected at Camp Lejeune. Specifically, the findings demonstrated that VOC exposure levels as low as 37-72 ppb could materially elevate the risk of leukemia. The study findings suggest even relatively low levels of VOC exposure in drinking water can materially increase leukemia risk. Additionally, the study highlighted the carcinogenic potential of TCE and PCE, which had been demonstrated in experimental animal studies. Although the authors of this study cautioned that they could not definitively infer causation, this study – when considered as part of my weight-of-the-evidence analysis – provides support for a causal relationship between TCE, PCE, and leuekemia even at low levels of exposure.

2. Aschengrau et al., 1993

Aschengrau *et al.* reviewed the cancer risk experienced by a cohort of individuals exposed to PCE on Cape Cod, Massachusetts, after “it was discovered that PCE was leaching into drinking water.” [Aschengrau A. Arch Environ Health: Intern J 1993;48:284-92 at 284]. Following this discovery, the Massachusetts Department of Health observed "elevations in cancer mortality" in the affected areas, particularly "consistently elevated mortality rates" for leukemia. [Aschengrau at 285]. In the towns with the highest PCE concentrations, levels ranged from 1.5-80 µg per liter at medium and high-use sites to 1,600-7,750 µg per liter at low-use sites. These levels are comparable to the concentrations found at Camp Lejeune's Hadnot Point and Tarawa Terrace systems.

The authors defined the risk of leukemia (and other cancers) for the Cape Cod cohort. People exposed to *any* amount of PCE had a relative risk of leukemia of 1.72 (95% CI 0.5-4.71), which demonstrates a 72% increased risk. Given the study's small sample size, these results are not statistically significant, but "a finding that does not achieve statistical significance nonetheless can provide important evidence for a causal association." [ATSDR 2017 at 8]. This evidence is still valuable in my weight-of-the-evidence analysis despite being underpowered.

When people were exposed to high amounts of PCE, their measured risk of leukemia was even higher. High PCE exposure, defined as above the 90^{th} percentile which is equivalent to a cumulative exposure of 27-44 milligrams, produced a risk ratio of 5.78 (95% CI 0.98 - 22.97), suggesting a 478% increased risk of leukemia. As the cumulative amount of PCE increased, so did the risk of leukemia. The authors concluded "increased leukemia risk was dose related."

Researchers conducting the study concluded that public drinking water contaminated with PCE is associated with a heightened risk of leukemia. [Aschengrau 1993 at 291]. The study also introduced a metric called Relative Delivered Dose (RDD) to estimate the total amount of PCE consumed by individuals. The 90th percentile for cumulative exposure ranged from 27.1 to 44.1 mg. For comparison, these levels are in the same range as the cumulative exposures experienced by individuals at Camp Lejeune.

For example, if a Marine at Camp Lejeune consumed water from Tarawa Terrace in 1984, when PCE concentrations were about 150 ppb (equivalent to 0.150 mg/liter), and drank 4.29 liters of water per day (calculated based on drinking 6 liters per day for three days a week and 3 liters per day for the other four days), they would have a cumulative exposure of 44 mg over 68 days. *See* [ATSDR 2017 at 3] ("A marine in training at Camp Lejeune consumes an estimated 6 liters of water per day for three days per week and 3 liters per day the rest of the week (ATSDR 2016). Under warm weather conditions, a Marine may consume between 1 and 2 quarts of water per hour and shower twice a day."). This exposure would place the Marine in the 90th percentile of cumulative exposure in the Aschengrau study, meaning they would have received more PCE than 90% of participants in that study.

A Marine present at Camp Lejeune during lower rates of PCE concentration still could have received comparable levels. For example, if the Marine's exposure was from Hadnot Point rather than Tarawa Terrace, where PCE concentrations reached a lower maximum of around 39 ppb (39 µg per liter, equivalent to 0.039 milligrams per liter), and the Marine consumed 4.29 liters per day would accumulate a total of 44 mg of PCE in approximately 263 days. A duration of 263 days to reach 44 mg of PCE is easily within the mean time at Camp Lejeune for Marines of 18 months.

I could continue at length using many other examples. The takeaway is clear: it is realistic to assume Camp Lejeune personnel received cumulative PCE exposure similar to that observed in the 90th percentile of the Aschengrau study. This study provides evidence that people exposed to comparable amounts of PCE as people at Camp Lejeune are at an increased risk of leukemia.

3. Cohn et al., 1994

The Cohn 1994 study [Cohn P. Environ Health Perspect. 1994;102:556-61] examined water contamination in 75 New Jersey towns, focusing on TCE and PCE. Using water modeling, the researchers estimated chemical concentrations, reporting maximum levels of 67 ppb for TCE, 14 ppb for PCE, and 92.9 ppb for total volatile organic compounds (VOCs), all of which are comparable to or lower than the levels documented at Camp Lejeune [Cohn 1994 at 557].

The study analyzed both leukemia and non-Hodgkin lymphoma (NHL) rates in towns with varying contaminant concentrations. For leukemia, the authors found a “statistically significant association” between higher leukemia incidence in females and residence in towns with VOC concentrations exceeding 20 ppb [Cohn 1994 at 558]. This finding demonstrates that exposure to at least 20 ppb of VOCs is sufficient to increase leukemia risk. Additionally, females exposed to at least 5 ppb of TCE had a relative risk (RR) of 1.43 (95% CI 1.07–1.90), while males exhibited a risk of 1.10 (95% CI 0.84–1.43). For PCE, females exposed to at least 5 ppb experienced a 20% increased risk of leukemia [Cohn 1994 at 560].

In addition to leukemia, the study also assessed NHL. The authors found that females living in towns with total VOC concentrations above 20 ppb faced an increased risk of NHL, with a relative risk of 1.24 (95% CI 0.97–1.57) [Cohn 1994 at 558]. For TCE, females exposed to at least 5 ppb had a relative risk of 1.36 (95% CI 1.08–1.70), while males exposed to the same level demonstrated a risk of 1.20 (95% CI 0.94–1.52). For PCE, males exposed to at least 5 ppb faced a 10% increased risk of NHL, and exposure to PCE was significantly associated with high-grade NHL among females [Cohn 1994 at 559-560]. These findings suggest that relatively low levels of exposure to TCE and PCE are sufficient to elevate NHL risk.

The authors noted the potential for synergistic effects when individuals are exposed to both TCE and PCE, as these chemicals share toxic metabolic pathways. They concluded that "the carcinogenic activity of TCE and PCE may be compounded by joint exposure" [Cohn 1994 at 561]. This is especially relevant to Camp Lejeune, where residents and workers were simultaneously exposed to both chemicals, likely amplifying their cancer risk.

The relevance of the study to Camp Lejeune is further reinforced by a statement in the Bove 2014b manuscript, which emphasized that "the maximum detected level of TCE in the Hadnot Point drinking water was considerably higher than the maximum levels detected in the drinking water of the New Jersey towns" [Bove 2014b at 11]. Given that Camp Lejeune’s VOC levels frequently far exceeded the thresholds identified in the Cohn study, the findings provide strong evidence linking the base’s water contamination to cases of leukemia and NHL.

4. Woburn, Massachusetts Contamination

In the late 1970s and 1980s, Woburn, Massachusetts, experienced a notable cancer cluster linked to water contamination from industrial activities, including tanning and degreasing processes. Investigations identified two heavily contaminated wells, G and H, containing 267 ppb of TCE and 21 ppb of PCE, respectively. [Lagakos SW. J Am Stat Assoc. 1986;81:583-596 at 583; Costas K. Sci Total Environ. 2002;300:23–35]. These levels are similar to or lower than those recorded at Camp Lejeune.

Following the discovery, state reports indicated that Woburn's cancer mortality rates were significantly higher than neighboring areas. "A local clergyman reported 10 cases of childhood leukemia in one area over 15 years," and a Boston pediatric hematologist identified six cases in a six-block radius since 1972. [Parker GS. Woburn Cancer Incidence and Environmental Hazards 1969–1978. 1981 at 2]. The Massachusetts Department of Public Health confirmed the childhood leukemia cluster in 1981. [Costas 2002 at 1].

Subsequent epidemiological studies consistently linked the water contamination to leukemia. For example, "exposures to the solvents TCE and PCE were linked to a leukemia cluster." [Cohn 1994 at 556; Fagliano 1990 at 1209].

Parker 1981**:** The Massachusetts Department of Public Health, in collaboration with the CDC, investigated childhood leukemia rates in Woburn and found them to be significantly higher than expected during the study period. The increase was particularly pronounced in the eastern part of the town, where 12 cases of childhood leukemia were recorded compared to an expected 5.3 cases. These findings indicate that the levels of TCE and PCE in the contaminated wells, which ranged from tens to hundreds of parts per billion, were sufficient to contribute to the development of leukemia in the affected population.

Lagakos 1986**:** The Lagakos 1986 study was initiated in response to an alarming rise in childhood leukemia cases in Woburn, Massachusetts, which drew attention following the discovery of significant contamination in the town's drinking water. The researchers sought to investigate this concerning increase and found a clear connection between exposure to water from Wells G and H and higher rates of leukemia in children. Their analysis demonstrated that both cumulative exposure and categorical measures of contamination were strongly associated with the elevated leukemia rates.

The study also observed a decline in leukemia cases after the contaminated wells were shut down, further reinforcing the link between the contamination and adverse health outcomes. Between 1964 and 1983, 20 cases of childhood leukemia were documented, more than double the expected number of 9.1 for the population.

These findings highlight that the levels of TCE and PCE in Wells G and H—ranging from 10s to 100s of ppb—were sufficient to significantly increase the risk of leukemia in the exposed population.

Cutler 1986**:** The 1986 study by Cutler examined the relationship between environmental hazards and childhood leukemia in Woburn, Massachusetts, focusing on the period from 1969 to 1979. The researchers found that leukemia rates during this time were significantly higher than expected. In one particular census tract supplied with water from the contaminated wells, the rate of childhood leukemia was 7.5 times the expected number. These findings provide strong evidence that the levels of TCE and PCE in the wells, ranging from tens to hundreds of parts per billion, were sufficient to contribute to the development of leukemia in the affected population. [Cutler JJ. Public Health Rep 1986; 101:201-5].

Costas 2002**:** In 2002, a follow-up evaluation of the cancer cluster in Woburn was conducted by the Massachusetts Bureau of Environmental Health. The findings revealed that as the volume of contaminated water from wells G and H delivered to households increased, so did the risk of childhood leukemia. The study indicated that mothers who likely consumed water from these wells during pregnancy faced a significantly higher risk of their children developing leukemia compared to those who did not. Specifically, the relative risk of leukemia for children whose mothers consumed the most contaminated water exceeded 14.0 (95% CI 0.92–224.52)—an increase of several thousand percent. [Costas 2002 at 31]

The authors also observed a dose-response relationship, showing that greater exposure to contaminated drinking water during pregnancy correlated with higher risks of childhood leukemia. [Costas 2002 at 30] These findings underscore that the levels of chemicals present in the water at Woburn were sufficient to induce leukemia. While the study focused on maternal exposure during pregnancy, it highlights the hazardous nature of these chemicals and their capacity to trigger the cellular changes that lead to leukemia.

IX. EVIDENCE FROM CAMP LEJEUNE STUDIES CONFIRMS THAT THESE CHEMICALS CAUSE LEUKEMIA AND NHL AT DETECTED CONCENTRATIONS

Extensive research has already shown that TCE, benzene, and PCE are capable of causing leukemia and NHL, with the risks evident at levels comparable to those found in Camp Lejeune's water. What sets Camp Lejeune apart is the rare availability of human epidemiological studies directly examining individuals exposed to these chemicals at the site. These studies are relevant to show the effects of these exposures, confirming a link between the contaminated water and an increased risk of leukemia and NHL among those exposed.

One key part of the Camp Lejeune studies is that it moves beyond theoretical cancer risk calculations. Cancer slope models, often derived from animal studies and used to predict risks like 1-in-a-million, significantly understate the real-world risk observed in Camp Lejeune's exposed population. The epidemiological findings provide a much clearer picture of the actual health outcomes, showing risks far higher than those theoretical models suggest. This direct evidence gives us a understanding of the true impact of the contamination.

The Camp Lejeune studies also give insight into the cumulative effects of multiple chemical exposures. Many Camp Lejeune residents were exposed to TCE, PCE, benzene, and/or vinyl chloride simultaneously. Studies and scientific literature suggest that these exposures are not merely additive but could interact synergistically, creating a combined risk that is greater than the sum of individual risks. [Rosenfeld 2024 at 14] This interaction amplifies the potential harm, reinforcing the need to consider the full scope of the exposure rather than isolating each chemical's effect.

Moreover, the Camp Lejeune data provides conclusive evidence that the chemical concentrations present were sufficient to induce leukemia and NHL. The unique epidemiological focus on Camp Lejeune offers rare and strong data that support and strengthens the existing body of evidence, leaving little doubt about the harm posed to humans by these contaminants at the levels detected in the water at Camp Lejeune.

A. BOVE 2014A STUDY: *CANCER MORTALITY STUDY OF MARINES AND NAVY PERSONNEL EXPOSED TO CONTAMINATED DRINKING WATER AT CAMP LEJEUNE, NORTH CAROLINA*

The *Bove 2014a* study examined cancer mortality rates among military personnel stationed at Camp Lejeune compared to those at Camp Pendleton. Both bases housed similar military populations, but only Camp Lejeune personnel were exposed to contaminated water containing TCE, PCE, benzene, and vinyl chloride. By leveraging this distinction, the study assessed the impact of chemical exposure on leukemia-related mortality risk.

The researchers found that individuals in the Camp Lejeune cohort resided on base for an average of 18 months. The study reported an increased risk of death from leukemia of 11% among Marines stationed at Camp Lejeune compared to those at Camp Pendleton, with a hazard ratio of 1.11 (95% CI: 0.75–1.62). This elevated mortality risk was linked to the exposure to contaminated water, as no significant differences in other key characteristics between the populations were identified.

Cumulative exposure levels to the chemicals were measured in micrograms per liter per month (µg/L-month). For example, if an individual was exposed to 300 µg/L of TCE during one month and 400 µg/L during the next, their cumulative exposure over two months would total 700 µg/L-month. These cumulative exposures were categorized into low, medium, and high levels for TCE, PCE, benzene, and total volume of organic compounds (TVOC):

TCE: Low exposure (1–3,100 µg/L-month), medium exposure (3,100–7,700 µg/L-month), and high exposure (7,700–39,745 µg/L-month).

PCE: Low exposure (1–155 µg/L-month), medium exposure (155–380 µg/L-month), and high exposure (380–8,585 µg/L-month).

Benzene: Low exposure (2–45 µg/L-month), medium exposure (45–110 µg/L-month), and high exposure (110–601 µg/L-month).

TVOC: Low exposure (1–4,600 µg/L-month), medium exposure (4,600–12,250 µg/L-month), and high exposure (12,250–64,016 µg/L-month).

The study explored leukemia mortality risk in relation to cumulative exposure levels. Among Camp Lejeune personnel exposed to TCE at low to high levels (1–39,745 µg/L-month), the hazard ratio for leukemia-related death was 1.40 (95% CI: 0.93–2.12), reflecting a 40% increase in mortality risk. Similar patterns were observed for PCE (hazard ratio 1.37; 95% CI: 0.90–2.08), benzene (1.47; 95% CI: 0.97–2.23), and TVOC (1.45; 95% CI: 0.97–2.17). Importantly, no increased leukemia mortality risk was detected for individuals with minimal exposure (less than 1 µg/L-month for TCE, PCE, or TVOC, and less than 2 µg/L-month for benzene).

Those exposed to TCE at 1–3,100 µg/L-month had a hazard ratio of 2.0 (95% CI: 1.0–4.0), indicating a 100% increased risk of leukemia mortality, while those exposed to more than 7,700 µg/L-month had a hazard ratio of 1.81 (95% CI: 0.85–3.85). Similarly, for benzene, exposure levels of 2–45 µg/L-month corresponded to a hazard ratio of 2.54 (95% CI: 1.27–5.08), reflecting a 154% increased mortality risk. TVOC exposure between 1–4,600 µg/L-month was associated with a hazard ratio of 2.50 (95% CI: 1.24–5.03), representing a 150% increased risk of leukemia mortality.

The findings demonstrated a non-linear exposure-response relationship, with significant increases in mortality risk found in different cumulative exposure levels. The results further highlight that even low levels of chemical exposure—such as 1 µg/L-month of TCE or TVOC and 2 µg/L-month of benzene—are sufficient to increase the risk of leukemia mortality.

The Bove 2014a study offers strong evidence that the contamination at Camp Lejeune significantly increased the risk of leukemia-related mortality among exposed personnel. The findings underscore that even short-term exposure to relatively low levels of TCE, PCE, benzene, and vinyl chloride can contribute to an elevated mortality risk, reinforcing the carcinogenic potential of these chemicals at the concentrations found in the Camp Lejeune water supply.

B. BOVE 2014B STUDY: CANCER MORTALITY STUDY OF CIVILIAN EMPLOYEES EXPOSED TO CONTAMINATED DRINKING WATER AT CAMP LEJEUNE, NORTH CAROLINA

The *Bove 2014b* study compared civilian employees at Camp Lejeune with their counterparts at Camp Pendleton. This retrospective cohort study sought to determine whether exposure to contaminated drinking water at Camp Lejeune increased mortality risk from cancers and other chronic diseases. [Bove 2014b at 2]

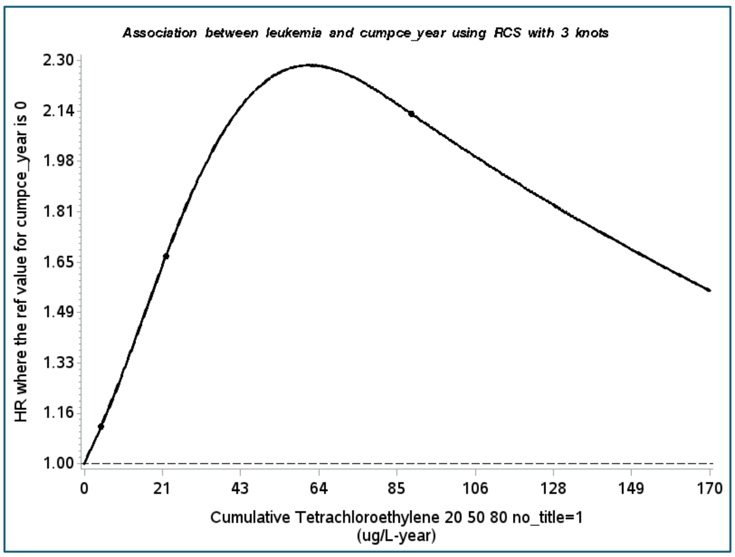
Since nearly all civilian workers at Camp Lejeune lived off-base, their exposure to the contaminated water occurred primarily during work hours. This setup provides compelling evidence of the potential health effects of intermittent exposure to the contaminants.

When comparing Camp Lejeune civilians to those at Camp Pendleton, the study found a hazard ratio of 1.59 (95% CI 0.66–3.84) for leukemia, representing a 59% increased mortality risk. This finding underscores the potential for Camp Lejeune's chemical contamination to contribute to leukemia, with an average exposure duration of 2.5 years.

The study also assessed leukemia risk across varying degrees of chemical exposure and identified a monotonic exposure-response relationship. [Bove 2014b at 9] Civilians in higher exposure categories showed the following hazard ratios:

- PCE: HR 1.82 (95% CI 0.36–9.32)
- Benzene: HR 1.25 (95% CI 0.31–5.10)
- TVOC: HR 1.68 (95% CI 0.33–8.67)

To dig even deeper, the authors employed splines to illustrate the relative risk of leukemia based on cumulative PCE exposure.



These splines revealed that leukemia rates began to rise significantly at approximately 5 µg/L-years of PCE exposure. The relative risk increased to 1.65 at 21 µg/L-years, and by about 60 µg/L-years, the relative risk climbed above 2.0

C. ATSDR 2018 STUDY: MORBIDITY STUDY OF FORMER MARINES, EMPLOYEES, AND DEPENDENTS POTENTIALLY EXPOSED TO CONTAMINATED DRINKING WATER AT U.S. MARINE CORPS BASE CAMP LEJEUNE

The 2018 morbidity study, conducted by ATSDR, examined whether exposure to the contaminated drinking water at Camp Lejeune was associated with medically confirmed diseases. The study surveyed over 200,000 Marines stationed at Camp Lejeune from 1972 to 1985 and a comparator group of 50,000 Marines stationed at Camp Pendleton during the same period. Additionally, it included more than 8,000 civilians who worked at Camp Lejeune and 7,000 civilians from Camp Pendleton.

The authors used water distribution models along with data on residential locations and periods of residence to calculate cumulative and average residential exposure to TCE, PCE, and other contaminants in the water. [2018 ATSDR at 6]. By comparing Marines and civilians at Camp Lejeune with those at Camp Pendleton, the study assessed the relationship between varying levels of chemical exposure and the risk of both leukemia and NHL.

Leukemia Findings: Civilians exposed to medium levels of TCE and PCE combined (10,868–50,563 ppb-months for TCE or 457–2,118 ppb-months for PCE) had an odds ratio of 1.41 (95% CI: 0.38–5.28), reflecting a 41% increased risk of leukemia compared to Camp Pendleton civilians. Those with high combined exposure levels (above 50,563 ppb-months for TCE or above 2,118 ppb-months for PCE) showed an odds ratio of 1.32 (95% CI: 0.15–11.40), indicating a 32% increased risk. [2018 Morbidity Study at 86].

When comparing civilians at Camp Lejeune to their counterparts at Camp Pendleton, the overall odds ratio was 1.10 (95% CI: 0.36–3.38), providing evidence that exposure to the contaminated water—and to the chemicals it contained during the time of the study period—was sufficient to increase the risk of leukemia.

The authors also examined leukemia rates in civilians at Camp Lejeune with varying degrees of exposure to TCE and PCE. For civilians in the medium exposure group (10,868–50,563 ppb-months of TCE or 457–2,118 ppb-months of PCE), the odds ratio was 1.69, indicating a 69% increased risk of leukemia. For those with even higher exposure levels, the odds ratio was 1.58 (95% CI: 0.16–15.30), reflecting a 58% increased risk. [2018 Morbidity Study at 88]. These findings demonstrate that exposure to as little as 10,868 ppb-months of TCE or 457 ppb-months of PCE is sufficient to elevate leukemia risk.

NHL Findings: Classification of NHL presented a significant challenge in the study. According to the authors, "the medical confirmation process was unable to distinguish the type of lymphoma for most of the reported cases," and therefore, Hodgkin lymphoma, non-Hodgkin lymphoma (NHL), and lymphomas of unspecified type were grouped together as "lymphoma." [ATSDR Morbidity Study 2018 at 24].

For Marines stationed at Camp Lejeune, the odds ratio for NHL was 1.10 (95% CI: 0.8–1.5) compared to those at Camp Pendleton. Among civilians, the odds ratio was 1.3 (95% CI: 0.6–8.1), indicating an increased risk of NHL associated with exposure to contaminated water at Camp Lejeune during the study period. [ATSDR Morbidity Study 2018 at 73].

The authors also analyzed NHL risk among civilians at Camp Lejeune based on their levels of exposure to TCE and PCE. For civilians with medium combined exposure (10,868–50,563 ppb-months of TCE or 457–2,118 ppb-months of PCE), the odds ratio was 1.70 (95% CI: 0.68–4.24), corresponding to a 70% increased risk of NHL compared to civilians at Camp Pendleton. Civilians with high combined exposure (above 50,563 ppb-months of TCE or 2,118 ppb-months of PCE) had an odds ratio of 1.71 (95% CI: 0.46–6.39), reflecting a 71% increased risk. [ATSDR Morbidity Study 2018 at 86].

Finally, the study compared NHL rates among Camp Lejeune personnel exposed to higher levels of TCE and PCE to those stationed at Camp Lejeune but exposed to lower levels. For civilians with medium exposure (10,868–50,563 ppb-months of TCE or 457–2,118 ppb-months of PCE), the odds ratio was 1.64, corresponding to a 64% increased risk of NHL. For those with even higher exposure levels, the odds ratio was 1.86 (95% CI: 0.43–8.11), reflecting an 86% increased risk. [2018 Morbidity Study at 88].

These findings demonstrate that exposure to as little as 10,868 ppb-months of TCE or 457 ppb-months of PCE is sufficient to increase the risk of NHL.

D. BOVE 2024A STUDY: LONG-TERM CANCER MORTALITY AMONG MILITARY PERSONNEL EXPOSED TO CONTAMINATED DRINKING WATER AT CAMP LEJEUNE

The *Bove 2024a* Study investigated cancer mortality using a longer time horizon than earlier studies. This research compared Navy and Marine personnel stationed at Camp Lejeune from 1972 to 1985 with a comparator group stationed at Camp Pendleton during the same period.

The study found that military personnel at Camp Lejeune had a hazard ratio of 1.10 (95% CI 0.87–1.40) for leukemia mortality compared to those at Camp Pendleton, reflecting a 10% increased risk of dying from leukemia. Additionally, for acute myeloid leukemia specifically, the hazard ratio was 1.11 (95% CI 0.78–1.59).

E. BOVE 2024B STUDY: CANCER INCIDENCE AMONG INDIVIDUALS EXPOSED TO CONTAMINATED DRINKING WATER AT CAMP LEJEUNE

The *Bove 2024b* cancer incidence study analyzed cancer rates among Marines, Navy personnel, and civilians at Camp Lejeune compared to a similar cohort at Camp Pendleton. The study assessed cancer incidence from 1996 to 2017 to evaluate whether being stationed or employed at Camp Lejeune increased the risk of cancer. Camp Pendleton, which was not known to have contaminated drinking water but housed a comparable population, served as the control group, with the key difference being the exposure to hazardous chemicals experienced by the Camp Lejeune cohort.

The study found that people stationed at Camp Lejeune had a higher risk of leukemia. Among military personnel, the overall hazard ratio (HR) for leukemia was 1.07 (95% CI: 0.91–1.25), while civilians had an AML hazard ratio of 1.35 (95% CI: 0.59–3.09). These results demonstrate that exposure to the contaminated water at Camp Lejeune during 1975–1985 increased the risk of leukemia.

To explore exposure further, the authors used “duration of assignment” or “duration of employment” as a surrogate for cumulative exposure. For Marines and Navy personnel, low exposure was defined as 1–6 quarters, medium as 7–10 quarters, and high as more than 10 quarters on base. For civilian workers, low/medium exposure was defined as 1–21 quarters, and high exposure was more than 21 quarters on base.

For Marines and Navy personnel with low-duration exposure (1–6 quarters), the study reported a leukemia hazard ratio of 1.11 (95% CI: 0.92–1.33). The risk was even greater for AML, with a hazard ratio of 1.38 (95% CI: 0.97–1.90). Civilians with high-duration exposure (>21 quarters) showed a hazard ratio of 1.43 (95% CI: 0.72–2.86) for all leukemias, with an even higher hazard ratio of 2.53 (95% CI: 0.76–8.37) for AML specifically. [Bove 2024b at Table 6]

The findings once again showed that individuals stationed at Camp Lejeune faced a higher risk of developing NHL. In the primary comparison, Marines had an odds ratio of 1.01 (95% CI: 0.90–1.14), while civilians had an odds ratio of 1.19 (95% CI: 0.83–1.71). These results demonstrate that exposure to the contaminated water at Camp Lejeune—and to the levels of chemicals present in the water between 1975 and 1985—elevates the risk of NHL.

For Marines with "low duration" exposure (defined as 1–6 quarters on base), the odds ratio for NHL overall was below 1.0 (95% CI: 0.78–1.12) compared to Marines at Camp Pendleton. However, the risk increased for specific NHL subtypes, such as Burkitt lymphoma (HR: 2.01, 95% CI: 0.87–4.66) and marginal zone B-cell lymphoma (HR: 1.39, 95% CI: 0.82–2.35). [Bove 2024b at Table 5]. These findings indicate that spending 1–6 quarters on base during 1975–1985—or receiving an equivalent level of chemical exposure during that time—is sufficient to increase the risk of certain NHL subtypes.

For civilians with "low/medium duration" exposure (defined as 1–21 quarters working on base), the odds ratio for NHL was 1.31 (95% CI: 0.84–2.03). [Bove 2024b at Table 6]. These results show that working as a civilian on base for 1–21 quarters is enough to raise the risk of non-Hodgkin lymphoma.

Limitations to this study exist. The study relied on cause of death information from death certificates, which are subject to errors. This could lead to non-differential disease misclassification, potentially biasing the hazard ratios towards the null. The cohort was also generally young. Almost all of the Marines/Navy personnel subgroup was aged < 65 years by the end of follow-up, which reduced the number of deaths for each cause. This limited the study's ability to fully evaluate mortality, particularly for diseases that typically occur later in life. Also, for some causes of death, particularly in the civilian workers' analyses, there was poor precision of hazard ratios due to the small sample size and resulting small numbers of cases. Lastly, while the study design attempted to minimize the healthy worker bias by comparing to a similar military base, the healthy worker effect could still influence the results, particularly for the civilian worker cohort. The study emphasized that the findings are relevant to all individuals exposed to Camp Lejeune's contaminated water and recommended continued follow-up for those potentially affected.

F. ROSENFELD 2024 STUDY: CAMP LEJEUNE MARINE CANCER RISK ASSESSMENT FOR EXPOSURE TO CONTAMINATED DRINKING WATER FROM 1955 TO 1987

The 2024 study by Rosenfeld *et al*. employed cancer-slope and other health-assessment methodologies to evaluate the cancer risk for Marines stationed at Camp Lejeune between 1953 and 1987. The authors determined that even a single month of working on the base during the period from 1980 to 1984 could result in a cancer risk exceeding the 1 in a million de minimis threshold. [Rosenfeld 2024 at 10]. For marines with six months on the base, the risk increased up to sixfold compared to the one-month exposure scenario. [Rosenfeld 2024 at 11].

The cancer-slope calculations have limitations acknowledged above in this report. Cancer-slope calculations are used to estimate potential risk rather than to establish causation. The theoretical risks calculated for Camp Lejeune exceeded the de minimis threshold, indicating potential harm. Human epidemiological studies show that the actual risks observed in exposed populations are higher than those estimated by these models. This demonstrates that the contamination at Camp Lejeune had measurable impacts beyond those predicted by theoretical assessments.

The findings from Rosenfeld *et al*. are consistent with epidemiological data showing that even short-term exposure to contaminated water at Camp Lejeune carried notable risks.

X. MECHANISM OF ACTION

A. TCE

The mechanism by which TCE causes leukemia and NHL involves several pathways:

Immunotoxicity: TCE exposure has been shown to cause immunosuppressive effects, including a decline in lymphocyte subsets, such as CD4+ T cells, CD8+ T cells, natural killer (NK) cells, and B cells. This immunosuppression is associated with decreased levels of soluble CD27 and CD30, which are important for lymphocyte activation and function. [Bassig BA. Carcinogen 2016;37:692–700]. This immunosuppressive effect is significant even at levels below the current Occupational Safety and Health Administration (OSHA) permissible exposure limit. These findings support the biologic plausibility that TCE exposure broadly impacts immune system components and is associated with NHL risk. [Lan Q. Carcinogenesis 2010;31:1592–6].

Altered B-cell Activation: TCE exposure has been linked to changes in B-cell activation markers and serum immunoglobulin levels. Specifically, there is a significant reduction in serum levels of IgG and IgM among TCE-exposed workers, indicating impaired immune function. These findings strengthen the biologic plausibility that TCE acts as a lymphomagen, particularly in its association with NHL. [Zhang L. Carcinogenesis 2013;34:799–802].

Epigenetic Modifications: TCE exposure can lead to DNA hypomethylation and histone hyperacetylation, which can alter the expression of tumor-related genes such as N-Ras, c-Jun, c-Myc, c-Fos, and IGF-II. These epigenetic changes can promote carcinogenesis by dysregulating gene expression. [Phillips RV. Epigenetics 2019;14:1112–24].

Genotoxicity: TCE and its metabolites can form DNA adducts, which can cause cell mutations. The formation of TCE epoxide, a reactive intermediate, is particularly implicated in this process. This metabolite can bind covalently to DNA and proteins, potentially leading to carcinogenesis. [Bannerjee South Cancer Res 1978;38:776-80].

Oxidative Stress: Oxidative stress is another mechanism whereby TCE causes leukemia.

Several studies have demonstrated that TCE exposure leads to the generation of reactive oxygen species, which can result in oxidative stress and subsequent DNA damage. For instance, Hu et al. found that TCE exposure in human HepG2 cells caused significant DNA strand breaks and chromosome damage, which were linked to oxidative stress and lipid peroxidation. [Hu C. Mut Res 2008;652:88-94]. Furthermore, Varshney et al. demonstrated that oxidative metabolites of TCE, such as trichloroacetic acid and dichloroacetic acid, induce genotoxic effects in human peripheral blood lymphocytes, further supporting the role of oxidative stress in TCE-induced DNA damage. [Varshney M. Environ Sci Pollut Res Inter 2013;20:8709-16]. These findings collectively demonstrate that oxidative stress is a significant mechanism through which TCE exerts its genotoxic effects, including leading to leukemia.

B. PCE

There are several mechanisms by which PCE causes leukemia and NHL. These include, but are not limited to:

Oxidative Stress: PCE exposure increases reactive oxygen species and lipid peroxidation in lymphocytes, leading to oxidative damage to DNA and other cellular components. This oxidative stress can result in mutations and genomic instability, promoting leukemic transformation and lymphomagenesis. [Ghahri A. J Biochem Molec Toxicol 2022;36:e23000].

Genotoxicity: PCE is associated with NHL through its genotoxic effects, which include significant increases in structural chromosome aberrations and micronucleus formation in human peripheral blood lymphocytes. These findings highlight its genotoxic potential, as such DNA damage can result in mutations that contribute to the malignant transformation of lymphocytes. [Azimi J. Inter J Occup Environ Med 2017;8:224-31]. Additionally, PCE and its metabolites can form DNA adducts, which cause cell mutations. The formation of reactive intermediates, such as TCE epoxide, further contributes to these mutagenic effects. [Bannerjee South Cancer Res 1978;38:776-80].

Alteration of Gene Expression: PCE modulates the expression of genes involved in cancer induction, cell differentiation, cell-cycle progression, and apoptosis. For example, PCE exposure affects genes like c-jun and c-fos, which regulate cell proliferation, as well as BAX and BCL-2, which are central to apoptotic processes. These alterations can lead to uncontrolled cell growth and survival, contributing to both leukemogenesis and lymphomagenesis. [Diodovich C. Arch Toxicol 2005;79:508-14].

Metabolic Activation: PCE is metabolized via cytochrome P450-dependent oxidation and glutathione conjugation pathways. The metabolites, such as trichloroacetate and dichloroacetate, are associated with renal toxicity and have been implicated in carcinogenesis. These metabolites can cause direct DNA damage or interfere with cellular signaling pathways, contributing to leukemia and NHL development. [Lash LH and Parker JC. Pharmacol Rev 2001;53:177-208].

Protein Adduct Formation: PCE metabolites form protein adducts, such as N epsilon-(dichloroacetyl)-L-lysine, which have been detected in the liver, kidney, and blood of exposed rats and humans. These adducts can disrupt normal cellular functions and contribute to carcinogenesis. [Pähler A. Toxicol Sci 1999;48:5-13].

C. BENZENE

Benzene is metabolized primarily in the liver to phenolic metabolites, such as phenol, hydroquinone, catechol, and 1,4-benzoquinone. These metabolites are then transported to bone marrow, where they undergo further conversion to reactive intermediates, including semiquinone radicals and quinones, via peroxidase enzymes. This is a proposed mechanism for benzene to cause leukemia [Smith MT. Environ Health Perspect 1996;104:1219-25; McHale CM. Carcinogenesis 2012;33:240-52].

Oxidative Stress and Chromosomal Aberrations: These reactive intermediates generate reactive oxygen species (ROS) through redox cycling, leading to oxidative stress. ROS can cause significant damage to cellular structures such as DNA, proteins, and lipids. Specifically, benzene metabolites induce DNA strand breakage, chromosomal aberrations, and mutations that can result in mitotic recombination, chromosome translocation, and aneuploidy. [Hiraku Y and Kawanishi S. Cancer Res 1996;56:5172-8; Grigoryan H. Carcinogenesis 2018;39:661-668].

In the context of NHL, benzene exposure is associated with specific chromosomal rearrangements commonly seen in NHL, such as translocations like t(14;18) and deletions like del(6q). These genetic alterations disrupt normal cellular functions and promote lymphomagenesis. [Zhang L. Environ Molec Mutagenesis 2007;48:467-74].

Epigenetic Modification and Genomic Instability: Benzene metabolites can interfere with critical cellular processes by damaging tubulin, histone proteins, and topoisomerase II, further contributing to genomic instability. Additionally, benzene exposure leads to cumulative genetic and epigenetic alterations in hematopoietic stem cells (HSCs) and their microenvironment, promoting the development of leukemic clones with selective growth advantages. [McHale CM. Carcinogenesis 2012;33:240-52; Spatari G. Cancers 2021;13:2392].

Benzene can also induce epigenetic changes in the context of NHL, including DNA hypomethylation and hypermethylation of CpG islands in promoter regions of tumor suppressor genes. These modifications activate oncogenes and silence tumor suppressor genes, contributing to lymphomagenesis. [Spatari G. Cancers 2021;13:2392].

Immune Dysregulation and Immunotoxicity: Benzene exposure dysregulates the aryl hydrocarbon receptor and reduces immunosurveillance, which facilitates the clonal evolution of leukemic cells. [McHale CM. Carcinogenesis 2012;33:240-52].

In NHL, benzene exposure causes immunosuppression and chronic inflammation. It significantly reduces the number of white blood cells, including lymphocytes such as CD4+ T-cells, B-cells, and natural killer cells, while simultaneously increasing proinflammatory biomarkers. This combination of immunosuppression and chronic inflammation impairs immunosurveillance and promotes cancer invasion. [Guo H Occup Environ Med 2021;78:377–84.].

D. VINYL CHLORIDE

Vinyl chloride is metabolized in the liver by cytochrome P450 enzymes, particularly CYP2E1, to form reactive intermediates such as chloroethylene oxide and chloroacetaldehyde. These metabolites are highly reactive and can form DNA adducts, specifically etheno adducts such as 1,N6-ethenoadenine and 3,N4-ethenocytosine. These adducts are mutagenic and can lead to point mutations in critical genes involved in cell cycle regulation and apoptosis, such as proto-oncogenes and tumor suppressor genes. [Whysner J. Pharmacol Ther 1996;71:7-28; Bartsch H. Environ Health Perspect 1976;17:193-8; Bolt HM. Crit Rev Toxicol 2005;35:307-23].

Genotoxicity and DNA Adduct Formation: The formation of these DNA adducts, and the resulting mutations, can disrupt normal cellular processes, leading to uncontrolled cell proliferation and the development of leukemia. Additionally, the genotoxic effects of vinyl chloride metabolites have been demonstrated in various studies, showing their ability to induce mutations and chromosomal aberrations in both in vitro and in vivo models. [Green T, Hathway DE. Chemico-Biol Interact 1978;22:211-24; Bolognesi C. Mut Res Rev Mut Res 2017;774:1-11].

In the context of NHL, these same reactive intermediates, such as chloroethylene oxide and chloroacetaldehyde, induce genetic damage by forming DNA adducts. These adducts lead to mutations in critical genes that regulate the cell cycle and apoptosis, mirroring the carcinogenic processes observed in leukemia. [Bartsch H. Environ Health Perspect 1976;17:193-8; Whysner J. Pharmacol Ther 1996;71:7-28].

These mutations can result in chromosomal aberrations and micronucleus formation, which are key events in carcinogenesis and are observed in lymphocytes of workers exposed to vinyl chloride. Genotoxicity studies demonstrate the ability of these metabolites to induce chromosomal damage in mammalian cells, further supporting their role in NHL development. [Bolognesi C. Mut Res Rev Mut Res 2017;774:1-11; Feng N. Biomark 2014;19:281-6; Ji F. Carcinogenesis 2010;31:648-53].

Immune Dysregulation: Epidemiological studies have also identified an association between vinyl chloride exposure and an increased risk of lymphatic and hematopoietic cancers, including NHL. The immunosuppressive effects of vinyl chloride and its metabolites contribute to this risk by impairing immune surveillance, thereby enabling the proliferation of malignant lymphocytes. [Infante PF. Mut Res 1976;41:131-41; Hardell L. Environ Health Perspect 1998;106 Suppl 2:679-81].

XI. STUDIES THAT DID NOT SHOW AN ASSOCIATION BETWEEN CAMP LEJEUNE CHEMICALS AND LEUKEMIA

In my review of the literature, I also considered studies that did not demonstrate an association between the Camp Lejeune water contaminants and leukemia. I note a few below:

Morgan *et al.* studied the mortality of aerospace workers exposed to TCE and did not find an association between TCE exposure and leukemia with a standardized mortality rate of 1.05 (95%

CI 0.50-1.93). [Morgan RW Epidemiol 1998;9:424-31], although the wide confidence interval allows that the association is significant.

There are also studies of PCE which have not found an association with leukemia. For example, a case-control study in Montreal by Christensen *et al.* evaluated the association between exposure to chlorinated solvents and cancer. [Christensen KY. J Occup Environ Med 2013;55:198-208] The study found no significant findings related to leukemia.

A Swedish study by Selden and Ahlborg used a historically prospective cohort design to focus on people who worked in dry-cleaning or laundry establishments. [Seldén AI and Ahlborg G. Inter Arch Occup Environ Health 2011;84:435-43] They found no clear association between PCE exposure and subsequent cancer morbidity, including leukemia, with an overall standardized incidence rate of 1.01 (95% CI 0.51–1.81).

Studies evaluating the association of benzene with leukemia have occasionally found no association. For instance, Raabe and Wong conducted a meta-analysis of cell-type-specific leukemia risks in petroleum workers and found no increase in AML or other leukemia subtypes, attributing this to the low levels of benzene exposure in the petroleum industry. [Raabe GK and Wong O. Environ Health Perspect 1996;104:1381-92]

XII. STUDIES THAT DID NOT SHOW AN ASSOCIATION BETWEEN CAMP LEJEUNE CHEMICALS AND NHL

In my review of the scientific literature and in writing this report I considered studies that did not demonstrate an association between the Camp Lejeune water contaminants and NHL.

The 2013 study by Vlaanderen *et al.* did not observe evidence for an association between exposure to TCE and NHL or multiple myeloma in the Nordic Occupational Cancer cohort. [Vlaanderen J. Occup Environ Med 2013;70:393-40]. Also, Press *et al.* conducted a population-based cancer cluster investigation and found no consistent, sustained, or more recent elevation in NHL occurrence in a neighborhood with TCE contamination. [Press DJ. Cancer Cause Control 2016;27:607-13].

With regards to PCE and NHL, a study by Callahan did not find an association between PCE exposure and NHL in their analysis of occupational exposure to various chlorinated solvents, including perchloroethylene. [Callahan CL. Occup Environ Med 2018;75:415-20].

In 2009, Lamm *et al* published a systematic review and meta-analysis of case-control studies and concluded that chronic myelogenous leukemia (CML) does not appear to be related to benzene exposure. [Lamm SH. Chem-Biol Interact 2009;182:93-7]

XIII. ADDITIVE AND SYNERGISTIC EFFECTS OF SOLVENTS AND TOXINS

Adding to the complexity of the Camp Lejeune fact set and the potential for toxicity was that the Camp Lejeune water was contaminated with at least four different chlorinated hydrocarbons--

PCE, TCE, DCE, VC – as well as by benzene. The ATSDR data reflects that when contemporaneous samples of the potable water were taken and analyzed in the early 1980s, all five chemicals were detected including at levels above today's maximum contaminant levels (MCLs).[2] Several of the chemicals were detected during the same overlapping time periods at Hadnot Point. Further, numerous individuals residing at Tarawa Terrace would have gone about their days at Hadnot Point before going home in the evening, thereby receiving exposures to mixtures of the chemicals already mixed together in the Hadnot Point water treatment system and the Tarawa Terrace water system. It is reasonably inferable that all or most individual exposures were to more than one of the relevant chemicals in drinking water.

Further, it should be noted that these chemicals are molecules. The structural similarity between the 4 chlorinated VOCs at issue herein is striking. The differences between the molecular series proceeding from PCE to VC may be conceptualized roughly as starting with a structure with four chlorine atoms (thus the "tetra" (Latin for four) in tetrachloroethylene), then deleting one chlorine atom from the structure (leading to TCE, "tri"), then deleting one more chlorine atom (reducing to DCE, "di"), and then deleting one more (leaving vinyl chloride).

As one may intuit from the above rough conceptualization, under the right environmental conditions, PCE may degrade into TCE, and so forth, over time. Thus, in groundwater conditions, PCE initially undergoes a classical decomposition as a result of dehalogenated reduction to TCE and the Cl^- ion under aerobic conditions around Eh +100 (+50) to 0 mV. While maintaining the double bond between the carbon atoms, TCE decays under slightly reducing conditions of around Eh -50 to -100 mV to dichloroethene (DCE) and Cl^-. [Pierri D. Environ Adv 2021;5:100090]. The fact that PCE may degrade into TCE over time supports the contention that ultimately Camp Lejeune residents exposed to one of the chemicals were likely to have also been exposed to others (highlighting the question of additive effect).

PCE and TCE also upon ingestion can generate common metabolites, which can themselves be mutagenic, genotoxic, or carcinogenic.[3] "Trichloroethylene (TCE) and tetrachloroethylene (PCE) are structurally similar chemicals" and "are structurally similar chlorinated olefins." [Luo YS. Toxicol 2018;409:33-43]. An analysis of the comparative toxicokinetics of TCE and PCE reveals that upon absorption, TCE and PCE are metabolized through oxidative and glutathione conjugation pathways. [Cichocki JA,. J Pharmacol Exp Ther 2016;359:110123]. Initial oxidation occurs on the double bond by cytochrome P450s (CYPs) to generate an epoxide, which can be further metabolized. Trichloroacetic acid (TCA) is a major oxidative metabolite of both TCE and

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[2] *See* Figure 4 in Maslia ML. Water 2016;8:449. *See also id.* at Table 2, listing selected "measured and reconstructed (simulated) concentrations of tetrachloroethylene (PCE), trichloroethylene (TCE), *trans*-1,2-dichloroethylene (1,2-tDCE), vinyl chloride (VC), and benzene at the Hadnot Point water treatment plant."

[3] A genotoxin is a chemical or agent that can damage DNA or chromosomes in a cell, potentially causing mutations that lead to cancer or birth defects. A genotoxic agent can bind directly to DNA or indirectly damage it by affecting enzymes involved in DNA replication. Genotoxicity is a more general term than mutagenicity. A mutagen is a mutation-causing agent, such as a chemical, which results in an increased rate of mutations in an organism's genetic code. All mutagens are also genotoxins. A genotoxic carcinogen or mutagenic carcinogen can include a chemical that can damage the genetic material of a cell in a manner that can contribute to lead to cancer.

PCE, and is a common urinary biomarker of exposure. [Forkert PG. Drug Metab Dispos 2003;31:306-11]. As of 2014, TCA was classified by the EPA as a possible human carcinogen based on evidence of carcinogenicity in experimental animals. [IARC Monograph 106, 2014]. As of 2012, TCA was considered to be a confirmed carcinogen in experimental animals.

In addition to metabolization producing TCA, TCE is also metabolized into the oxidative metabolite, trichloroethanol (TCOH), which is a TCE-specific metabolite that is formed through oxidation of TCE to chloral hydrate (CH), while PCE oxidation occurs through trichloroacetyl chloride.[4] TCOH and related chemicals have been studied for their carcinogenic potential.[5]

There are other common metabolites as between PCE and TCE. For instance, upon absorption, both TCE and PCE can enzymatically conjugate with glutathione to form dichloro- or trichloro-glutathione conjugates (DCVG or TCVG).[6] These can be further metabolized via hepatic or renal gamma-glutamyl transferase and di-peptidase to form corresponding cysteine conjugates, DCVC or TCVC, which are then n-acetylated via N-acetyltransferase to generate NAcDCVC or NAcTCVC, respectively.[7] In addition, both NAcDCVC and NAcTCVC can be deacetylated via acylase to yield DCVC or TCVC, respectively. Apart from N-acetylation, DCVC and TCVC can be further bio-activated via cysteine conjugate β lyase to generate reactive thioketenes, or flavin-containing monooxygenase to form corresponding sulfoxides.[8]

In short, the science reflects that unsurprisingly structurally similar chemicals – e.g., PCE and TCE – once absorbed into the body by ingestion, inhalation or dermal exposure routes, can be broken down or metabolized into other substances. Some of these metabolites or breakdown products are common as between the parent chemicals.

When exposure to more than one chemical occurs (as, here, to e.g. PCE and TCE), there is the potential for 3 major types of interactions: either a) the toxic effects are additive (e.g.: 1 + 1 = 2); or b), the effects are less than truly additive (e.g.: 2 + 2 = 3);[9] or c), the effects are synergistic (e.g.: 1 + 1 = 3). Any significant deviation from additivity would be classified as synergy or antagonism. Synergy can be defined as a combination effect that is greater than the additive effect expected. Synergy can also be called superadditivity.

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[4] Luo 2018, citing Chiu WA. Toxicol Sci 20078;95:23-36.

[5] *See* Robert Kapp, Encyclopedia of Toxicology (Second Edition), 2005, discussing 2,2,2-Trichloroethanol and noting that acyl chlorides and free radicals that are formed from both 1,1,1-trichloroethane and 1,1,2-trichloroethane are believed to bind nucleic acids and proteins causing various cytoxic, mutagenic, and carcinogenic effects.

[6] Luo 2018, citing Lash LH. Environ Health Perspect 2000;108:177-200.

[7] *Id.*

[8] Luo 2018, citing Lash LH. Mutat Res Rev Mutat Res 2014;762:22-36.

[9] For example, assume that drinking only chemical X for a year causes a 2% chance of cancer, and drinking only chemical Y for a year causes a 3% chance of cancer; and because of some interaction between them, if one drinks both X and Y for a year, the cancer risk rises but only to 4%. Under "normal" additive conditions, using the simple math the additive effect should have been 5% instead.

As discussed above, the studies involving exposure to multiple toxins reveals that it makes the toxicity and carcinogenicity worse. For instance:

- A study of drinking water contamination and leukemia and non-Hodgkin lymphoma (NHL) incidence (1979-1987) was conducted in a 75-town study area in New Jersey including the counties of Bergen, Essex, Morris and Passaic. [Cohn P. Environ Health Perspect. 1994;102:556-61]. The abstract of a subsequent 1994 article on the work reads: "A study of drinking water contamination and leukemia and non-Hodgkin's lymphoma (NHL) incidence (1979-1987) was conducted in a 75-town study area. Comparing incidence in towns in the highest **trichloroethylene (TCE)** stratum (>5 microg/l) to towns without detectable TCE yielded an age-adjusted rate ratio (RR) for total leukemia among females of 1.43 (95% CI 1.07-1.90). For females under 20 years old, the RR for acute lymphocytic leukemia was 3.26 (95% CI 1.27-8.15). Elevated RRs were observed for chronic myelogenous leukemia among females and for chronic lymphocytic leukemia among males and females. NHL incidence among women was also associated with the highest TCE stratum (RR = 1.36; 95% CI 1.08-1.70). For diffuse large cell NHL and non-Burkitt's high-grade NHL among females, the RRs were 1.66 (95% CI 1.07-2.59) and 3.17 (95% CI 1.23-8.18), respectively, and 1.59 (95% CI 1.04-2.43) and 1.92 (95% CI 0.54-6.81), respectively, among males. **Perchloroethylene (PCE)** was associated with incidence of non-Burkitt's high-grade NHL among females, but **collinearity with TCE made it difficult to assess relative influences. The results demonstrate a link between TCE/PCE and leukemia/ NHL incidence**. However, the conclusions are limited by potential misclassification of exposure due to lack of individual information on long-term residence, water consumption, and inhalation of volatilized compounds." (Emphases added). The discussion section inter alia notes: "This predicted added risk is in the same range as the increased leukemia and NHL incidence rates observed in the highest TCE stratum in this study. The rodent bioassays have been criticized because high concentrations must be used to generate a statistically sufficient number of cancers in a small group of animals with a normal life span of 2 years. However, human exposures to drinking water contaminants **include ingestion, inhalation, and dermal exposures that frequently include more than one contaminant and may involve susceptible subpopulations such as fetuses and neonates. The carcinogenic activity of TCE and PCE may be compounded by joint exposure because TCE and PCE appear to share toxic metabolic pathways.**" [Cohn 1994 at 561]. (Emphasis added).

Documented evidence of various particular additive or synergistic effects of two different exposures, contaminants or stressors, include, in one study, evidence of how obesity was observed to increase the risk of arsenic-associated lung and bladder cancer by over 10-fold in individuals with elevated arsenic exposure compared to non-obese individuals. [Steinmaus C. Environ Res. 2015;142:594–601]. Studies indicate that arsenic's carcinogenicity is synergistically higher in obese individuals, smokers, and those with concurrent occupational exposures. [Steinmaus 2015; Ferreccio C. Epidemiol 2013;24:898–905]. As another specific example of apparent synergistic carcinogenic effect, a 2000 publication described a supra-additive genotoxicity of a combination of γ-irradiation and ethyl methanesulfonate in exposed mouse cells.[10]

One of the first synergistic interactions described between environmental pollutants was with a mixture of asbestos and cigarette smoke, which promotes the development of lung cancer.[11] The science of additive and synergistic interactions between multiple chemical contaminants such as, e.g., the PCE, TCE, benzene, and vinyl chloride, is evolving. However, the science published in the area to date is compelling and supports a qualitative conclusion (particularly under an "equipoise" or "as likely as not" standard) that Camp Lejeune Plaintiffs were exposed by multiple routes of exposure to multiple chemicals with (as likely as not) additive if not multiplicative effect.

Concepts of additive effect of multiple exposures to different carcinogens and environmental contaminants over time is related to the hypothesis of carcinogenesis as additive across various exposures and stressors. In this regard, cumulative risk assessment has been defined as the assessment of "combined risks from aggregate exposures to multiple agents or stressors, where agents or stressors may include chemical and nonchemical stressors." U.S. EPA. Framework for cumulative risk assessment. U.S Environmental Protection Agency, Office of Research and Development, National Center for Environmental Assessment; Washington, DC: 2003.

XIV. BRADFORD HILL ANALYSIS - BENZENE AND LEUKEMIA

I generally followed the weight of the evidence approach to investigating and analyzing the data on benzene exposure and adverse health effects in the Camp Lejeune cohort, and leukemia specifically. I have also evaluated adverse health effects and water through consideration of the Bradford Hill Viewpoints. Published as nine viewpoints in 1965, the Bradford Hill viewpoints are often used to determine if observed epidemiologic associations are causal. Those nine principles are: strength of association; consistency; specificity; temporality; biological gradient; plausibility; coherence; experiment; and analogy. Applying these viewpoints to the association between the chemicals at Camp Lejeune and leukemia, there is substantial evidence supporting causality:

Strength of Association: Strength of association is demonstrated by statistical significance. That is, an odds ratio for the occurrence of an adverse health effect in those exposed to benzene of greater than 1.1 (given the as likely as not standard applicable to Camp Lejeune). It should be

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[10] *See* Stopper H. Mutagenesis 2000;15:235-8 (from the Abstract: "While testing for genotoxicity is usually performed on single chemicals, exposure of humans always comprises a number of genotoxic agents. The investigation of potentially synergistic effects of combinations therefore is an important issue in toxicology. Combinations of 511 keV γ-radiation with the chemical alkylating agent ethyl methane-sulfonate were investigated in the in vitro micronucleus test in mouse lymphoma L5178Y cells. With combinations in the low dose linear effect range for the individual agents (0.25–2 Gy and 0.8–3.2 mM, respectively), supra-additivity by 34–86% was seen. The synergism was more pronounced at the higher dose levels. Supra-additivity was confirmed in experiments using cytochalasin B and analyzing binucleate cells only, to control for putative effects on the cell cycle. Statistical significance was shown by a 2-factor analysis of variance with interaction….").

[11] *See* Alejandro F. GeoHealth 2022;6 (so stating).

noted that statistical significance is not itself determinative of causation; rather, it helps to explain the likelihood one would see a disease in a given population versus a control group. Therefore, studies with confidence intervals that include 1.0 do not establish that an agent does not cause a given disease, but rather that the subject disease may not be more prevalent in the exposed group than in a control group. Studies of Camp Lejeune personnel as well studies of occupational exposure and other environmental pollution, reliably demonstrate risks of greater than 1.1 for exposure to benzene and leukemia. For instance, a meta-analysis reported a summary effect size of 1.72 for any leukemia with benzene exposure. [Khalade A. Environ Health 2010;9:31].

Consistency: The Bradford Hill term of consistency refers to the concept that studies done in different populations or that studies of different designs yield similar results. This viewpoint is also met in that varied studies consistently demonstrate leukemia (particularly AML) after exposure to benzene. The association has been consistently observed across various studies and populations.

Specificity: Specificity in Bradford Hill's time meant that exposure causes a single disease without any other likely explanation other than the exposure under consideration. However, we now know that a particular exposure may cause more than one disease state. For instance, it is known that benzene is known to cause several cancers and other adverse health effects. Therefore, the specificity viewpoint is difficult to meet with regards to benzene.

Temporality: Temporality is the easiest of the Bradford Hill viewpoints to understand, and the one viewpoint that must be met. Simply put, the exposure must precede the development of the disease. This viewpoint is also met in the issue at hand with regards to the Camp Lejeune water contamination.

Biological Gradient: The concept of a biological gradient is that a dose-response exists. That is, that the greater a dose (*i.e.*, exposure), the more likely a response (*i.e.*, presence of disease). However, we now know that complex dose-response relationships can occur (*e.g.*: hormesis) and that dose-response relationships are not all (or necessarily) linear. Further complicating the dose-response relationship is that amongst the exposed people at Camp Lejeune there were children as well as adults. It is unknown the degree to which children have altered absorption or kinetics of benzene, particularly when one considers the three different methods of chemical absorption at Camp Lejeune. While granular dose-response data are not available for the Camp Lejeune cohorts, data from occupational exposures and other environmental contamination sites do provide evidence of a positive dose-response for exposure to benzene and the occurrence of leukemia, with higher exposures leading to greater risks. [Khalade A. Environ Health 2010;9:31].

Plausibility: Biologic plausibility refers to the concept that a relationship between an exposure and an adverse health outcome can be attributed to causation based on existing biomedical and epidemiological knowledge. In the above report, some of the research into the mechanism of action and varied outcomes after benzene exposures were detailed. Benzene is metabolized into toxic intermediates that can cause DNA damage and chromosomal aberrations, which are mechanisms known to contribute to leukemogenesis. [Smith MT. Ann Rev Public Health 2010;31:133-48]. There have been several epidemiological studies performed with benzene exposure. Given this abundant evidence, it is my opinion that the biologic plausibility standard has been met with regards to benzene exposure and leukemia.

Coherence: The Bradford Hill viewpoint of coherence is very similar to biological plausibility. That is, that "the cause-and-effect interpretation of the data should not seriously conflict with the generally known facts of the natural history and biology of the disease." [Bradford Hill 1965]. Benzene is a known carcinogen. There are mechanistic and human studies evaluating the effect of benzene on gene expression and chromosomal abnormalities, and the occurrence of leukemia. It is my opinion that the viewpoint of coherence has also been met.

Experimental Evidence: Bradford Hill also identified experimentation as a viewpoint to evaluate with regards to causation. Put simply, conduct experiments whereby you either purposely expose individuals to a toxin (such as benzene), or you eliminate such an exposure and determine the effect on adverse health outcome occurrence. Clearly one cannot ethically subject individuals for any significant length of time to benzene by any method of exposure. However, there are decades of epidemiologic research which demonstrate that benzene causes cancer, and specifically that benzene causes leukemia. Therefore, it is my opinion that the experimentation viewpoint has also been met.

Analogy: With analogy, Bradford Hill meant to say that when there is strong evidence of an exposure-disease dyad, one should be more inclined to accept causation with a similar exposure and/or disease. There is ample scientific evidence of solvents (including benzene) causing various cancers, and benzene specifically causing leukemia. With the wide range and varied adverse effects (including carcinogenesis) of benzene, it is my opinion that the analogy viewpoint has also been met.

When the body of research on benzene is considered in light of the Bradford Hill viewpoints, I am able to opine that exposure to benzene causes leukemia. However, it is also important to note that the Bradford Hill viewpoints were not intended to be rigid guidelines or a checklist that must be completed in order to determine causation. Rather, they are suggested guidelines to consider when determining causation.

XV. BRADFORD HILL ANALYSIS – BENZENE AND NHL

I generally followed the weight of the evidence approach to investigating and analyzing the data on benzene exposure and adverse health effects in the Camp Lejeune cohort, and NHL specifically. I have also evaluated adverse health effects and water through consideration of the Bradford Hill Viewpoints.

Strength of Association: Strength of association is demonstrated by statistical significance. That is, an odds ratio for the occurrence of an adverse health effect in those exposed to benzene of greater than 1.1 (given the as likely as not standard applicable to Camp Lejeune). It should be noted that statistical significance is not itself determinative of causation; rather, it helps to explain the likelihood one would see a disease in a given population versus a control group. Therefore, studies with confidence intervals that include 1.0 do not establish that an agent does not cause a given disease, but rather that the subject disease may not be more prevalent in the exposed group than in a control group. Studies of Camp Lejeune personnel as well studies of occupational exposure and other environmental pollution, demonstrate risks of greater than 1.1 for exposure to benzene and NHL. For instance, Bassig *et al.* found a significant association between occupational benzene exposure and NHL risk (HR 1.5; 95% CI 1.2-2.0) [Bassig BA. Int J Cancer 2024;155:2159–68]

Consistency: The Bradford Hill term of consistency refers to the concept that studies done in different populations or that studies of different designs yield similar results. This viewpoint is also met in that varied studies demonstrate NHL after exposure to benzene. For example, the Vlaanderen *et al.* 2011 manuscript (which included studies from at least 4 countries) found increased meta-relative risks for NHL with higher study quality in [Vlaanderen J. Environ Health Perspect 2011;119:159-67]. And the aforementioned Bassig 2024 study which demonstrated an association between benzene exposure and NHL was conducted in China.

Specificity: Specificity in Bradford Hill's time meant that exposure causes a single disease without any other likely explanation other than the exposure under consideration. However, we now know that a particular exposure may cause more than one disease state. For instance, it is known that benzene is known to cause several cancers and other adverse health effects. Therefore, the specificity viewpoint is difficult to meet with regards to benzene.

Temporality: Temporality is the easiest of the Bradford Hill viewpoints to understand, and the one viewpoint that must be met. Simply put, the exposure must precede the development of the disease. This viewpoint is also met in the issue at hand with regards to the Camp Lejeune water contamination.

Biological Gradient: The concept of a biological gradient is that a dose-response exists. That is, that the greater a dose (*i.e.,* exposure), the more likely a response (*i.e.*, presence of disease). However, we now know that complex dose-response relationships can occur (*e.g.*: hormesis) and that dose-response relationships are not all (or necessarily) linear. Further complicating the dose-response relationship is that amongst the exposed people at Camp Lejeune there were children as well as adults. It is unknown the degree to which children have altered absorption or kinetics of benzene, particularly when one considers the three different methods of chemical absorption at Camp Lejeune. Studies do provide evidence of a positive dose-response for exposure to benzene and the occurrence of NHL, with higher exposures leading to greater risks. For instance, the Bassig 2024 study found a significant exposure-response relationship for cumulative occupational benzene exposure and NHL risk among Chinese men and women. The study reported hazard ratios of 1.5 (95% CI 1.2-2.0) for ever occupational exposure to benzene, with significant trends for increasing duration and cumulative exposure. Another study by Bassig *et al.* in the Shanghai Women's Health Study also demonstrated a significant trend in NHL risk with increasing years of benzene exposure and cumulative exposure levels. Women in the highest tertile of cumulative exposure had a hazard ratio of 2.16 (95% CI 1.17-3.98) compared to unexposed women [Bassig BA. Environ Health Perspect 2015;123:971–977]

Plausibility: Biologic plausibility refers to the concept that a relationship between an exposure and an adverse health outcome can be attributed to causation based on existing biomedical and epidemiological knowledge. In the above report, some of the research into the mechanism of action and varied outcomes after benzene exposures were detailed. Benzene is metabolized into toxic intermediates that can cause DNA damage and chromosomal aberrations, which are mechanisms known to contribute to leukemogenesis. [Smith MT. Ann Rev Public Health 2010;31:133-48]. There have been several epidemiological studies performed with benzene exposure. Given this abundant evidence, it is my opinion that the biologic plausibility standard has been met with regards to benzene exposure and NHL.

Coherence: The Bradford Hill viewpoint of coherence is very similar to biological plausibility. That is, that "the cause-and-effect interpretation of the data should not seriously conflict with the generally known facts of the natural history and biology of the disease." [Bradford Hill 1965]. Benzene is a known carcinogen. There are mechanistic and human studies evaluating the effect of benzene on gene expression and chromosomal abnormalities, and the occurrence of NHL and other hematologic cancers. It is my opinion that the viewpoint of coherence has also been met.

Experimental Evidence: Bradford Hill also identified experimentation as a viewpoint to evaluate with regards to causation. Put simply, conduct experiments whereby you either purposely expose individuals to a toxin (such as benzene), or you eliminate such an exposure and determine the effect on adverse health outcome occurrence. Clearly one cannot ethically subject individuals for any significant length of time to benzene by any method of exposure. However, there are decades of epidemiologic research which demonstrate that benzene causes cancer, and specifically that benzene causes NHL. Therefore, it is my opinion that the experimentation viewpoint has also been met.

Analogy: With analogy, Bradford Hill meant to say that when there is strong evidence of an exposure-disease dyad, one should be more inclined to accept causation with a similar exposure and/or disease. There is ample scientific evidence of solvents (including benzene) causing various cancers, and benzene specifically causing NHL. With the wide range and varied adverse effects (including carcinogenesis) of benzene, it is my opinion that the analogy viewpoint has also been met.

When the body of research on benzene is considered in light of the Bradford Hill viewpoints, it is my opinion that exposure to benzene causes NHL. However, it is also important to note that the Bradford Hill viewpoints were not intended to be rigid guidelines or a checklist that must be completed in order to determine causation. Rather, they are suggested guidelines to consider when determining causation.

XVI. BRADFORD HILL ANALYSIS – TCE AND LEUKEMIA

I generally followed the weight of the evidence approach to investigating and analyzing the data on TCE, and adverse health effects in the Camp Lejeune cohort, and leukemia specifically. I have also evaluated adverse health effects and water through consideration of the Bradford Hill Viewpoints.

Strength of Association: Strength of association is demonstrated by statistical significance. That is, an odds ratio for the occurrence of an adverse health effect in those exposed to the contaminated Camp Lejeune water of greater than 1.1 (given the as likely as not standard of the Camp Lejeune Justice Act). The strength of association between TCE exposure and leukemia varies across studies. For instance, Cohn *et al.* (Cohn 1994) reported an age-adjusted risk ratio for total leukemia among females of 1.43 (95% CI 1.07-1.90) in areas with high TCE contamination. However, Alexander *et al.* found no significant association in their meta-analysis (SRRE = 1.11; 95% CI 0.93-1.32). (Alexander 2006)

Consistency: The Bradford Hill term of consistency refers to the concept that studies done in different populations or that studies of different designs yield similar results. The evidence for consistency is mixed. Some studies, like those by Cohn et al. (Cohn 1994) and Karami et al. [Karami S. Occup Environ Med 2013;70:591-9] demonstrate an association between TCE and hematopoietic cancers, including leukemia. Conversely, other studies, such as Alexander et al., do not support a significant association.

Specificity: Specificity in Bradford Hill's time meant that exposure causes a single disease without any other likely explanation other than the exposure under consideration. However, we now know that a particular exposure may cause more than one disease state. For instance, it is known that the water contaminants from Camp Lejeune (and TCE specifically) is known to cause several cancers and other adverse health effects. Therefore, the specificity viewpoint is difficult to meet with regards to TCE and leukemia.

Temporality: Temporality is the easiest of the Bradford Hill viewpoints to understand, and the one viewpoint that must be met. Simply put, the exposure must precede the development of the disease. This viewpoint is also met in the issue at hand with regards to the Camp Lejeune water contamination with TCE.

Biological Gradient: The concept of a biological gradient is that a dose-response exists. That is, that the greater a dose (*i.e.,* exposure), the more likely a response (*i.e.*, presence of disease). However, we now know that complex dose-response relationships can occur (*e.g.*: hormesis) and that dose-response relationships are not all (or necessarily) linear. Further complicating the dose-response relationship is that amongst the exposed people at Camp Lejeune there were children as well as adults. It is unknown the degree to which children have altered absorption or kinetics of TCE, particularly when one considers the three different mechanisms of chemical absorption at Camp Lejeune. While granular dose-response data are not available for the Camp Lejeune cohorts, some studies indicate a dose-response relationship. For example, Cohn *et al.* observed higher RRs for leukemia with higher TCE exposure levels.

Plausibility: Biologic plausibility refers to the concept that a relationship between an exposure and an adverse health outcome can be attributed to causation based on existing biomedical and epidemiological knowledge. In the above report, some of the research into the mechanism of action and varied outcomes after TCE exposures were detailed. Biological plausibility is supported by mechanistic studies showing TCE's impact on immune function and hematopoietic cells. For instance, Lan et al. demonstrated that TCE exposure is associated with declines in lymphocyte subsets, which could contribute to leukemia development. [Lan Q. Carcinogenesis 2010;31:1592-6]

Coherence: The Bradford Hill viewpoint of coherence is very similar to biological plausibility. That is, that "the cause-and-effect interpretation of the data should not seriously conflict with the generally known facts of the natural history and biology of the disease." [Bradford Hill 1965]. The association between TCE and leukemia is coherent with existing knowledge of TCE's toxicological effects, including its classification as a carcinogen by the US Environmental Protection Agency. [Chiu WA. Environ Health Perspect 2013;121:303-11]

Experimental Evidence: Bradford Hill also identified experimentation as a viewpoint to evaluate with regards to causation. Put simply, conduct experiments whereby you either purposely expose individuals to a toxin (such as TCE), or you eliminate such an exposure and determine the effect on adverse health outcome occurrence. Clearly one cannot ethically subject individuals for any significant length of time to TCE by any method of exposure. However, there are decades of epidemiologic research which demonstrate that the Camp Lejeune water contamination chemicals cause cancer, and specifically that TCE causes leukemia. Therefore, it is my opinion that the experimentation viewpoint has also been met.

Analogy: With analogy, Bradford Hill meant to say that when there is strong evidence of an exposure-disease dyad, one should be more inclined to accept causation with a similar exposure and/or disease. There is ample scientific evidence of chlorinated and other solvents (including TCE, PCE, and benzene) causing various cancers, with TCE, PCE, and benzene specifically causing leukemia. With the wide range and varied adverse effects (including carcinogenesis) of the chlorinated solvents, it is my opinion that the analogy viewpoint has also been met.

When the body of research on TCE exposure is considered in light of the Bradford Hill viewpoints, it is my opinion that exposure to TCE causes leukemia. However, it is also important to note that the Bradford Hill viewpoints were not intended to be rigid guidelines or a checklist that must be completed in order to determine causation. Rather, they are suggested guidelines to consider when determining causation.

XVII. BRADFORD HILL ANALYSIS – TCE AND NHL

I generally followed the weight of the evidence approach to investigating and analyzing the data on TCE and NHL specifically. However, I have also evaluated adverse health effects and water through consideration of the Bradford Hill viewpoints.

Strength of association is demonstrated by statistical significance. That is, an odds ratio for the occurrence of an adverse health effect in those exposed to the contaminated Camp Lejeune water of greater than 1.1. It should be noted that statistical significance is not itself determinative of causation; rather, it helps to explain the likelihood one would see a disease in a given population versus a control group. Therefore, studies with confidence intervals that include 1.0 do not establish that an agent does not cause a given disease, but rather that the subject disease may not be more prevalent in the exposed group than in a control group. Studies of Camp Lejeune personnel as well studies of occupational exposure and other environmental pollution, reliably demonstrate risks of greater than 1.1 for exposure to TCE and NHL. For example, a pooled analysis of four international case-control studies found elevated risks of specific NHL subtypes with TCE exposure [Cocco P. Occup Environ Med 2013;70:795-802].

Consistency: The Bradford Hill term of consistency refers to the concept that studies done in different populations or that studies of different designs (for instance, cohort studies and case-control tests) yield similar results. A manuscript by the U.S. EPA authored by Scott and Jinot found a summary risk estimates for overall exposure to TCE of 1.23 for NHL (95% CI 1.07-1.42), and for the highest exposure group the RR was 1.43 (95% CI 1.13-1.82). [Int J Environ Res Public Health 2011;8:4238-72].

Specificity: Specificity in Bradford Hill's time meant that an exposure causes a single disease without any other likely explanation other than the exposure under consideration. However, we now know that a particular exposure may cause more than one disease state. For instance, it is known that TCE is known to cause several cancers and other adverse health effects. Therefore, the specificity viewpoint is difficult to meet with TCE and NHL.

Temporality: Temporality is the easiest of the Bradford Hill viewpoints to understand, and the one viewpoint that must be met. Simply put, the exposure must precede the development of the disease. This viewpoint is also met in the issue at hand with regards to the Camp Lejeune water contamination.

Biological Gradient: The concept of a biological gradient is that a dose-response exists. That is, that the greater a dose (i.e., exposure), the more likely a response (i.e., presence of disease). However, we now know that complex dose-response relationships can occur (e.g.: hormesis) and that dose-response relationships are not all (or necessarily) linear. Further complicating the dose-response relationship is that amongst the exposed people at Camp Lejeune there were children as well as adults. It is unknown the degree to which children have altered absorption or kinetics TCE, particularly when one considers the three different mechanisms of TCE absorption at Camp Lejeune. A pooled analysis of four international case-control studies found that the risk of follicular lymphoma increased with higher probability and intensity of TCE exposure, and this risk was further elevated with longer duration of exposure. [Cocco P. Occup Environ Med 2013;70:795-802]. This study also noted increased risks for NHL overall, follicular lymphoma, and CLL with combined metrics of duration, frequency, and intensity of exposure.

Plausibility: Biologic plausibility refers to the concept that a relationship between an exposure and an adverse health outcome can be attributed to causation based on existing biomedical and epidemiological knowledge. In the above report, some of the research into the mechanism of action and varied outcomes after TCE exposure was detailed. Mechanistic studies have shown that TCE exposure is associated with declines in lymphocyte subsets and markers of B-cell activation, which are biologically plausible mechanisms for NHL development [Lan Q. Carcinogenesis 2010;31:1592-6]. Furthermore, there have been several epidemiological studies which demonstrate the increase in NHL risk with TCE. Given this abundant evidence, it is my opinion that the biologic plausibility standard has been met with regards to exposure and NHL.

Coherence: The Bradford Hill viewpoint of coherence is very similar to biological plausibility. That is, that "the cause-and-effect interpretation of the data should not seriously conflict with the generally known facts of the natural history and biology of the disease" [Bradford Hill 1965]. TCE is a known carcinogen. There are mechanistic, animal, and human studies evaluating the effect of the chemicals on gene expression and chromosomal abnormalities, and the occurrence of cancer, including NHL. It is my opinion that the viewpoint of coherence has also been met.

Experimental Evidence: Bradford Hill also identified experimentation as a viewpoint to evaluate with regards to causation. Put simply, conduct experiments whereby you either purposely expose individuals to a toxin (such as TCE), or you eliminate such an exposure and determine the effect on adverse health outcome occurrence. Clearly one cannot ethically subject individuals for any significant length of time to TCE by any method of exposure. However, there is a plethora of research which demonstrate that TCE causes cancer, and specifically that TCE causes NHL. Therefore, it is my opinion that the experimentation viewpoint has also been met.

Analogy: With analogy, Bradford Hill meant to say that when there is strong evidence of an exposure-disease dyad, one should be more inclined to accept causation with a similar exposure and/or disease. There is ample scientific evidence of chlorinated and non-chlorinated solvents (including TCE) causing various cancers, with TCE specifically causing NHL. With the wide range and varied adverse effects (including carcinogenesis) of the chlorinated solvents including TCE, it is my opinion that the analogy viewpoint has also been met.

When the body of research on TCE exposure is considered in light of the Bradford Hill viewpoints, it is my opinion that exposure to TCE causes NHL. However, it is also important to note that the Bradford Hill viewpoints were not intended to be rigid guidelines or a checklist that must be completed in order to determine causation. Rather, they are suggested guidelines to consider when determining causation.

XVIII. BRADFORD HILL ANALYSIS – PCE AND LEUKEMIA

I generally followed the weight of the evidence approach to investigating and analyzing the data on PCE exposure and adverse health effects in the Camp Lejeune cohort, and leukemia specifically. I have also evaluated adverse health effects and water through consideration of the Bradford Hill Viewpoints.

Strength of Association: Strength of association is demonstrated by statistical significance. That is, an odds ratio for the occurrence of an adverse health effect in those exposed to the contaminated Camp Lejeune water of greater than 1.1 (given the as likely as not standard of the Camp Lejeune Justice Act). It should be noted that statistical significance is not itself determinative of causation; rather, it helps to explain the likelihood one would see a disease in a given population versus a control group. Therefore, studies with confidence intervals that include 1.0 do not establish that an agent does not cause a given disease, but rather that the subject disease may not be more prevalent in the exposed group than in a control group. Studies of Camp Lejeune personnel as well studies of occupational exposure and other environmental pollution, reliably demonstrate risks of greater than 1.1 for exposure to the Camp Lejeune solvents and leukemia. The study by Cohn *et al.* reported an association between PCE exposure and non-Burkitt's high-grade NHL among females. Furthermore, the Aschengrau 1993 study found that high PCE exposure yielded a risk ratio of 5.78 (95% CI 0.98 - 22.97) for leukemia. As the cumulative amount of PCE increased, so did the risk of leukemia. The authors concluded "increased leukemia risk was dose related."

Consistency: The Bradford Hill term of consistency refers to the concept that studies done in different populations or that studies of different designs yield similar results. The findings for PCE and leukemia are not consistent across all studies. While Cohn *et al.* (Cohn 1994) demonstrated a link, the cohort study by Seldén and Ahlborg (2011) on Swedish dry-cleaners and laundry workers found no clear association between PCE exposure and subsequent cancer morbidity, including leukemia. The consistency viewpoint is therefore difficult to meet for PCE and leukemia.

Specificity: Specificity in Bradford Hill's time meant that exposure causes a single disease without any other likely explanation other than the exposure under consideration. However, we now know that a particular exposure may cause more than one disease state. PCE exposure has been linked to various cancers, including NHL and liver cancer, but not exclusively to leukemia. Therefore, the specificity viewpoint is not met.

Temporality: Temporality is the easiest of the Bradford Hill viewpoints to understand, and the one viewpoint that must be met. Simply put, the exposure must precede the development of the disease. This viewpoint is also met in the issue at hand with regards to the Camp Lejeune water contamination and leukemia.

Biological Gradient: The concept of a biological gradient is that a dose-response exists. That is, that the greater a dose (*i.e.*, exposure), the more likely a response (*i.e.*, presence of disease). However, we now know that complex dose-response relationships can occur (*e.g.*: hormesis) and that dose-response relationships are not all (or necessarily) linear. Further complicating the dose-response relationship is that amongst the exposed people at Camp Lejeune there were children as well as adults. It is unknown the degree to which children have altered absorption or kinetics of PCE, particularly when one considers the three different mechanisms of PCE at Camp Lejeune. As mentioned above, the Aschengrau 1993 study found that as the cumulative amount of PCE increased, so did the risk of leukemia, with the authors concluding "increased leukemia risk was dose related." Therefore, it is my opinion that a biological gradient exists for PCE and leukemia.

Plausibility: Biologic plausibility refers to the concept that a relationship between an exposure and an adverse health outcome can be attributed to causation based on existing biomedical and epidemiological knowledge. In the above report, some of the research into the mechanism of action and varied outcomes after PCE exposures were detailed. Specifically, PCE is metabolized into toxic intermediates that can cause DNA damage and chromosomal aberrations, which are mechanisms known to contribute to leukemogenesis. [Smith MT. Ann Rev Public Health 2010;31:133-48]. Given these data, it is my opinion that the plausibility viewpoint has been met.

Coherence: The Bradford Hill viewpoint of coherence is very similar to biological plausibility. That is, that "the cause-and-effect interpretation of the data should not seriously conflict with the generally known facts of the natural history and biology of the disease." [Bradford Hill 1965]. The water contaminants at Camp Lejeune (including PCE) are known or probable carcinogens. There are numerous mechanistic and human studies evaluating the effect of the chemicals on gene expression and chromosomal abnormalities, and the occurrence of leukemia. It is my opinion that the viewpoint of coherence has also been met.

Experimental Evidence: Bradford Hill also identified experimentation as a viewpoint to evaluate with regards to causation. Put simply, conduct experiments whereby you either purposely expose individuals to PCE, or you eliminate such an exposure, and determine the effect on adverse health outcome occurrence. Clearly one cannot ethically subject individuals for any significant length of time to PCE by any method of exposure. However, there are decades of epidemiologic research which demonstrate that the Camp Lejeune water contamination chemicals (including PCE) cause cancer. So, while there is limited direct experimental evidence for PCE exposure and leukemia, it is my opinion that this Bradford Hill factor has been met.

Analogy: With analogy, Bradford Hill meant to say that when there is strong evidence of an exposure-disease dyad, one should be more inclined to accept causation with a similar exposure and/or disease. There is ample scientific evidence of chlorinated and other solvents (including TCE, PCE, and benzene) causing various cancers, with TCE and benzene specifically causing leukemia. Other chlorinated solvents like TCE have been associated with cancer, which provides analogy for PCE and leukemia.

When the body of research on PCE exposure is considered in light of the Bradford Hill viewpoints, it is my opinion that exposure to PCE causes leukemia. However, it is also important to note that the Bradford Hill viewpoints were not intended to be rigid guidelines or a checklist that must be completed in order to determine causation. Rather, they are suggested guidelines to consider when determining causation.

XIX. BRADFORD HILL ANALYSIS – PCE AND NHL

I generally followed the weight of the evidence approach to investigating and analyzing the data on PCE exposure and adverse health effects in the Camp Lejeune cohort, and NHL specifically. However, I have also evaluated adverse health effects and water through consideration of the Bradford Hill viewpoints.

Strength of association is demonstrated by statistical significance. That is, an odds ratio for the occurrence of an adverse health effect in those exposed to the contaminated Camp Lejeune water of greater than 1.1 under the as likely as not standard. It should be noted that statistical significance is not itself determinative of causation; rather, it helps to explain the likelihood one would see a disease in a given population versus a control group. Therefore, studies with confidence intervals that include 1.0 do not establish that an agent does not cause a given disease, but rather that the subject disease may not be more prevalent in the exposed group than in a control group. Studies of Camp Lejeune personnel as well studies of occupational exposure and other environmental pollution, reliably demonstrate risks of greater than 1.1 for exposure to PCE and NHL. For instance, Selden and Ahlborg published findings from a cohort of more than 10,000 dry-cleaning and laundry workers that had occupational exposure to PCE and found elevated rates of NHL (SIR 2.05; 95% CI 1.30–3.07). [Selden AI and Ahlborg G. Int Arch Occup Environ Health 2011;84:435–43]. Additionally, Boice *et al.* (Boice 1999) found an increased standardized mortality rate of 1.70 (95% CI 0.73-3.34) for occupational exposure to PCE and NHL.

Consistency: The Bradford Hill term of consistency refers to the concept that studies done in different populations or that studies of different designs (for instance, cohort studies and case-control tests) yield similar results. This viewpoint is also met in that human studies utilizing varied methods demonstrate an increased risk of NHL after exposure to PCE. For example, the Selden and Ahlborg study was conducted in Sweden, while the Vlaanderen 2013 study was conducted in Scandinavia and found that high exposure to PCE was associated with an elevated hazard ratios for NHL of 1.23 (95% CI 1.00-1.52). Furthermore, Boice *et al.* study from 1999 found an increased standardized mortality rate of 1.70 (95% CI 0.73-3.34) for U.S. workers exposed to PCE. Thus, the scientific literature supports an association between occupational PCE exposure and NHL.

Specificity: Specificity in Bradford Hill's time meant that an exposure causes a single disease without any other likely explanation other than the exposure under consideration. However, we now know that a particular exposure may cause more than one disease state. For instance, it is known that PCE is known to cause several cancers and other adverse health effects. Therefore, the specificity viewpoint is difficult to meet with PCE.

Temporality: Temporality is the easiest of the Bradford Hill viewpoints to understand, and the one viewpoint that must be met. Simply put, the exposure must precede the development of the disease. This viewpoint is also met in the issue at hand with regards to the Camp Lejeune water contamination.

Biological Gradient: The concept of a biological gradient is that a dose-response exists. That is, that the greater a dose (i.e., exposure), the more likely a response (i.e., presence of disease). However, we now know that complex dose-response relationships can occur (e.g.: hormesis) and that dose-response relationships are not all (or necessarily) linear. Further complicating the dose-response relationship is that amongst the exposed people at Camp Lejeune there were children as well as adults. It is unknown the degree to which children have altered absorption or kinetics of PCE, particularly when one considers the three different mechanisms of PCE absorption at Camp Lejeune. The 2013 study by Vlaanderen *et al*. explored exposure-response relations for PCE in the Nordic Occupational Cancer cohort. They found that hazard ratio for NHL was elevated in groups with high exposure to PCE compared to occupationally unexposed subjects. Additionally, hazard ratios for NHL increased with increasing continuous exposure to PCE, indicating a dose-response relationship

Plausibility: Biologic plausibility refers to the concept that a relationship between an exposure and an adverse health outcome can be attributed to causation based on existing biomedical and epidemiological knowledge. In the above report, some of the research into the mechanism of action and varied outcomes after PCE exposure were detailed. Mechanistic studies have shown that PCE causes immunotoxicity, chromosomal aberrations, and epigenetic modifications (to name a few). Furthermore, there have been several epidemiological studies which demonstrate the increase in NHL risk with PCE exposure. Given this evidence, it is my opinion that the biologic plausibility standard has been met with regards to PCE exposure and NHL.

Coherence: The Bradford Hill viewpoint of coherence is very similar to biological plausibility. That is, that "the cause-and-effect interpretation of the data should not seriously conflict with the generally known facts of the natural history and biology of the disease" [Bradford Hill 1965]. PCE is a known carcinogen. There are mechanistic and human studies evaluating the effect of PCE on gene expression and chromosomal abnormalities, and the occurrence of cancer, including NHL. It is my opinion that the viewpoint of coherence has also been met.]

Experimental Evidence: Bradford Hill also identified experimentation as a viewpoint to evaluate with regards to causation. Put simply, conduct experiments whereby you either purposely expose individuals to a toxin (such as PCE), or you eliminate such an exposure and determine the effect on adverse health outcome occurrence. Clearly one cannot ethically subject individuals for any significant length of time to PCE by any method of exposure. However, epidemiologic research demonstrate that PCE causes cancer, and specifically that PCE causes NHL. Therefore, it is my opinion that the experimentation viewpoint has also been met.

Analogy: With analogy, Bradford Hill meant to say that when there is strong evidence of an exposure-disease dyad, one should be more inclined to accept causation with a similar exposure and/or disease. There is ample scientific evidence of chlorinated and other solvents (including TCE, PCE, and benzene) causing various cancers, with TCE, PCE, and benzene specifically causing NHL. With the wide range and varied adverse effects (including carcinogenesis) of the chlorinated solvents, it is my opinion that the analogy viewpoint has also been met.

When the body of research on PCE exposure is considered in light of the Bradford Hill viewpoints, it is my opinion that exposure to PCE causes NHL. However, it is also important to note that the Bradford Hill viewpoints were not intended to be rigid guidelines or a checklist that must be completed in order to determine causation. Rather, they are suggested guidelines to consider when determining causation.

XX. BRADFORD HILL ANALYSIS – TVOC AND LEUKEMIA

I generally followed the weight of the evidence approach to investigating and analyzing the data on TVOC exposure and adverse health effects in the Camp Lejeune cohort, and leukemia specifically. I have also evaluated adverse health effects and water through consideration of the Bradford Hill Viewpoints.

Strength of Association: Strength of association is demonstrated by statistical significance. That is, an odds ratio for the occurrence of an adverse health effect in those exposed to the contaminated Camp Lejeune water of greater than 1.1 (given the as likely as not standard of the

Camp Lejeune Justice Act). It should be noted that statistical significance is not itself determinative of causation; rather, it helps to explain the likelihood one would see a disease in a given population versus a control group. Therefore, studies with confidence intervals that include 1.0 do not establish that an agent does not cause a given disease, but rather that the subject disease may not be more prevalent in the exposed group than in a control group. Studies of Camp Lejeune personnel (Bove 2014) as well studies of other environmental pollution, reliably demonstrate risks of greater than 1.1 for exposure to the Camp Lejeune solvents and leukemia. For instance, Liu et al. found a pooled relative risk for leukemia of 1.03 per 1 μg/m^3 increase in benzene. [Liu N. Indoor Air. 2022;32:e13038]

Consistency: The Bradford Hill term of consistency refers to the concept that studies done in different populations or that studies of different designs yield similar results. This viewpoint is also met in that human studies consistently demonstrate leukemia after exposure to the water contaminants found at Camp Lejeune as TVOC. The association has been consistently observed across various studies and populations. For instance, Zhang et al. reported an increased risk of childhood acute leukemia with higher TVOC levels, supporting the consistency viewpoint. [Zhang Y. J Environ Sci Health Part A 2021;56:190-8]

Specificity: Specificity in Bradford Hill's time meant that exposure causes a single disease without any other likely explanation other than the exposure under consideration. However, we now know that a particular exposure may cause more than one disease state. For instance, it is known that the water contaminants from Camp Lejeune are known to cause several cancers and other adverse health effects. Additionally, the Camp Lejeune contaminants can be combined as TVOC, which by definition is non-specific. Therefore, the specificity viewpoint is difficult to meet with the chemical contaminants at Camp Lejeune.

Temporality: Temporality is the easiest of the Bradford Hill viewpoints to understand, and the one viewpoint that must be met. Simply put, the exposure must precede the development of the disease. This viewpoint is also met in the issue at hand with regard to the Camp Lejeune water contamination.

Biological Gradient: The concept of a biological gradient is that a dose-response exists. That is, that the greater a dose (*i.e.,* exposure), the more likely a response (*i.e.*, presence of disease). However, we now know that complex dose-response relationships can occur (*e.g.*: hormesis) and that dose-response relationships are not all (or necessarily) linear. Further complicating the dose-response relationship is that amongst the exposed people at Camp Lejeune there were children as well as adults. It is unknown the degree to which children have altered absorption or kinetics of the TVOCs, particularly when one considers the three different mechanisms of chemical absorption at Camp Lejeune. Liu *et al.* (Liu 2022) did find a dose-response relationship with benzene (which is a component of TVOC) and leukemia.

Plausibility: Biologic plausibility refers to the concept that a relationship between an exposure and an adverse health outcome can be attributed to causation based on existing biomedical and epidemiological knowledge. In the above report, some of the research into the mechanism of action and varied outcomes after TCE, PCE, benzene, and vinyl chloride exposures were detailed. Specifically, the chemicals are metabolized into toxic intermediates that can cause DNA damage and chromosomal aberrations, which are mechanisms known to contribute to leukemogenesis. [Smith MT. Ann Rev Public Health 2010;31:133-48]. Given this abundant evidence, it is my opinion that the biologic plausibility standard has been met with regards to exposure and leukemia.

Coherence: The Bradford Hill viewpoint of coherence is very similar to biological plausibility. That is, that "the cause-and-effect interpretation of the data should not seriously conflict with the generally known facts of the natural history and biology of the disease." [Bradford Hill 1965]. The water contaminants at Camp Lejeune are known or probable carcinogens. There are mechanistic and human studies evaluating the effect of the chemicals on gene expression and chromosomal abnormalities, and the occurrence of leukemia. It is my opinion that the viewpoint of coherence has also been met.

Experimental Evidence: Bradford Hill also identified experimentation as a viewpoint to evaluate with regards to causation. Put simply, conduct experiments whereby you either purposely expose individuals to a toxin (such as TCE, PCE, benzene, and vinyl chloride), or you eliminate such an exposure and determine the effect on adverse health outcome occurrence. Clearly one cannot ethically subject individuals for any significant length of time to these chemicals by any method of exposure. However, there are decades of epidemiologic research which demonstrate that the Camp Lejeune water contamination chemicals cause cancer, and specifically leukemia. Therefore, it is my opinion that the experimentation viewpoint has also been met.

Analogy: With analogy, Bradford Hill meant to say that when there is strong evidence of an exposure-disease dyad, one should be more inclined to accept causation with a similar exposure and/or disease. There is ample scientific evidence of chlorinated solvents (and benzene) causing various cancers, and specifically causing leukemia. With the wide range and varied adverse effects (including carcinogenesis) of the chlorinated solvents and benzene, it is my opinion that the analogy viewpoint has also been met.

When the body of research on TVOC exposure is considered in light of the Bradford Hill viewpoints, it is my opinion that exposure to these chemicals as TVOC causes leukemia. However, it is also important to note that the Bradford Hill viewpoints were not intended to be rigid guidelines or a checklist that must be completed in order to determine causation. Rather, they are suggested guidelines to consider when determining causation.

XXI. BRADFORD HILL ANALYSIS – TVOC AND NHL

I generally followed the weight of the evidence approach to investigating and analyzing the data on TVOC exposure and adverse health effects in the Camp Lejeune cohort, and NHL specifically. However, I have also evaluated adverse health effects and water through consideration of the Bradford Hill viewpoints.

Strength of association is demonstrated by statistical significance. That is, an odds ratio for the occurrence of an adverse health effect in those exposed to the contaminated Camp Lejeune water of greater than 1.1. under the as likely as not standard. It should be noted that statistical significance is not itself determinative of causation; rather, it helps to explain the likelihood one would see a disease in a given population versus a control group. Therefore, studies with confidence intervals that include 1.0 do not establish that an agent does not cause a given disease, but rather that the subject disease may not be more prevalent in the exposed group than in a control group. Studies of Camp Lejeune personnel as well studies of occupational exposure and other environmental pollution, reliably demonstrate risks of greater than 1.1 for exposure to TVOC and NHL. For instance, Miligi *et al.* found that individuals with medium/high levels of exposure to benzene, had an increased risk of NHL, with odds ratio of 1.6 (95% CI 1.0-2.4). [Miligi L. Epidemiol 2006;17:552-61] Similarly, Cocco *et al.* reported that exposure to benzene and other solvents was associated with an increased risk of B-cell NHL, particularly CLL and follicular lymphoma (Cocco 2013).

Consistency: The Bradford Hill term of consistency refers to the concept that studies done in different populations or that studies of different designs (for instance, cohort studies and case-control tests) yield similar results. This viewpoint is also met in that human studies utilizing varied methods reliably demonstrate an increased risk of NHL after exposure to the water contaminants found at Camp Lejeune.

Specificity: Specificity in Bradford Hill's time meant that an exposure causes a single disease without any other likely explanation other than the exposure under consideration. However, we now know that a particular exposure may cause more than one disease state. For instance, it is known that the water contaminants from Camp Lejeune are known to cause several cancers and other adverse health effects. Therefore, the specificity viewpoint is difficult to meet with TVOCs.

Temporality: Temporality is the easiest of the Bradford Hill viewpoints to understand, and the one viewpoint that must be met. Simply put, the exposure must precede the development of the disease. This viewpoint is also met in the issue at hand with regards to the Camp Lejeune water contamination.

Biological Gradient: The concept of a biological gradient is that a dose-response exists. That is, that the greater a dose (i.e., exposure), the more likely a response (i.e., presence of disease). However, we now know that complex dose-response relationships can occur (e.g.: hormesis) and that dose-response relationships are not all (or necessarily) linear. Further complicating the dose-response relationship is that amongst the exposed people at Camp Lejeune there were children as well as adults. It is unknown the degree to which children have altered absorption or kinetics of the contaminants, particularly when one considers the three different mechanisms of chemical absorption at Camp Lejeune. While granular dose-response data of TVOCs are not available for the Camp Lejeune cohorts, data from other studies do provide evidence of a positive dose-response for exposure to the chemicals at Camp Lejeune and the occurrence of NHL. For example, Wang *et al.* conducted a population-based case-control study among Connecticut women, finding that increased risk of NHL was associated with higher levels of occupational exposure to organic solvents. Specifically, they observed a significant increase in NHL risk with increasing average intensity, average probability, cumulative intensity, and cumulative probability levels of organic solvent exposure. [Wang R. Am J Epidemiol 2009;169:176-85]

Plausibility: Biologic plausibility refers to the concept that a relationship between an exposure and an adverse health outcome can be attributed to causation based on existing biomedical and epidemiological knowledge. In the above report, some of the research into the mechanism of action and varied outcomes after TCE, PCE, and benzene exposures were detailed. Mechanistic studies have shown that TCE exposure is associated with declines in lymphocyte subsets and markers of B-cell activation, which are biologically plausible mechanisms for NHL development [Lan Q. Carcinogenesis 2010;31:1592-6]. Furthermore, there have been several epidemiological studies which demonstrate the increase in NHL risk with TCE, PCE, and benzene exposure. Given this abundant evidence, it is my opinion that the biologic plausibility standard has been met with regards to exposure and NHL.

Coherence: The Bradford Hill viewpoint of coherence is very similar to biological plausibility. That is, that "the cause-and-effect interpretation of the data should not seriously conflict with the generally known facts of the natural history and biology of the disease" [Bradford Hill 1965]. The water contaminants at Camp Lejeune are known or probable carcinogens. There are mechanistic and othernstudies evaluating the effect of the chemicals on gene expression and chromosomal abnormalities, and the occurrence of cancer, including NHL. It is my opinion that the viewpoint of coherence has also been met.

Experimental Evidence: Bradford Hill also identified experimentation as a viewpoint to evaluate with regards to causation. Put simply, conduct experiments whereby you either purposely expose individuals to the Camp Lejeune toxins, or you eliminate such an exposure and determine the effect on adverse health outcome occurrence. Clearly one cannot ethically subject individuals for any significant length of time to these chemicals by any method of exposure. However, there are decades of epidemiologic research which demonstrate that the Camp Lejeune water contamination chemicals cause cancer, and specifically that they causes NHL. Therefore, it is my opinion that the experimentation viewpoint has also been met.

Analogy: With analogy, Bradford Hill meant to say that when there is strong evidence of an exposure-disease dyad, one should be more inclined to accept causation with a similar exposure and/or disease. There is ample scientific evidence of chlorinated solvents (including TCE and PCE) and benzene causing various cancers, with TCE, PCE, and benzene specifically causing NHL. With the wide range and varied adverse effects (including carcinogenesis) of the chlorinated and non-chlorinated solvents, it is my opinion that the analogy viewpoint has also been met.

When the body of research on TCE, PCE, and benzene exposure is considered in light of the Bradford Hill viewpoints, it is my opinion that exposure to these chemicals causes NHL. However, it is also important to note that the Bradford Hill viewpoints were not intended to be rigid guidelines or a checklist that must be completed in order to determine causation. Rather, they are suggested guidelines to consider when determining causation.

XXII. CONCLUSION

The water at Camp Lejeune was contaminated for decades with TCE, PCE, vinyl chloride, and benzene. It is my opinion that the TCE, PCE, and benzene water contaminants have been shown to cause adverse health effects, including leukemia and NHL, in occupational studies, environmental studies outside of Camp Lejeune, and specifically in Marines and civilians who were based at Camp Lejeune, especially given the reduced standard at issue in this litigation, an as likely or not standard, or equipoise.

It is also my opinion that the levels of exposure to these chemicals at Camp Lejeune are hazardous to humans, and specifically as likely as not cause leukemia and NHL. Epidemiologic studies of occupational exposure to these chemicals, as well as environmental contamination by these chemicals, provide evidence that the level of exposure to these chemicals on Camp Lejeune were sufficient to cause leukemia and NHL.

Respectfully,

Steven B. Bird, MD

Appendix A

Nov 2024

Steven B. Bird, M.D.

PERSONAL INFORMATION

Address:	Department of Emergency Medicine University of Massachusetts Medical School 55 Lake Avenue North LA-167 Worcester, MA. 01655 USA
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Telephone:	(508) 421-1422
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Fax:	(508) 421-1490
E-mail:	steven.bird@umassmemorial.org

EDUCATION

M.D., *Alpha Omega Alpha* Northwestern University Chicago, Illinois	1991 – 1995
B.S. Biology, *cum laude* Yale University New Haven, Connecticut	1987 – 1991

POST-GRADUATE TRAINING

Fellow in Toxicology University of Massachusetts Medical School Worcester, MA	2002 – 2004
Chief Resident in Emergency Medicine University of Massachusetts Medical School Worcester, MA	2001 – 2002
Resident in Emergency Medicine University of Massachusetts Medical School Worcester, MA	1999 – 2002
US Naval Flight Surgeon Marine Corps Air Station Futenma Okinawa, Japan	1996 – 1999
Resident in Surgery Naval Hospital San Diego San Diego, CA	1995 – 1996

LICENSURE AND BOARD CERTIFICATION

American Board of Emergency Medicine, 2003 and 2013

American Board of Toxicology, 2004 and 2014

Massachusetts Physician License # 205932

ACADEMIC APPOINTMENTS

Professor of Emergency Medicine Department of Emergency Medicine University of Massachusetts Medical School Worcester, MA	3/2016 - current
Associate Professor of Emergency Medicine Department of Emergency Medicine University of Massachusetts Medical School Worcester, MA	1/2010 – 3/2016
Assistant Professor of Emergency Medicine Department of Emergency Medicine University of Massachusetts Medical School Worcester, MA	9/2004 – 1/2010
Instructor of Emergency Medicine Department of Emergency Medicine University of Massachusetts Medical School Worcester, MA	8/2002 – 8/2004

DEPARTMENTAL, SCHOOL, and HOSPITAL APPOINTMENTS

Chief of Medical Toxicology UMassMemorial Health Worcester, MA	3/2024 – current
IT Steering Council UMassMemorial Health Worcester, MA	2/2020 – 11/2024
Space Allocation and Utilization Committee UMass Medical School & UMassMemorial Health Worcester, MA	2/2020 – 2022
Clinician Experience Officer (CXO) UMassMemorial Health Worcester, MA	9/2019 – 11/2024
Medical Center/Medical Group Leadership Team UMassMemorial Health Worcester, MA	9/2019 – 11/2024
Joint Leadership Team UMass Medical School & UMassMemorial Health	9/2019 – 11/2024

Worcester, MA

Chair, Division Director of EMS Search Committee Department of Emergency Medicine University of Massachusetts Medical School Worcester, MA	3/2017 - 1/2018
Comprehensive Stroke Center Director Search Comm. University of Massachusetts Medical School Worcester, MA	8/2016 - 12/2016
Clinician Health and Well-Being Committee Co-Chair University of Massachusetts Medical School Worcester, MA	8/2015 – 11/2024
Dept of Neurosurgery Chair Search Committee University of Massachusetts Medical School Worcester, MA	9/2014 - 6/2016
Dept of EM Clinical Quality Review Committee UMassMemorial Health Worcester, MA	7/2013 - current
Medical Staff President UmassMemorial Health Worcester, MA	7/2013 - 6/2015
Chief Medical Officer Search Committee UMassMemorial Health Worcester, MA	6/2013 - 9/2013
Vice Chair of Education Department of Emergency Medicine University of Massachusetts Medical School Worcester, MA	3/2012 - 9/2019
Chair of Hospital Credentials Committee UMassMemorial Health Worcester, MA	7/2011 - 6/2013
Medical Staff President-Elect UMassMemorial Health Worcester, MA	7/2011 - 6/2013
Assistant Director of Clinical Operations Department of Emergency Medicine University of Massachusetts Medical School Worcester, MA	3/2011 - 11/2013
Program Director for Emergency Medicine Residency University of Massachusetts Medical School Worcester, MA	3/2011 - 8/2019
Medical Staff Executive Committee UMassMemorial Medical Center Worcester, MA	6/2010 – 11/2024

Attending Emergency Physician University of Massachusetts Medical Center Worcester, MA	7/2002 - current
Attending Emergency Physician Marlborough Hospital Marlborough, MA	7/2002 - current
Attending Emergency Physician Clinton Hospital Clinton, MA	7/2002 - current

MEMBERSHIPS AND SOCIETIES

Council of Residency Directors for Emergency Medicine	2011- 2019
American College of Medical Toxicology	2001 - current
Massachusetts College of Emergency Physicians	1999 - current
Society for Academic Emergency Medicine	1998 - current
American College of Emergency Physicians	1998 - current

HONORS AND AWARDS

Outstanding Contribution to Medical Toxicology Research American College of Medical Toxicology	2021
National Leadership Award UMass Department of Emergency Medicine	2019
Emergency Medicine Residency Teaching Award UMass Emergency Medicine Residency	2018
Emergency Medicine Residency Teaching Award UMass Emergency Medicine Residency	2016
Lean Yellow Belt	2015
Best Scientific Presentation American College of Medical Toxicology Annual Meeting	2014
Team Award for Quality Care UMassMemorial Healthcare	2012
Lean White Belt	2012
Best New Speaker Award American College of American Physicians Annual Meeting Perfect audience evaluation score of 100%.	2012

Young Investigator Award 2007
Society for Academic Emergency Medicine

Best Resident Basic Science Presentation 2002
Society for Academic Emergency Medicine

Excellence in Research Award 2002
New England Regional Research Directors

Navy and Marine Corps Achievement Medal 1999

Alpha Omega Alpha 1994

Yale University Richter Fellow 1990

PROFESSIONAL ACTIVITIES

Departmental/Institutional

Division Chief of Medical Toxicology 3/2024 – current
UMassMemorial Health
Worcester, MA

- Responsible for executive direction and execution of 9-person Division of Medical Toxicology and its 4 fellows.

Claims Committee 4/2021 - current
UMassMemorial Health
Worcester, MA

- Member of the Claims Committee of our self-insured captive
- Review all claims and lawsuits brought against UMassMemorial Health and covered individuals
- Evaluate each claim and lawsuit and give recommendations to the Director of Risk Management and the CEO with regards to defense, settlement, or trial, as well as recommend financial limits on any settlement

Clinician Experience Officer (CXO) 9/2019 – 11/2024
UMassMemorial Health, Medical Group, and Medical School
Worcester, MA

- CXO for jointly funded position of the health system, group practice, and medical school. Responsible for all wellness and engagement activities for all physicians, advanced practice providers, residents, and fellows.
- Led efforts that saw our Press Ganey physician engagement at the University Campus climb from the 1st percentile to the 18th percentile.
- Reports directly to hospital president, Dean, and group practice president.
- Member of Medical Center/Medical Group Leadership Team as well as Joint Leadership Team (involving medical school).
- Successfully led to UMass joining the Stanford Physician Wellness Academic Consortium in June 2020.
- Created a cadre of wellness coaches to allow for free wellness coaching for all faculty, residents, and fellows.
- Jointly-led the Caring for the Caregiver efforts during COVID-19 pandemic.

Peer Support Program 6/2016 – 11/2024
UMassMemorial Health
Worcester, MA

- Creator, with the assistance of a competitive grant from risk management, of a peer support network at UMassMemorial Healthcare. The peer support network is a group of 25 physicians trained in providing assistance to physicians facing difficulties related to poor patient outcomes, litigation, and other stressors. The Peer Support Program receives a new referral roughly once every 2 weeks.

Clinician Health and Well-Being Committee 8/2015 – 11/2024
UMassMemorial Health
Worcester, MA

- Selected by System CMO to co-chair the Clinician Health and Well-Being Committee (CHWC). The mission of this committee is to proactively identify, counsel, and refer physicians before an adverse event occurs.

Wellness Committee Chair 4/2015 - current
Department of Emergency Medicine
University of Massachusetts Medical School
Worcester, MA

- Created a wellness committee for our residency and department. Invited national speakers on the topic and facilitated a "Notes Day" (modeled on the process improvement structure of Pixar) to help identify local, institutional, and departmental factors associated with physician burnout. Instituted wellness initiatives within the residency, including a wellness and empathy curriculum.

Vice Chair of Education 3/2012 - 9/2019
Department of Emergency Medicine
University of Massachusetts Medical School
Worcester, MA

- Responsible for all aspects of education within the Department of Emergency Medicine, including undergraduate, graduate, and allied health professional education. The Department has 40 residents in a PGY1-3 residency; 70+ faculty members; 911fellows; and UMass and visiting medical students.

- Oversaw the development and implementation of mandatory UMass medical student class "Emergency Clinical Problem Solving". This class began in May, 2013, and is required for all 125 4th year medical students. Responsible for 4th-year medical student elective in Emergency Medicine. Direct report for 5 physicians and oversees staff of 4 administrative assistants.

President of the Medical Staff 7/2013 - 6/2015
UMassMemorial Health

- Served a two-year term as president of the medical staff. Responsible for review of all new and renewal applications to the medical staff. Coordinated with Chief Medical Officer all institution peer reviews, including the Chief Physician Officer, hospital general counsel, applicable department chairs, and the individual physician in question. As president of the medical staff I also presided over quarterly medical staff meetings, participated in Joint Commission preparation focus groups, and assisted the Chief Medical Officer and Group Practice President as needed.

Clinical Competency Committee 3/2012 – 7/2024
Emergency Medicine Residency

University of Massachusetts Medical School
Worcester, MA

- Responsible for determining the competency and promotion for 36 emergency medicine residents and coordinates decisions with the Graduate Medical Education office.

Chair, Medical Staff Credentialing Committee 7/2011 - 6/2013
UMassMemorial Health

- Served two years as Chair of the Medical Center's credentialing. Reviewed all new and renewal applications to the medical staff. Coordinated with Chief Medical Officer and Department Chairs or Division Chiefs for candidates that are conditionally approved or not recommended for approval.

Assistant Director of Clinical Operations 3/2011 - 12/2013
Department of Emergency Medicine
University of Massachusetts Medical School
Worcester, MA

- Worked closely with the Director of Clinical Operations to strategize long-term vision and processes for the Department's clinical activities. Interviewed all candidates for faculty positions and fellowships. Responsible for the yearly performance evaluations for 5 faculty members.
- Instrumental in the initiation of the Departmental Peer Review Process, a nationally recognized model of peer review and process improvement.

Emergency Medicine Residency Curriculum Committee 2011 - current
University of Massachusetts Medical School
Worcester, MA

- Responsible for overhaul of entire 18-month emergency medicine residency curriculum.

Peer Review Committee 2011 - current
Department of Emergency Medicine
University of Massachusetts Medical School

- A nationally recognized peer review process whose monthly meeting of approximately 12 individuals confidentially and anonymously reviews concerns of care. Feedback delivered to individual practitioners and findings presented at weekly departmental Morbidity and Mortality conference.

Medical Staff Executive Committee 2010 – 11/2024
UMass Memorial Medical Center
Worcester, MA

- Executive committee of the medical staff. Reviews and approves all hospital policies. Responsible for approval of medical staff privileges and recommending/monitoring physicians' compliance with Physician Health Services as needed.

Research Committee 2003 - current
Department of Emergency Medicine
University of Massachusetts Medical School
Worcester, MA

- Committee charged with providing guidance and vision for Departmental research; reviewing internal and extramural proposals; and awarding internal funding.

Emergency Medicine Residency Selection Committee 2002 - 2023
University of Massachusetts Medical School
Worcester, MA

- 21 years of service on committee that reviews, interviews, and ranks medical students applying to UMass for emergency medicine through the NRMP Match. Chair of this committee from 2011-2019.

Chair of Physician Incentive Compensation Committee 2006 - 2011
Department of Emergency Medicine
UMassMemorial Health
Worcester, MA

- Responsible for the development and growth of the emergency medicine physician incentive compensation plan. Grew this plan from a total of $70,000 per year in 2005 to over $1.1 million in 2011 (and now up to nearly $2 million). Responsible for determination of incentive plan metrics, monitoring performance of those metrics across 70+ faculty, and yearly reporting of the metrics.

Procedural Sedation Committee 2004 - 2010
UMassMemorial Health
Worcester, MA

- Committee responsible for writing institutional policies regarding procedural sedation. Also responsible for reviewing quality data and any adverse events related to procedural sedation for the hospital and clinics.

National

Board of Directors – Immediate-Past President 5/2019 – 5/2020
Society for Academic Emergency Medicine

- Immediate-Past President of the 6700-member Society for Academic Emergency Medicine. Responsible for guiding the 9-member Board of Directors on overall strategic plan for the organization, as well as guiding a $4.5 million budget.

Board of Directors – President 5/2018 - 5/2019
Society for Academic Emergency Medicine

- President of the 6700-member Society for Academic Emergency Medicine. Responsible for guiding the 9-member Board of Directors on overall strategic plan for the organization, as well as guiding a $4.5 million budget.

Board of Directors – President-Elect 5/2017 - 5/2018
Society for Academic Emergency Medicine

- Elected to the President-Elect role of SAEM in March 2017. Will assume role of President in May 2018.

AAMC Standardized Video Interview Workgroup 1/2017 - 8/2019

- Member of workgroup convened by the AAMC to define rubric for scoring of the Standardized Video Interview (SVI) project. Furthermore, we analyzed interim data from a trial of the SVI and have informed the AAMC on methods to improve the SVI, as well as creating a research agenda around the SVI.

National Academy of Medicine (NAM) 1/2017 – 8/2024
Clinician Well-Being Action Collaborative

- I represent the field of emergency medicine on this national collaborative involving the entire house of medicine. The mission of the NAM Clinician Well-Being Action Collaborative (chaired by Drs. Victor Zhou, Thomas Nasca, and Darrel Kirch) is to create a body of knowledge, research agenda, and implementation science to mitigate burnout amongst physicians, promote wellness, and return joy to the practice of medicine. I am one of just 3 emergency physicians involved in this national effort.

Board of Directors – Secretary-Treasurer 5/2016 – 5/2017
Society for Academic Emergency Medicine

- Member of the Board of Directors. Responsible for financial oversight of the largest academic emergency medicine society in the U.S., with annual budget of over $4 million. Participate in the strategic direction of the Society.

Board of Directors 2011 - 2013 & 2016 - 2019
Emergency Medicine Foundation

- Member of the Board of Directors of the EMF, a 501c3 research funding organization affiliated with the American College of Emergency Physicians. Responsible for directing areas of research focus as well as fund raising and approving grant funding of approximately $1 million per year.

Board of Directors 5/2014 – 5/2020
Society for Academic Emergency Medicine Foundation

- Member of the Board of Directors of the SAEM Foundation, a 501c3 research funding organization with a corpus of over $11 million. Responsible for directing areas of research focus as well as fund raising.

Board of Directors (member-at-large) 5/2014 - 5/2016
Society for Academic Emergency Medicine

- Member of the Board of Directors. Responsible for oversight and providing strategic direction for the largest academic emergency medicine society in the U.S.

Search Committee 10/2014 - 5/2015
CEO of the Society for Academic Emergency Medicine

  - Member of 10-person search committee for new CEO of the Society for Academic Emergency Medicine. Resulted in the hiring of CEO Megan Schagrin.

Search Committee 9/2014 - 7/2015
Academic Emergency Medicine Editor-in-Chief

  - Member of 6-person search committee for new Editor-in-Chief of Academic Emergency Medicine.

NIH Special Emphasis Panel Review Member 2012 - 2016

  - Serves as review for NIH panel ZRG1 MDCN-B

Finance Committee 2011 - 2013

American College of Emergency Physicians

- Committee responsible for generating and approving ACEP's yearly budget of roughly $22 million. Interacted directly with ACEP's Executive Director, CFO, and Board of Directors.

Annual Meeting Program Committee 2008 - 2014
Society for Academic Emergency Medicine

- Co-chair of scientific subcommittee. Responsible for coordinating reviewers and reviewing more than 1,200 abstracts to the SAEM annual meeting. Responsible for organization of the entire scientific aspects of the meeting (determining oral presentations, poster presentations, assigning moderators, meeting room assignments at host hotels, etc.

Grants Committee 2004 - 2014
Society for Academic Emergency Medicine

- Responsible for reviewing grant applications to SAEM. Served as chair of the Institutional Research Training Grant category in 2010, the Education Research Grant in 2011, and the Spadafora Medical Toxicology Grant in 2012. Made recommendations for funding to the SAEM Board of Directors for grants totaling approximately $400,000/year.

Scientific Review Committee 2003 - 2011
American College of Emergency Physicians

- Responsible for reviewing grant applications to Emergency Medicine Foundation. Made recommendations for funding to the EMF Board of Directors for grants totaling more than $1,000,000/year.

Research Committee 2003 - 2004
Society for Academic Emergency Medicine

International

Southeast Asia Toxicology Research Consortium 2004 – 2019

Scholarly

Editorial Board 2019 - current
The Journal of Wellness

Editorial Board 2009 - current
Academic Emergency Medicine

Editorial Board 2009 - 2013
The Open Toxinology Journal

Editorial Board – founding member 2005 - 2011
Journal of Medical Toxicology

Manuscript reviewer for *JAMA; Academic Emergency Medicine; Annals of Emergency Medicine; Pediatrics; Journal of Emergency Medicine; Journal of Medical Toxicology; Clinical Toxicology; The Open Toxinology Journal; PLoS One*

Invited Attendance

Extracorporeal Removal of Toxins in Poisoning (ExTRIP) working group
Montreal, Canada, October 2019

American College of Medical Toxicology Chemical Agents of Opportunity symposium
Nashville, TN, May 2019

12th International Symposium on Protection Against Chemical Warfare Agents
Munich, Germany, April 2019

Western Regional SAEM Conference, Napa, CA, March 2019

NINDS CounterACT meeting, Boston, MA, June 2017

10th International Symposium on Protection Against Chemical Warfare Agents
Munich, Germany, April 2017

NINDS CounterACT meeting, Davis, CA, June 2016

NINDS CounterACT meeting, New York, NY, June 2015

NINDS CounterACT meeting, Denver, CO, June 2014

13th Congress of APAMT, Shenyang, China, September 2014

NIH Workshop on Neurologic Effects of Nerve Agents, Bethesda, MD, February 2014

NY Chapter of the American College of Emergency Physicians, Lake George, NY, July 2013

NINDS CounterACT meeting, Bethesda, MD June 2013

NINDS CounterACT meeting, San Francisco, CA June 2012

11th National Congress of the Iranian Society of Toxicology, Mashad, Iran, August 2011

5th Congress of APAMT, Colombo, Sri Lanka, August 2006

8th International Symposium on Protection Against Chemical Warfare Agents
Munich, Germany, May 2004

SIGNIFICANT MENTORING

Sneha Shah, MD	AMA Women's Section Award	2014
John Haran, MD	SAEM Research Training Grant	2014-2015
Chad Darling, MD	K23 from NHLBI	2010-2015

Romolo Gaspari, MD K08 from NINDS 2007-2012

COMMUNITY ACTIVITIES

St. John's High School Gala – Planning committee 2018 - 2020

- Assisted in securing sponsorships and auction items, selling tables, and planning the annual St. John's High School Galal. This event raised more than $250,000.

Yale Alumni Schools Committee – Central Mass 2009-2012

- Responsible for coordinating, assigning, and reviewing approximately 40 Yale alumni interviews of applicants to Yale University.

Spring Street School Chess Club 2009-2014

- Organized, coached, and facilitated the chess club for Spring Street School in Shrewsbury, Massachusetts, for grades 1-4. Increased participation in this chess club to nearly 40% of students in the school, creating the largest elementary chess club in New England.

Central Mass Heart Ball – Planning committee 2010 & 2011

- Responsible for securing sponsorships and auction items, selling tables, and planning the annual American Heart Association Ball. This event raises more than $300,000 annually.

TEACHING RESPONSIBILITIES

Grand Rounds/Invited Lectures
University of Vermont Grand Rounds. "Chest Pain Testing in the ED" December 11, 2017, Burlington, VT.

University of West Virginia Grand Rounds. "Rationale Testing in the ED" August 24, 2017, Morgantown, WV.

Society for Academic Emergency Medicine Annual Meeting, "Before Taking Care of Others You Must Take Care of Yourself" May 2017, Orlando, FL

Society for Academic Emergency Medicine Annual Meeting, "Accepting Risk and the Myth of Zero" May 2017, Orlando, FL

Falmouth Hospital Emergency Care Conference, "Emerging Drugs of Abuse and Testing Conundrums" March 2017, Falmouth, MA

University of Vermont Larner School of Medicine, Emergency Medicine Update, "Visual Toxicology". February 2017, Stowe, VT

University of Vermont Larner School of Medicine, Emergency Medicine Update, "Pattern Recognition in Toxicology". February 2017, Stowe, VT

North American Congress of Clinical Toxicology, "Neurotoxicology of Organophosphorus Pesticides". October 2016, Boston, MA

Controversies and Consensus in Emergency Medicine conference, "Safely Decreasing Stress Testing from the Emergency Department". September 2016, Northampton, MA

Society for Academic Emergency Medicine Annual Meeting, “Accepting Risk and the Myth of Zero” May 2016, New Orleans, LA

Society for Academic Emergency Medicine Annual Meeting, “Metacognition: How Physicians Think” May 2016, New Orleans, LA

Boston Medical Center faculty retreat, “Wellness, Resiliency, and Empathy”, April 2016, Newport, RI

American College of Emergency Physicians Annual Meeting, “Beyond the Bends” October 2015, Boston, MA

American College of Emergency Physicians Annual Meeting, “Dangerous Drug Interactions” October 2015, Boston, MA

American College of Emergency Physicians Annual Meeting, “Nature’s Deadliest Creatures” October 2015, Boston, MA

ACEP Toxicology Interest Group, “From Benchtop to Sri Lanka: One Toxicologists Journey” October 2015, Boston MA

Society for Academic Emergency Medicine Annual Meeting, “Do Your Patients Know You Care? Methods to Convey Empathy” May 2015, San Diego, CA

American College of Emergency Physicians Annual Meeting, “Dangerous Drug Interactions” October 2014, Chicago, IL

American College of Emergency Physicians Annual Meeting, “Environmental Emergencies” October 2014, Chicago, IL

Rhode Island Hospital/Brown University. “How Physicians Think” September 2014, Providence, RI.

Asia Pacific Association of Medical Toxicology, “Translational Therapies for Acute Organophosphorus Inhibitor Poisoning” September 2014, Shenyang, China.

Sapporo Medical University, “Novel Therapies for Acetylcholinesterase Inhibitor Poisoning” September 2014, Sapporo, Japan.

Society for Academic Emergency Medicine Annual Meeting, “Metacognition: Thinking About How You Think” May 2014, Dallas, TX

American College of Emergency Physicians Annual Meeting, “Dangerous Drug Interactions That Can Kill Your Patients” October 2013, Seattle, WA

American College of Emergency Physicians Annual Meeting, “Cutting-Edge Ideas in Toxicology” October 2013, Seattle, WA

Albany Medical College Department of Emergency Medicine, “How to Give a Presentation” August 2013, Albany, NY

Boston Medical Center Department of Emergency Medicine. “Metacognition” August 2013, Boston, MA

New York chapter of the American College of Emergency Physicians: “New and Emerging Drugs of Abuse” July 2013, Lake George, NY

New York chapter of the American College of Emergency Physicians: "Drug-Drug Interactions in the Emergency Department" July 2013, Lake George, NY

American College of Emergency Physicians Annual Meeting: "What Goes Down, Must Come Up: Diving Medical Emergencies" October 2011, San Francisco, CA

American College of Emergency Physicians Annual Meeting: "Marine Envenomations" October 2011, San Francisco, CA

North Country Hospital: "Pattern Recognition in Adverse Drug Events" February 2011, Newport, Vermont

Washington University School of Medicine: ""Translational Research in Emergency" September 2010, St. Louis, MO

University of Massachusetts Medical School: "Translational Research in Emergency Medicine and Building an Academic Career" July 2009 Worcester, MA

Children's Hospital Boston - Pediatric Emergency Medicine and Massachusetts Poison Control Center; "Acetylcholinesterase Inhibitors" May 2008, Boston, MA

University of Iowa, Department of Emergency Medicine. "Organophosphates and Chemical Nerve Agents." November 2005, Iowa City, IA

University of Iowa, Department of Emergency Medicine. "Antidepressant Poisoning." April 2006, Iowa City, IA

University of Iowa, Department of Emergency Medicine. "Pattern Recognition in Toxicology." April 2006, Iowa City, IA

University of Massachusetts Medical School: "Translational Research in Emergency Medicine: from Benchtop to Sri Lanka" June 2007 Worcester, MA

Brigham and Women's Hospital, Division of Emergency Medicine: "Cardiovascular Poisonings" May 2006, Boston, MA

Center for Disease Control and Prevention. Agency for Toxic Substances and Disease Registry. "Agents of Opportunity: Toxic Gases"
March 2005, Hartford, CT

Brigham and Women's Hospital, Division of Emergency Medicine: "Procedures in Toxicology" February 2005, Boston, MA

Baystate Medicine Center, Department of Emergency Medicine "Poison Control Center Functions" March 2004, Springfield, MA

Portsmouth Naval Medical Center: "Pattern Recognition in Toxicology"
March 2003, Portsmouth, VA

Harvard School of Public Health: "Neurotoxicology"
October 2003, Boston, MA

Classroom Lectures (selected)
University of Massachusetts Emergency Medicine Residency: "Toxicology In-Service Review" February 2016, Worcester, MA

University of Massachusetts Emergency Medicine Residency: "How to Give a Presentation"

August 2015, Worcester, MA

University of Massachusetts Emergency Medicine Residency: "Toxicology In-Service Review" February 2015, Worcester, MA

University of Massachusetts Emergency Medicine Residency: "Metacognition"
June 2013, Worcester, MA

University of Massachusetts Emergency Medicine Residency: "Toxicology In-Service Review" February 2013, Worcester, MA

University of Massachusetts Emergency Medicine Residency: "Dysbarism"
Sept 2012, Worcester, MA

University of Massachusetts Emergency Medicine Residency: "Impact Factor and Bibliometric Indices"
July 2012, Worcester, MA

University of Massachusetts Emergency Medicine Residency: "How to Give a Presentation"
Sept 2011, Worcester, MA

University of Massachusetts Emergency Medicine Residency: "Pattern Recognition in Toxicology"
July 2011, Worcester, MA

University of Massachusetts Emergency Medicine Residency: "Ethanol Forensics"
Apr 2011, Worcester, MA

University of Massachusetts Emergency Medicine Residency: "Acetaminophen Toxicity"
Aug 2007, Worcester, MA

University of Massachusetts Emergency Medicine Residency: "Endocrine Emergencies"
Feb 2007, Worcester, MA

University of Massachusetts Emergency Medicine Residency: "Pattern Recognition in Toxicology"
July 2006, Worcester, MA

University of Massachusetts Emergency Medicine Residency: "Toxic Alcohols"
April 2004, Worcester, MA

University of Massachusetts Emergency Medicine Residency: "Central Venous Access"
August 2003, Worcester, MA

University of Massachusetts Emergency Medicine Residency: "Introduction to the Poisoned Patient"
July 2003, Worcester, MA

Massachusetts College of Pharmacy: "Summertime Poisonings"
July 2003, Worcester, MA

Massachusetts College of Pharmacy: "Introduction to the Poisoned Patient"
May 2003, Worcester, MA

Emergency Medical Services: "A Trip Through the Medicine Cabinet"
December 2002, Williamstown, MA

University of Massachusetts Emergency Medicine Residency: "Acetaminophen"
August 2002, Worcester, MA

University of Massachusetts Emergency Medicine Residency: "Anti-hypertensive Poisonings"
January 2002, Worcester, MA

Clinical Teaching and Supervision
Responsible for all aspects of training for 36 emergency medicine residents

Oversees residents and medical students approximately 50 hours/month in the emergency department

Oversees 3 medical toxicology fellows and one emergency medicine resident per month on the toxicology consultation service

Participates in weekly toxicology conference for residents, fellows, and pharmacists

PAPERS IN PEER-REVIEWED JOURNALS

1. S Howard-Wilson, J Ching, S Gentile, M Ho . . . **Bird SB** et al. Efficacy of a Multimodal Digital Behavior Change Intervention on Lifestyle Behavior, Cardiometabolic Biomarkers, and Medical Expenditure: Protocol for a Randomized Controlled Trial. JMIR Research Protocols 13 (1), e50378

2. Ligibel JA, Goularte N, Berliner JI, **Bird SB**, Brazeau CMLR, Rowe SG, Stewart MT, Trockel MT. Well-being parameters and intention to leave current institution among academic physicians. *JAMA Open Network* 2023; 6: e2347894-e2347894

3. Ghannoum G, Gosselin S, Hoffman RS et al. Extracorporeal treatment for ethylene glycol poisoning: systematic review and recommendations from the EXTRIP workgroup. *Critical Care* 2023;27:56.

4. Lu D, Lee J, Alvarez A, Sakamoto J, **Bird SB**, Vandana S, Laa M, Nordenholz M, Manfredi R, Blomkalns Factors Driving Burnout and Professional Fulfillment Among Emergency Medicine Residents: A National Wellness Survey. *Acad Emerg Med Ed Training* 2022; 6:S5-S12.

5. Bouchard J, Yates C, Calello DP et al. Extracorporeal Treatment for Gabapentin and Pregabalin Poisoning: Systematic Review and Recommendations From the EXTRIP Workgroup. *Am J Kid Dis*. 2022;79: 88-104.

6. Lu D, Lee J, Alvarez A, Sakamoto J, **Bird SB**, Vandana S, Laa M, Nordenholz M, Manfredi R, Blomkalns A. Drivers of Professional Fulfillment and Burnout Among Emergency Medicine Faculty: A National Wellness Survey by the Society for Academic Emergency Medicine. *Acad Emerg Med* 2022; published online March 19, 2022. ttps://doi.org/10.1111/acem.14487

7. Ghannoum G, Berling I, Lavergne V et al. Recommendations from the EXTRIP workgroup on extracorporeal treatment for baclofen poisoning. *Kid Interl* 2021;100:720-36.

8. Brower KJ, Brazeau CMLR, Kiely SC, et al. The Evolving Role of the Chief Wellness Officer in the Management of Crises by Health Care Systems: Lessons from the Covid-19 Pandemic. *NEJM Catalyst*. 2021; 5. DOI:https://doi.org/10.1056/CAT.20.0612.

9. Bouchard J, Shepherd G, Hoffman RS, et al. Extracorporeal treatment for poisoning to beta-adrenergic antagonists: systematic review and recommendations from the EXTRIP workgroup. *Crit Care* 2021;25**:** 201-. https://doi.org/10.1186/s13054-021-03585-7.

10. Wong A. Hoffman RS, Walsh SJ, et al. Extracorporeal treatment for calcium channel blocker poisoning: systematic review and recommendations from the EXTRIP workgroup. *Clin Toxicol* 2021;59: 361-375.

11. Mowry JB, Shepherd G, Hoffman RS, et al. Extracorporeal Treatments for Isoniazid Poisoning: Systematic Review and Recommendations from the EXTRIP Workgroup. *Pharmacotherapy* 2021; 00:1-16.

12. Berling I, King JD, Shepherd G, et al. Extracorporeal Treatment for Chloroquine, Hydroxychloroquine, and Quinine Poisoning: Systematic Review and Recommendations from the EXTRIP Workgroup. *J Am Soc Nephrol* 2020 Oct;31(10):2475-2489. doi: 10.1681/ASN.2020050564

13. Nordenholz KE, Alvarez A, Lall MD, **Bird S**, Blomkalns AL. Optimizing Wellness in Academic Emergency Medicine. *J Wellness* 2020. DOI: 10.18297/jwellness/vol2/iss2/8

14. Gallahue FE, Deiorio NM, Blomkalns A, **Bird SB**, et al. The AAMC Standardized Video Interview – Lessons Learned from the Residency Selection Process. *Acad Med* 2020. doi: 10.1097/ACM.000000000000357

15. Melnyk BM, Kelly SA, Stephens J . . . **Bird SB**. Interventions to Improve Mental Health, Well-Being, Physical Health, and Lifestyle Behaviors in Physicians and Nurses: A Systematic Review. *Am J Health Prom*, 2020 Nov;34(8):929-941.

16. Greenberger SM, Finnell JT, Chang BP, Garg N, Quinn SM, **Bird SB,** et al. Changes to the ACGME Common Program Requirements and Their Potential Impact on Emergency Medicine Core Faculty Protected Time. *Acad Emerg Med Ed & Training*. Nov 23, 2019. ttps://doi.org/10.1002/aet2.10421

17. **Bird SB**, Hern HG, Blomkalns A et al. Innovation in Residency Selection: The AAMC Standardized Video Interview. *Acad Med*. 2019;94:1489-97. doi:10.1097/ACM.0000000000002705

18. Gallahue FE, Hiller KM, **Bird SB** et al. The AAMC Standardized Video Interview: Reactions and Use by Residency Programs During the 2018 Application Cycle. *Acad Med* 2019;94:1506-12. doi: 10.1097/ACM.0000000000002714

19. Dyrbye LN, Meyers D, Ripp J, Dalal N, **Bird SB**, Sen S. A pragmatic approach for organizations to measure health care professional well-being. *National Acad Medicine*, Oct 2018, pp 1-11.Doi.org/10.31478/201809g

20. Deiorio NM, Jarou ZJ, Alker A, **Bird SB**, et al. Applicant Reactions to the AAMC Standardized Video Interview During the 2018 Application Cycle. *Acad Med* 2019 Oct;94(10):1498-1505. doi: 10.1097/ACM.0000000000002842.

21. Jarou Z, Karl E, Alker A, **Bird SB**, et al. Factors Affecting Standardized Video Interview Performance: Preparation Elements and the Testing Environment. *EM Resident*, April 17, 2018.

22. **Bird SB**, Blaomkalns A, Deiorio NM, Gallague FE. Beyond test scores and medical knowledge: the standardized video interview, an innovative and ethical approach for holistic assessment of applicants. *Acad Med* 2018;93:151.

23. **Bird S**, Blomkalns A, Deiorio NM, Gallague FE et al. Stepping up to the plate: emergency medicine takes a swing at enhancing the residency selection process. *AEM Ed & Training* 2017;2: 61-5. Doi: 10.1002/aet2.10068.

24. Shah S, Church R, Butler M, **Bird SB**. Assessment of emergency medicine faculty milestone competencies. *Intl J Ed Res Tech* 2017; 8 (2): 1-7.

25. **Bird SB**. Neurologic and pregnancy effects of carbon monoxide exposure. *Toxicol Open Access*. 2017, 3:4. Doi: 10.4172/2476-2067.

26. Bunya N, Sawamoto K, Benoit H, **Bird SB**. The Effect of Parathion on Red Blood Cell Acetylcholinesterase in the Wistar Rat. *J Toxicol* 2016. doi.org/10.1155/2016/4576952

27. **Bird SB**, Krajacic P, Sawamoto K, Bunya N, Loro E, Khurana TS. Pharmacotherapy to protect the neuromuscular junction after acute organophosphate poisoning. *Proc Ann NY Acad Sci* 2016; 1674:86-93.

28. Marin JR, Lewiss RE, Shook JE, et al. Point-of-care ultrasonography by Pediatric Emergency medicine physicians. *Pediatrics* 2015;135:e1113-22.

29. Temple C, Gaspari R, **Bird S**. Caffeine reduces organophosphate induced respiratory failure; effect of caffeine on dichlorvos induced central respiratory failure in a rat model *Curr Topic Toxicol* 2015; 11, 15 – 21.

30. Reznek MA, Kotkowski KA, Arce MW, Jepson ZK, **Bird SB**, Darling CE. Patient safety incident capture resulting from incident reports: a comparative observational analysis. *BMC Emergency Medicine* 2015, **15**:6 doi:10.1186/s12873-015-0032-7.

31. Broach J, Krupa R, **Bird SB**, Manuell M. Regional preparedness for mass acetylcholinesterase inhibitor poisoning through plans for stockpiling and interhospital sharing of pralidoxime. *Am J Disaster Med*. 2014:9;4, 1-9. Doi:10.5055/ajdm.2014.0000

32. Jepson ZK,Darling CE, Kotkowski KA, **Bird SB**, Arce MA, Volturo GA, Reznek MA. Emergency department patient safety incident characterization: an observational analysis of the findings of a standardized peer review process. *BMC Emergency Medicine* 2014,14:20-27.DOI:101186/1471-227X-14-20

33. Neavyn MJ, Blohm E, Babu KM, **Bird SB**. Medical marijuana and driving. *J Med Toxicol*. 2014; available online March 2014. DOI 10.1007/s13181-014-0393-4.

34. Jackson CJ, Carville A, Ward J, Mansfield K, Ollis DL, Khurana T, **Bird SB**. Use of OpdA, an Organophosphorus (OP) hydrolase, prevents lethalilty in an african green monkey model of acute OP poisoning. *Toxicol* 2014;317:1-5. doi: 10.1016/j.tox.2014.01.003

35. Sawamoto K, **Bird SB**, Katayama Y, Uemura S, Tanno K, Narimatsu E. Outcome from severe accidental hypothermia with cardiac arrest resuscitated with extracorporeal cardiopulmonary resuscitation. *Am J Emerg Med* 2014; 32(4):320-4. doi: 10.1016/j.ajem.2013.12.023.

36. Neavyn MJ, Boyer EW, **Bird SB**, Babu KM. Sodium acetate as a replacement for sodium bicarbonate in medical toxicology. *J Med Toxicol*. 2013 Sep; 9(3):250-4 doi: 10.1007/s13181-013-0304-0.

37. Darling CE, Smith CS, Sun JE, Klauke CG, Lerner J, Cyr J, Paige P, Paige PG, **Bird SB**. Cost reductions associated with a quality improvement initiative for patients with ST-elevation myocardial infarction. *Jt Comm J Qual Patient Saf*. 2013;39:16-21. PMID 23367648

38. Dunn C, **Bird S**, Gaspari R. Intralipid Fat emulsion decreases respiratory failure in a rat model of parathion poisoning. *Acad Emerg Med*. 2012;19:504-509.

39. Rosenbaum C, **Bird SB**. Non-muscarinic targets of organophosphorus pesticides. *J Med Toxicol* 2010 Dec;6(4):408-12.

40. Jackson CJ, Scott C, Carville A, Mansfield K, Ollis DL, **Bird SB**. Pharmacokinetics of OpdA, an organophosphorus hydrolase, in the African green monkey. *Biochem Pharmacol* 2010;80:1075-9.

41. Gresham C, Rosenbaum C, Gaspari R, Jackson CJ, **Bird SB**. "Kinetics and efficacy of an organophosphorus hydrolase in a rodent model of methyl-parathion poisoning. *Acad Emerg Med* 2010; 17:736-740.

42. **Bird SB**, Dawson A, Ollis D. "Enzymes and bioscavengers for prophylaxis and treatment of organophosphate poisoning" *Front Biosci* 2010; S2:209-220.

43. Rosenbaum CR, Church R, **Bird SB**. "Timing and frequency of physostigmine redosing for antimuscarinic toxicity" *J Med Toxicol* Published online April 20, 2010. DOI 10.1007/s13181-010-0077-7

44. Weibrecht K, Dayno M, Darling C, **Bird SB**. ""Liver aminotransferases are elevated with rhabdomyolysis in the absence of liver injury" *J Med Toxicol.* Published online April 21, 2010. DOI 10.s131181-010-0075-9

45. **Bird S,** Sutherland T, Gresham C, Oakeshott J, Eddleston M. "OpdA, a recombinant bacterial organophosphorus hydrolase, prevents lethality in rats after poisoning with highly toxic organophosphours pesticides" *Toxicol* 2008;247: 88-92.

46. **Bird SB**. "Impact factors, H indices, and citation analyses in toxicology Journals" *J Med Toxicol* 2008;4: 261-274.

47. **Bird S,** Sivilotti M. "Self-plagiarism, textual reuse, and the intent to mislead." *J Med Toxicol* 2008;4: 69-70.

48. Young K, **Bird S**, et al. "Productivity and career paths of previous recipients of SAEM research grant awards" *Acad Emerg Med* 2008; 15: 560-566.

49. Ali F, Boyer E, **Bird S**. "Estimated risk of hepatotoxicity after an acute acetaminophen overdose in alcoholics" *Alcohol* 2008;42: 213-218.

50. Kent K, Ganetsky M, Cohen J **Bird S**. "Non-fatal ventricular dysrhythmias associated with severe salicylate toxicity" *Clin Toxicol* 2008; 46: 297-299.

51. **Bird SB**, Rosenbaum CR. "Onset of symptoms after methadone overdose." Am J Emerg Med. 2008;26: 242.

52. Miller M, Navarro M, **Bird S**, Donovan J. "Antiemetic use in acetaminophen poisoning: how does the route of N-acetylcysteine administration affect utilization?" *J Med Toxicol* 2007; 3: 152-156.

53. Sivilotti MLA, **Bird SB**, Lo JCY, Dickson EW. "Multiple centrally-acting antidotes protect against severe organophosphate toxicity" *Acad Emerg Med* 2006; 13: 359-364.

54. **Bird SB**, Lane DR. "House officer procedure documentation using a personal digital assistant: a longitudinal study" *BMC Medical Informatics and Decision Making* 2006; 6.

55. Weizberg M. Su M. Mazzola JL. **Bird SB**. Brush DE. Boyer EW. "Altered mental status from olanzapine overdose treated with physostigmine" *Clin Toxicol.* 44(3):319-25, 2006.

56. Babu KM, McCormick M, **Bird S**. "Pediatric dietary supplement use – an update. *Clin Ped Emerg Med* 2005; 6: 85-92.

57. Mazzola JL, **Bird SB**, Brush DE, Aaron CK, Boyer EW. "Levofloxacin-related seizure activity in a patient with Alzheimer's disease: assessment of potential risk factors" *Clin Psychopharm* 2005;25:287-288.

58. Brush DE, **Bird SB**, Boyer EW. "γ-Hydroxybutyrate use in older adults." *Ann Intern Med* 2004; 140:W70-71.

59. DE Brush, **SB Bird**, EW Boyer. "Monoamine oxidase inhibitor poisoning resulting from internet misinformation on illicit substances." *J Tox Clin Tox* 2004;42:191.

60. **Bird SB,** Boyer EW. "The pharmacology and toxicology of ranolazine: a new metabolic modulator" *IJMT* 2003;6.

61. Dickson EW, **Bird SB**, Gaspari R., Boyer E, Ferris C. "Diazepam attenuates central respiratory depression due to organophosphate poisoning". *Acad Emerg Med* 2003;10:1303-1306.

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TEXTBOOK EDITOR

Irwin and Rippe's Intensive Care Medicine. "Pharmacology, Overdoses and Poisonings" Toxicology section editor. Lippincott. 9th Ed.

Irwin and Rippe's Intensive Care Medicine. "Pharmacology, Overdoses and Poisonings" Toxicology section editor. Lippincott. 8th Ed.

Emergency Medicine Research Handbook for Residents and Medical Students. Emergency Medicine Residents' Association. 1st Ed.

Irwin and Rippe's Intensive Care Medicine. "Pharmacology, Overdoses and Poisonings" Toxicology section editor. Lippincott. 7th Ed.

Aghababian's Emergency Medicine: The Core Curriculum. Section editor of 25 chapters. Jones and Bartlett, 2nd Ed.

Irwin and Rippe's Intensive Care Medicine. "Pharmacology, Overdoses and Poisonings" Toxicology section editor. Lippincott. 6th Ed.

Aghababian's Emergency Medicine: The Core Curriculum. Section editor of 25 chapters. Jones and Bartlett, 1st Ed.

TEXTBOOK CHAPTERS

Bird SB. “Acetaminophen Poisoning” *Intensive Care Medicine*. Rippe, and Irwin, Eds. 9th edition.

Bird SB. “Anticonvulsant Poisoning” *Intensive Care Medicine*. Rippe, and Irwin, Eds. 9th edition.

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Bird SB. “Chromium” Goldfrank L. et al., editors. *Goldfrank's Toxicologic Emergencies,* McGraw Hill. 9th edition.

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Bird SB. “Acetaminophen Poisoning” *Intensive Care Medicine*. Rippe, and Irwin, Eds. 6th edition.

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ABSTRACTS (selected presentations at national or international meetings)

1. Bunya N, Benoit H, Krajacic P, Loro E, Gaspari R, Khurana T, **Bird SB**. Pancuronium Improves Survival in a Rat Model of Acute Parathion Poisoning. May 2016, SAEM Annual Meeting, New Orleans, LA

2. Shah SH, **Bird SB**. Do Your Patients Know You Care? SAEM Annual Meeting 2015, San Diego, CA.

3. Bunya N, Benoit H, Krajacic P, Loro E, Gaspari R, Khurana T, **Bird SB**. Development of a rodent model of the Intermediate Syndrome. June 2015, NY Academy of Sciences, NY.

4. Bunya N, Sawamoto K, Benoit H, Gaspari R, Khurana T, **Bird SB**. Novel Neuromuscular Protection to CounterACT Organophosphorus (OP) Poisoning. CounterACT meeting 2014, Denver, CO.

5. Shah SH, Heitmann D, Mangolds V, Zgurzynski P, **Bird SB**. Evaluating the Implementation of an Interprofessional Team STEPPS Curriculum for Medical Students Using High Fidelity Simulation. CORD Annual Meeting 2014, New Orleans, LA.

6. Shah SH, Church R, **Bird SB**. Evaluating Faculty Milestone Competencies. CORD Annual Meeting 2014, New Orleans, LA.

7. Sawamoto K, Krajacic P, McCall J, DeLa Puente R, Ford-Webb T, Gaspari R, Khurana T, **Bird SB**. Novel Neuromuscular Protection to CounterACT Organophosphorus (OP) Poisoning. CounterACT meeting 2012, San Francisco, CA

8. **Bird SB**, Carville A, Mansfield K, Ollis D. Use Of An Organophosphorus Hydrolase Prevents Lethality In An African Green Monkey Model Of Acute Organophosphorus Poisoning. SAEM 2011 Annual Meeting, Boston, MA

9. Sharma K, Nelson L, Kurt K, **Bird S**, Brent J, Wax P. The Practice of Medical Toxicology in the US. NACCT Annual Meeting 2010, Denver, CO.

10. Weibrecht K, Dayno M, Darling C, **Bird S**. Liver aminotransferases are elevated with rhabdomyolysis in the absence of liver injury. NACCT Annual Meeting 2009, San Antonio, TX.

11. Rosenbaum C, **Bird S**. Timing and Frequency of Physostigmine for Anticholinergic Toxicity. NACCT Annual Meeting 2008, Toronto, Canada.

12. Acute Hepatotoxicity Associated with Amiodarone Administration Courtney J, Ganetsky M, **Bird SB**, Boyer EW. Clin Toxicol 2006; 44.

13. Isoniazid-Induced Psychosis in an Adolescent Male Gresham HW, Babu KM, Ali F, **Bird SB**, Boyer EW. Clin Toxicol 2006; 44.

14. Non – Fatal Cardiac Dysrhythimias Associated with Severe Salicylate Toxicity Kent KJ, Cohen JE, Ganetsky M, **Bird SB.** Clin Toxicol 2006; 44.

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16. **Bird SB**, Lo JCY, Dickson EW, Sivilotti MLA. Multiple centrally-acting antidotes protect against severe organophosphate toxicity.,. J Toxicol Clin Toxicol 2005; 43.

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20. **Bird SB**, Mazzola JL, Brush DE, Boyer EW, Aaron CK. A Prospective Evaluation of Abbreviated Oral N-acetylcysteine (NAC) Therapy for Acetaminophen Poisoning. Acad Emerg Med 2003;10:521.

21. **Bird SB**, Gaspari RF, Barnett KA, Dickson EW. Diazepam Attenuates Acute Central Respiratory Depression from Acute Organophosphate Poisoning. Acad Emerg Med 2003;10:520-521.

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23. Lane DR, **Bird SB**, Zarum RS. Documentation of Emergency Medicine Resident Procedures Using a Personal Digital Assistant. Acad Emerg Med 2003;10:537-538.

24. **Bird SB**, Eddleston M, Sutherland TD, Ollis D. Pharmacokinetics of an Organophosphorus Hydrolase in the African Green Monkey. SAEM 2008 Annual Meeting, New Orleans, LA.

25. **Bird SB**, Gresham H, Sutherland T, Eddleston M. Use of a Recombinant Bacterial Hydrolase for Acute Dichlorovos Poisoning. NACCT 2006 Annual Meeting, San Francisco, CA

26. **Bird SB**, Gresham H, Sutherland T, Eddleston M, Eyer P. Use of a Recombinant Bacterial Hydrolase for Acute Parathion Poisoning. SAEM 2006 Annual Meeting, San Francisco, CA.

27. **Bird SB**, Gaspari RJ, Aaron CK, Boyer EW, Dickson EW. Synergistic Effects of Glycopyrrolate, Ipratropium, and Diazepam on Mortality in a Rat Model of Lethal Organophosphate Poisoning. European Association of Poison Control Centres and Toxicologists 2003 annual meeting, Rome, Italy.

28. **Bird SB**, Mazzola JL, Boyer EW, Brush DE, Aaron CK. A Prospective Evaluation Of Abbreviated Oral N-Acetylcysteine (NAC) Therapy For Acetaminophen (Paracetamol) Poisoning. European Association of Poison Control Centres and Toxicologists 2003 annual meeting, Rome, Italy.

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31. **Bird SB**. Critical Care Toxicology: Organophosphate Poisoning. 2002 North American Congress of Clinical Toxicology, Palm Springs, CA.

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34. **Bird SB**. Case Presentation Competition, 2002 Society for Academic Emergency Medicine annual meeting, St. Louis, Missouri.

35. **Bird SB**, Zarum RS. Emergency Medicine Resident Procedure Documentation is Not Increased Using a Handheld Computerized Device. 2002 Society for Academic Emergency Medicine annual meeting, San Francisco, CA.

36. **Bird SB**, Ni Y. Comparison of a Numeric Rating Scale and the Visual Analog Scale in Extremity Pain. American College of Emergency Physicians 2001 Annual Meeting, Las Vegas, NV.

37. **Bird SB**, Sullivan J, Mangolds G, Schmidt E, Nichols C, Dickson EW. Clinically Significant Changes in Pain Along the Entire Visual Analog Scale. American College of Medical Toxicology 2001 annual meeting, San Francisco, CA.

FUNDING (completed)

"A Fitbit Digital Health Intervention in the UMass ACO" $ 100,000
Jan 2021-Dec 2021
Massachusetts Digital Health Right Care 4 You Grant Program

"RCT of Wellness Coaches to Decrease Burnout" $ 12,000
Jan 2020-Dec 2020
Carl Atkins Risk Management Grant
UMassMemorial Healthcare

"Development of a Peer Support Network" $ 10,000
June 2016-May 2017
Carl Atkins Risk Management Grant
UMassMemorial Healthcare

"Pharmacotherapy to counterACT parathion-induced NMJ dysfunction"
Principal Investigator: **Steven B. Bird, MD**
U01 NIH/NINDS $3,082,749
Sept 2013 – Aug 2016

"Novel Neuromuscular Protection to CounterACT Acute Organophosphate Poisoning"
Principal Investigator: **Steven B. Bird, MD**
R21 NIH/NINDS $ 823,588
Oct 2011 – Sept 2013

"Use of a bacterial OP hydrolase antidote for parathion poisoning"
Principal Investigator: **Steven B. Bird, MD**
R21 NIH/NIEHS $ 446,875
Aug 2007 – Aug 2009

"Functional MRI Assessment of Acute Organophosphate Poisoning"
Principal Investigator: **Steven B. Bird, MD**
K08 NIH/NIEHS
Dec 2004 - Dec 2008 $ 580,669

"Recombinant Organophosphate Hydrolase for Acute Parathion Poisoning"
Principal Investigator: **Steven B. Bird, MD**
American College of Medical Toxicology
July 2005 – June 2006 $ 7,500

"Recombinant Organophosphate Hydrolase for Acute Dichlorvos Poisoning"
Principal Investigator: **Steven B. Bird, MD**
Emergency Medicine Foundation
July 2005 – June 2006 $ 5,000

"Ipratropium bromide as a treatment of organophosphate toxicity"

Principal Investigator: **Steven B. Bird, MD**
Emergency Medicine Foundation Resident Research Grant Award
2001 – 2002 $ 5,000

Appendix B

Steven B. Bird, MD

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List of all cases in which, during the previous 4 years, I have testified as an expert at trial or by deposition.

Howe v. Tiffany Warren and Ascension Medical Group; Case No. 2022-CV-944
In the 18th Judicial District Court of Sedgwick Co, Kansas
Deposition: November 2024

Garcia v. Webb County; Case No. 5-23-CV-00137
In the Southern District of Texas
Deposition: November 2024

Hodys v. Barnes; Case No. PC2017-5776
In the Superior Court of Providence, Rhode Island
Deposition: October 2024

Kimbrow v. Walgreens; Case No. 2023-L-0005405
In the Circuit Court of Cook County, Illinois
Trial: September 2024

Gross v. Walgreens; Case No. 2023-L-000469
In the Circuit Court of Cook County, Illinois
Trial: July 2024

Joiner v. Walgreens; Case 2023-L-004568
In the Circuit Court of Cook County, Illinois
Trial: July 2024

Valadez v. GSK; Case No. 2023-L-000483
In the Circuit Court of Cook County, Illinois
Trial: May 2024

Patrick Feindt, Jr. v. United States of America; Case No. 1:22-cv-397-LEK-KJM
In the District Court of Hawaii
Trial: May 2024

Mejia v. Stanford Hospital; Case No. FST-CV20-6046034S
In the Superior Court for Judicial District of Stamford/Norwalk of Connecticut
Trial: March 2024.

Hankins v. Jenkins; Case No. 2:22-CV-01590.
In the United States District Court for the Northern District of Alabama

Trial: March 2024

Kimbrow v. Walgreens; Case No. 2023-L-0005405
In the Circuit Court of Cook County, Illinois
Deposition: March 2023

Valadez v. GSK; Case No. 2023-L-000483
In the Circuit Court of Cook County, Illinois
Deposition: January 2023

Kasza v. Walgreens et al; Case No. 2023-L-005404
In the Circuit Court of Cook County, Illinois
Deposition: December 2023

Valdes v. GSK; Case No. 2021-021945-CA-01
In the 11th Judicial Circuit for Miami-Dade County Florida
Deposition: December 2023

Williams v. Walgreens et al.; Case No. 2023-L-004599
In the Circuit Court of Cook County, Illinois
Deposition: December 2023

Feindt v. United States of America: Case No. 22-cv-297lLEK-KJM
In the United States District Court of Hawaii
Deposition: November 2023

Wilson v. GSK; Case No. 22-CA-000284
In the 13th Judicial Circuit for Hillsborough County Florida
Deposition: November 2023

Hall v. Baptist Easley; Case No. 2018-CP-23—01576
In the Circuit Court for Greenville County of South Carolina
Trial: October 2023

Reinhart v. Short Mountain Trucking; Case No. 3:21-CV-03122
In the United States District Court for the Central District of Illinois, Springfield Division
Deposition: August 2023

Pagan v. Saranita; Case No. 12-CA-424 2015CA00424
In the Fifth Judicial Circuit Court for Lake County of Florida
Trial: July 2023

Heinrich v. Serens; Case No. 2904978/2018
In the Supreme Court for Onondaga County of New York
Trial: July 2023

Hall v. Baptist Easley; Case No. 2018-CP-23—01576
In the Circuit Court for Greenville County of South Carolina
Deposition: July 2023

Cooper v. Advocate Christ; Case No. 2019L004866
In the Circuit Court for Cook County of Illinois
Deposition: May 2023

Richey v. CSX Transportation; Case No. 19-CI-007780
In the Jefferson Circuit Court of Kentucky, Division Five
Deposition: April 2023

Bowditch v. MedStar; Case No. 2021 CA 003778 M
In the Superior Court in Washington D.C.
Deposition: April 2023

Pimentel v. HUMC; Case No. BER-L-93-20.
In the Superior Court for Bergen County of New Jersey
Deposition: January 2023

Devani v. Honor Health; Case No. CV2021-050489
In the Superior Court for Maricopa County of Arizona
Deposition: November 2022

Ruepke v. BNSF Railroad; Case No. 2019-L-007730
In the Circuit Court for Cook County of Illinois
Deposition: August 2022

Hartman v. Illinois Central Railroad; Case No. 2:20-cv-1633
In the United States District Court for the Eastern District of Louisiana
Deposition: June 2022

Hankins v. Jenkins; Case No. 2:22-CV-01590.
In the United States District Court for the Northern District of Alabama
Deposition: June 2022

Fravel v. Herard; Case No. 2021 L 32
In the Circuit Court of the 21st Judicial Circuit for Kankakee County of Illinois
Deposition: June 2022

Lloyd v. Memorial Hospital; Case No. 16-2019-CA-000961
In the Fourth Judicial Circuit for Duval County of Florida.
Deposition: June 2022

Shephard v. Mease; Case No. 17004700CI
In the Sixth Judicial Circuit for Pinellas County of Florida

Deposition: April 2022

State of Florida v. Baldie;
In the Ninth Judicial Circuit for Orange County of Florida
Trial: April 2022

Mejia v. Stanford Hospital; Case No. FST-CV20-6046034S
In the Superior Court for Judicial District of Stamford/Norwalk of Connecticut
Deposition: December 2021.

Florida v. Baldie; Case No. 2020-CF-004830-AO
In the Ninth Judicial Circuit for Orange County of Florida
Deposition: November 2021.

U.S. v. Carvajal; Case No. 1:20-CR-10023-GAO-1
In the United States District Court of Massachusetts
Trial: November 2021

Bacon v. AnMed Health Cannon; Case No. 2019-CP-39-00937
In the Circuit Court for Pickens County of South Carolina
Deposition: June 2021

Gordanier v. Waldo; Case No. 19AE-CC00286
In the Sixth Judicial Circuit for Platte County of Missouri
Deposition: May 2021

Rybar v. DePuy; Case No. 4:16-cv-01579-CEJ
In the Circuit Court for the City of St. Louis of Missouri
Deposition: April 2021

Steven B. Bird, MD