

Exhibit 83

General Causation Expert Report of Steven B. Bird, MD

Kidney Cancer

Prepared by:
Steven B. Bird, MD
6 Laurel Ridge Ln
Shrewsbury MA 01545

December 9, 2024

Contents

I.	Qualifications	5
II.	Methodology	5
III.	“As Likely as Not” Standard	6
IV.	Summary of Opinions	8
V.	The chemicals found at Camp Lejeune That Cause Cancer	11
A.	The Chemicals at Camp Lejeune Generally	11
1.	Chlorinated ethylene organic solvents (TCE, PCE, vinyl chloride, and their relatives).....	12
B.	The particular carcinogens present at camp Lejeune	13
1.	Trichloroethylene (TCE)	13
2.	Perchloroethylene (PCE)	14
3.	Benzene	15
4.	Vinyl Chloride	16
C.	Mechanisms of toxicity.....	16
1.	TCE and kidney cancer.....	16
2.	PCE and kidney cancer.....	17
3.	Benzene and kidney cancer	17
4.	Vinyl chloride and kidney cancer	17
VI.	Chemical Contamination in the water at Camp Lejeune Spanned Decades.....	18
A.	Hadnot Point: TCE Contamination	18
B.	Hadnot Point: Benzene Contamination.....	19
C.	Hadnot Point: PCE Contamination	19
D.	Hadnot Point: Vinyl Chloride contamination.....	19
E.	Tarawa Terrace: TCE Contamination.....	20
F.	Tarawa Terrace: PCE Contamination.....	20
G.	Tarawa Terrace: Vinyl Chloride contamination	21
H.	Holcomb Boulevard.....	21
I.	Risk Assessments	22
1.	Risks based on CREG limits underrepresent actual cancer risk	22
2.	Theoretical risks are grounded in conservative assumptions.....	22
3.	Human epidemiology provides superior evidence	23
4.	The limited relevant data from risk assessment in this case supports the conclusion that the toxins at Camp Lejeune are hazardous to human generally and can cause kidney cancer.....	23
VII.	Routes of Exposure to These Chemicals.....	24
A.	In general	25
B.	Absorption via ingestion	26

1.	TCE.....	26
2.	PCE.....	27
3.	Benzene	27
4.	Vinyl chloride	28
C.	Absorption via inhalation.....	28
1.	TCE.....	28
2.	PCE.....	29
3.	Benzene	29
4.	Vinyl chloride	30
D.	Absorption via dermal exposure.	30
1.	TCE.....	30
2.	PCE.....	30
3.	Benzene.	31
4.	Vinyl chloride.	31
VIII.	Literature Review.....	31
A.	Occupational Studies	31
B.	Water-Contamination Studies	32
1.	Aschengrau et al., 1993, <i>Cancer risk and tetrachloroethylene-contaminated drinking water in Massachusetts</i>	32
2.	Andrew et al., 2022, <i>Kidney Cancer Risk Associated with Historic Groundwater Trichloroethylene Contamination</i>	33
3.	Alanee et al., 2015, <i>Trichloroethylene Is Associated with Kidney Cancer Mortality: A Population-based Analysis</i>	33
C.	Evidence from Camp Lejeune Studies Confirms That These Chemicals Cause Kidney Cancer at Detected Concentrations.....	34
1.	Bove 2014A Study: <i>Cancer Mortality Study of Marines and Navy Personnel Exposed to Contaminated Drinking Water at Camp Lejeune, North Carolina</i>	34
2.	Bove 2014b Study: <i>Cancer Mortality Study of Civilian Employees Exposed to Contaminated Drinking Water at Camp Lejeune, North Carolina</i>	36
3.	ATSDR 2018 Study: <i>Morbidity Study of Former Marines, Employees, and Dependents Potentially Exposed to Contaminated Drinking Water at U.S. Marine Corps Base Camp Lejeune</i> ..	37
4.	Bove 2024a Study: <i>Long-term Cancer Mortality Among Military Personnel Exposed to Contaminated Drinking Water at Camp Lejeune</i>	38
5.	Bove 2024b Study: <i>Cancer Incidence Among Individuals Exposed to Contaminated Drinking Water at Camp Lejeune</i>	39
6.	Rosenfeld 2024 Study: <i>Camp Lejeune Marine Cancer Risk Assessment for Exposure to Contaminated Drinking Water From 1955 to 1987</i>	40
7.	Studies That Did Not Show an Association Between Camp Lejeune Chemicals and Kidney Cancer	40

IX. Other Relevant Considerations.....	41
A. Carcinogenic Latency	41
B. Additive and Synergistic Effects of Solvents and Toxins	42
C. Urothelial carcinoma of the renal pelvis.....	45
X. Bradford Hill Analysis	45
A. TCE.....	45
B. PCE	47
C. Vinyl Chloride.....	49
D. Benzene.....	51
E. TVOC.....	54
XI. Conclusion.....	55

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

II. METHODOLOGY

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

(TCE OR PCE OR benzene OR vinyl chloride OR trichloroethylene OR tetrachloroethylene OR perchloroethylene) AND cancer AND (kidney OR renal)

I also performed numerous searches using Google Scholar, which gives 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.

I reserve the right to supplement this report.

III. "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.

Equipose 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.

Ultimately, I have concluded that at a minimum, “as likely as not,” that the drinking water at Camp Lejeune and each of the four toxins at issue are hazardous to humans and are known to cause kidney cancer. For the Camp Lejeune drinking water and some of the toxins, a higher standard of “more likely than not,” is met as well.

IV. SUMMARY OF OPINIONS

1. In my view, the water at Camp Lejeune, which was contaminated with significant levels of benzene, trichloroethylene (TCE), perchloroethylene (PCE), and vinyl chloride, causes kidney cancer. Each of these toxins has sufficient scientific evidence to support its causality to kidney cancer. This is especially true given the reduced standard at issue in this litigation, an as likely as not standard or equipoise.
2. It is also my opinion that the levels of exposure to these chemicals at Camp Lejeune are hazardous to humans, and specifically cause kidney cancer. Epidemiologic studies of occupational exposure, as well as studies involving environmental contamination, provide evidence that the level of exposure to these chemicals at Camp Lejeune were sufficient to cause kidney cancer.

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 and are known to cause kidney cancer as likely as not. Numerous studies provide evidence of specific levels of exposure—some of which are similar in intensity with the contamination observed at Camp Lejeune—that are associated with increased risks for kidney cancer:

1. **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.
2. **Exposure to a TCE concentration of \geq 76 ppb:** Moore LE, Boffetta P, Karami S, et al. Occupational trichloroethylene exposure and renal carcinoma risk: evidence of genetic susceptibility by reductive metabolism gene variants. *Cancer Res*. 2010;70(16):6527-6536.
3. **Cumulative exposure of \geq 1,580 ppb-years:** Moore et al., 2010.
4. **Sustained exposure to 0-25 ppb of TCE:** Andrew AS, Li M, Shi X, Rees JR, Craver KM, Petali JM. Kidney Cancer Risk Associated with Historic Groundwater Trichloroethylene Contamination. *Int J Environ Res Public Health*. 2022;19(2):618.
5. **Exposure to a TCE concentration of 267 ppb:** Parker GS, Rosen, S. Woburn: Cancer Incidence and Environmental Hazards 1969-1978. Commonwealth of Massachusetts, Department of Public Health, 1981.
6. **Exposure to a PCE concentration of 21 ppb:** Parker and Rosen, 1981.
7. **Cumulative exposure of 1 - 3,100 μ g/L-month of TCE:** 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.
8. **Cumulative exposure of 1 - 155 μ g/L-month of PCE:** Bove et al, 2014a.
9. **Cumulative exposure of 1 – 4,600 μ g/L-month of exposure to all compounds at Camp Lejeune:** Bove et al, 2014a.
10. **Cumulative exposure of 3,100 – 7,700 μ g/L-month of TCE:** Bove et al, 2014a.

11. **Cumulative exposure of 155 - 380 µg/L-month of PCE:** Bove et al, 2014a.
12. **Cumulative exposure of 4,600 – 12,250 µg/L-month of exposure to all compounds at Camp Lejeune:** Bove et al, 2014a.
13. **Cumulative exposure greater than 7,700 µg/L-month of TCE:** Bove et al, 2014a.
14. **Cumulative exposure greater than 380 µg/L-month of PCE:** Bove et al, 2014a.
15. **Cumulative exposure greater than 12,250 µg/L-month of exposure to all compounds at Camp Lejeune:** Bove et al, 2014a.
16. **18 months of residence on base from 1975 to 1985:** Bove et al, 2014a.
17. **Employment on base for 2.5 years:** Bove FJ, Ruckart PZ, Maslia M, Larson TC. Mortality study of civilian employees exposed to contaminated drinking water at USMC Base Camp Lejeune: a retrospective cohort study. *Environ Health*. 2014;13:68.
18. **Cumulative exposure to 110 – 11,030 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.
19. **Cumulative exposure to 36 - 711 ppb-months of PCE:** ATSDR, 2018.
20. **Cumulative exposure greater than 11,030 ppb-months of TCE:** ATSDR, 2018.
21. **Cumulative exposure greater than 711 ppb-months of PCE:** ATSDR, 2018.
22. **1-6 quarters stationed on base as a service member from 1975 to 1985:** Bove FJ. 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* 2024b;132;10.
23. **More than 21 quarters spent on base as a civilian worker from 1975 to 1985:** Bove et al, 2024b.

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 sufficient 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 drinking water systems at Camp Lejeune considerably exceeded their respective MCLs.”

The evidence in this case mirrors one of the oldest examples of epidemiology detecting a causal association. In the mid-1800s, British physician John Snow compared the rates of cholera in people who drank water from a company who drew its water from “comparatively clean, Thames water upstream from London” and

another company who drew its water from “downstream of London and therefore contaminated with sewage.” [Rothman K. *Modern Epidemiology*, 4th Edition, 2021]. The cholera rates were higher in households who drank water from the downstream company, thereby demonstrating convincingly that contaminated water was causing the cholera.

The evidence for Camp Lejeune largely relies on similarly elegant “natural experiment” designs. The studies looked at the rates of kidney cancer in areas of high contaminant concentrations and compared those rates to areas of lower contaminant concentrations. Some of the studies did so for Camp Lejeune itself, comparing rates of kidney cancer in personnel stationed there to the kidney cancer rates in personnel stationed at bases where the water was not contaminated. Just as the differential cholera rates between the pumps demonstrated a causal relationship between cholera and the water in 1800s London, the differential kidney cancer rates between Camp Lejeune and other marine bases demonstrates a causal relationship here.

The significant evidence from the above valid and methodologically sound studies establishes that exposure to the levels of the toxins in the drinking water at Camp Lejeune were hazardous to human beings generally and are known causes of kidney cancer. Much of the evidence related to Camp Lejeune stems from sophisticated natural experiment designs, particularly research comparing kidney cancer incidence rates in regions with higher and lower or negligible exposure. Some studies specifically examined kidney cancer 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 kidney cancer hazards 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 kidney cancer, even though it is likely 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 kidney cancer 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 levels known to cause kidney cancer.

While epidemiological data often focuses on specific dose ranges where elevated risks have been observed, these should not be interpreted as definitive minimum thresholds below which no hazard exists. Rather, these ranges reflect only the levels studied. It is indeed very likely that lower concentrations also contribute to kidney cancer 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 kidney cancer. Epidemiological findings clearly demonstrate increased

kidney cancer hazards at these levels and provides strong support that levels lower than those found specifically in the epidemiology are also hazardous to humans generally and are known to cause kidney cancer.

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

V. THE CHEMICALS FOUND AT CAMP LEJEUNE THAT CAUSE CANCER

The major drinking-water contaminants of interest at Camp Lejeune are volatile organic chemicals (VOCs): mainly trichloroethylene (TCE) and tetrachloroethylene (also known as perchloroethylene or PCE), but also benzene and vinyl chloride (as well as other chemicals that I will not address in this report). All those except benzene are halogenated, short-chain aliphatic hydrocarbons (halocarbons) - benzene is an aromatic hydrocarbon.

A. The Chemicals at Camp Lejeune Generally

To understand how exposure to the contaminated water at Camp Lejeune can cause kidney cancer, it's useful to consider how the underlying chemicals present can affect human health generally. TCE, PCE, benzene, and vinyl chloride are all organic solvents.

A solvent is a substance that dissolves another substance. While water is the most common solvent, a number of substances (especially those with oils as part of their make-up), do not dissolve well in water. Organic solvents are a class of solvents made up of chemical compounds - primarily carbon and hydrogen (hence the term “hydrocarbon”) - sometimes combined with other elements (e.g., chlorine), and are often used to aid this process. These solvents dissolve fat and oil easily. In turn, organic solvents are also able to dissolve in fat.

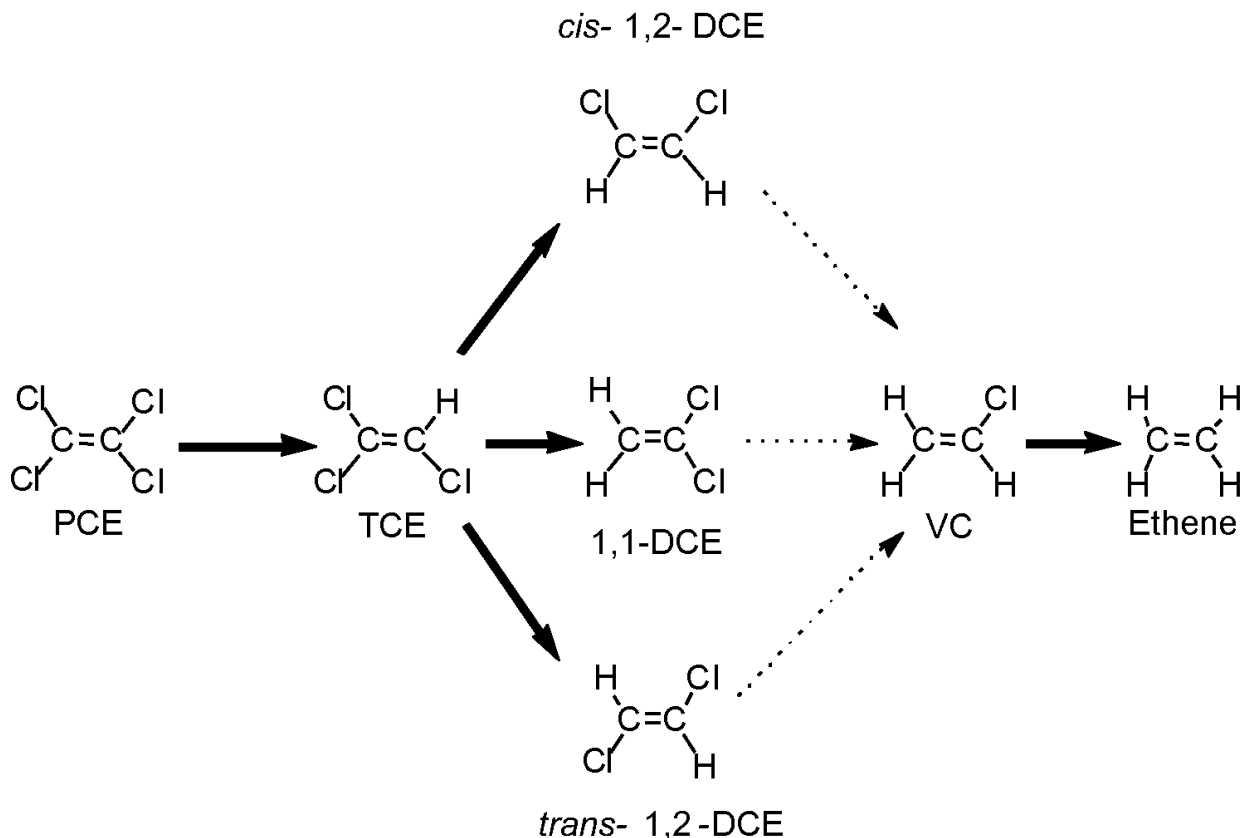
As a result of their ability to dissolve in fat (known as lipophilicity), organic solvents can permeate the human body. For example, organic solvents are uniquely able to affect the brain and nervous system by easily crossing the “blood brain barrier.” This natural protective barrier separates circulating blood from the fluid from the brain, isolating the central nervous system from the rest of the body. Because of the substantial fatty component in skin, organic solvents are also easily absorbed through the skin.

Many organic solvents are volatile (easily evaporated), leading to possible exposure through inhalation. Where these solvents are present in the water supply, they can easily move into the air under conditions such as showering, dishwashing, or toilet flushing. They can also enter homes through groundwater in a process known as vapor intrusion.

Because TCE, PCE, benzene, and vinyl chloride are organic solvents, their presence in a primary water source, like at Camp Lejeune, can result in exposure through ingestion of food and water, inhalation of indoor air, and absorption through the skin. It has been estimated that exposure through the air and skin from the drinking water source alone is roughly equal to, or may even exceed, exposure from ingestion.

1. Chlorinated ethylene organic solvents (TCE, PCE, vinyl chloride, and their relatives)

A subcategory of organic solvents is chlorinated volatile organic compounds (CVOCs), which can be divided into three groups based on their structures (methane, ethane, and ethylene). Of particular relevance in this case is the third subclass: chlorinated ethenes (also known as chlorinated ethylene). Chlorinated ethenes share on a common backbone: a variation on the underlying structure of the hydrocarbon known as ethylene. Ethylene is composed of two carbon atoms, connected by a double bond. Each carbon has two more places to connect other atoms. If all four connections are to hydrogen atoms, the result is ethylene (far right, figure below). Chlorinated ethenes result when a chlorine atom replaces at least one of the hydrogens.



In PCE, two chlorine atoms attach to each carbon atom, displacing all of the hydrogens completely. The other chlorinated ethenes are sometimes referred to as PCE's "daughter products" because through reductive dechlorination, PCE will degrade to TCE, then to a form of dichloroethylene (DCE), to vinyl chloride ("VC"), and finally to ethylene. In turn, ethylene can degrade to carbon dioxide and water.

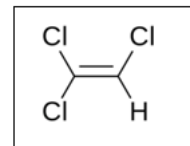
While very little data exists on how dichloroethylene affects humans and most regulatory bodies have not evaluated its carcinogenicity "due to lack of information," [ATSDR DEC ToxFAQ 2023, at 2], the National Toxicology Program classifies DCE as "reasonably anticipated to be a human carcinogen" due to studies in experimental animals. [National Toxicology Program 15th Report on Carcinogens, 2021]. This is consistent with PCE's other daughter products: TCE and vinyl chloride. [IARC Monograph 106, 2014 at 189] ("There is sufficient evidence in humans for the carcinogenicity of [TCE]"); [IARC Monograph 97, 2008 at 425] ("There is sufficient evidence in humans for the carcinogenicity of vinyl chloride."). PCE itself is classified as "probably carcinogenic to human." [IARC Monograph 106, 2014 at 329].

The closely related chemical structure of chlorinated ethenes, specifically the three present at Camp Lejeune, does not mean they cause the same biological effects but can inform a deeper understanding of the scientific literature, especially to the degree there are limits to current research.

B. The particular carcinogens present at camp Lejeune

1. Trichloroethylene (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.

There is also evidence that TCE can cause kidney cancer specifically. According to IARC, "There is sufficient evidence in humans for the carcinogenicity of trichloroethylene. Trichloroethylene causes cancer of the kidney." [IARC Monograph 106]. Similarly, ATSDR has concluded that "there is sufficient evidence for causation" for TCE and kidney cancer [ATSDR Assessment of the Evidence for the Drinking Water Contaminants at Camp Lejeune and Specific Cancers and Other Diseases, 2017]. Further, the National Toxicology Program has stated that TCE is known to be a human carcinogen based on sufficient evidence of carcinogenicity from studies in humans and that this conclusion is based on epidemiological studies showing that it causes kidney cancer in humans together with supporting evidence from toxicological, toxicokinetic, and mechanistic studies demonstrating the biological plausibility of its carcinogenicity in humans.

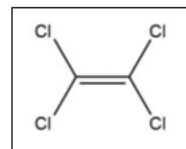
The classifications from the above organizations are based on an extensive body of literature from both human and animal studies. One such study was published in 2010 by Kelsh et al. [Kelsh MA. *Epidemiol* 2010;21: 95–102]. In this meta-analysis of occupational TCE exposure and kidney cancer, they evaluated 23 studies that met their inclusion criteria. The summary RR was 1.42 (95% CI 1.17-1.77). After removing 3 of the studies, the RR again was statistically significant with a RR 1.24 (95% CI 1.06-1.45).

In 2011, a manuscript from the Environmental Protection Agency (EPA) authored by Scott and Jinot sought to evaluate the evidence for kidney cancer, liver cancer, and non-Hodgkin lymphoma and TCE exposure [Scott CS. *Int J Environ Res Public Health* 2011;8:4238-72]. For overall TCE exposure and kidney cancer, the summary relative risk estimate from their random effects model was 1.27 (95% CI 1.13-1.43), with a higher RR for the highest exposure groups (1.58, 95% CI: 1.28-1.96). The authors concluded that "Other human, animal and pharmacokinetic data linking TCE and these cancers provide further support and biological plausibility to our findings."

Another study which demonstrated that TCE can cause kidney cancer was published in 2012 by Karami et al. [Karami S. *Occup Environ Med* 2012;69:858–867]. This meta-analysis of 28 papers resulted in an overall elevated relative risk of 1.26 (95% CI 1.02-1.56) for TCE exposure and renal cancer. When they evaluated cohort studies and case-control studies separately, each study design again revealed a statistically significant association. Furthermore, the authors concluded that exposure misclassification in previous studies would weaken estimates of kidney cancer from TCE specifically.

2. Perchloroethylene (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].

Epidemiologic studies involving PCE exposure have also demonstrated an association between PCE and kidney cancer. For instance, 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]. 284]. Following this discovery, the Massachusetts Department of Health observed “elevations in cancer mortality” in affected areas.

The authors then defined the risk of cancers for the Cape Cod cohort. People exposed to any amount of PCE had relative risk of kidney cancer of 1.23 (95% CI 0.40-3.11), suggesting a 23% 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 despite being underpowered.

Other studies that have shown an association between PCE and kidney cancer include a 2017 study Purdue *et al.* [Purdue MP. Occup Environ Med 2017;74:268–74] In this case-control study from the U.S. Kidney Cancer Study found an OR of 3.1 (95% CI 1.3-7.4) for high cumulative exposure to PCE and kidney cancer, indicating a strong association.

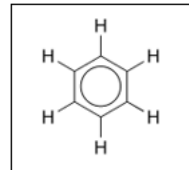
Other occupational studies of PCE exposure come from studies of the dry-cleaning industry. Ruder *et al.* conducted a study in their work at the National Institute for Occupational Safety and Health (NIOSH) of 1,708 dry-cleaning workers identified through union records and found a standardized mortality ratio for kidney cancer of 1.41 (95% CI 0.46-3.30). [Ruder AM. Am J Industr Med 2001;39:121-32]. In another mortality study, Callahan *et al.* performed long-term follow-up of 5369 dry cleaning union members in the United States [Callahan CL. Epidemiol 2019;30:285–90]. They found a positive dose-response to solvent exposure and death due to kidney cancer, with the highest exposure group demonstrating a hazard ratio of 13.2 (95% CI 1.9-90.8).

The Bove 2014b study examined cancer mortality in civilian workers at Camp Lejeune and compared the results to cancer mortality in civilians working at Camp Pendleton. [Bove FJ. Environ Health 2014;13:68]. They found an elevated standardized mortality ratio (SMR) of 1.30 (95% CI 0.52-2.67) for those workers at Camp Lejeune. When investigating the presence of a dose-response to the chemicals in the Camp Lejeune water, they found that “all kidney cancer deaths (n = 7) among the Camp Lejeune cohort had cumulative exposures above the median for PCE, TCE, and vinyl chloride. Only 1 kidney cancer was below the median for cumulative exposure to TVOC and two were below the median for benzene. Only 1 kidney cancer was

below the median average exposure to each of the contaminants. Because of the small numbers and high cumulative and average exposures of kidney cancers, categorical analyses **resulted in infinite HRs** for some of the contaminants.” (emphasis added).

3. 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 also a recognized carcinogen. According to IARC, there is sufficient evidence in humans for the carcinogenicity of benzene. [IARC Monograph 120 on Benzene, 2018]. Furthermore, the National Toxicology Program has proclaimed 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 has found that “benzene is characterized 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]

Several human studies have investigated the effect of benzene exposure on the development of renal cancer. In a case-control study from Germany, an association was found between benzene exposure and an increased risk of kidney cancer [Pesch B. *Int J Epidemiol* 2000;29:238-47]. The study included 935 cases and 4298 controls with exposure estimated according to occupational history and a job exposure matrix (JEM). They found that after controlling for age and smoking, an employment duration exceeding the 90th percentile of benzene exposure in the male British cohort were associated with renal cell carcinoma (OR 1.5; 95% CI 1.0-2.1).

In 2014, Bove 2014a reported on a cohort study of United States Marine and Navy personnel who served during 1975–1985 and were stationed at either Camp Lejeune (with its contaminated water), and Camp Pendleton (which did not have contaminated water). [Bove FJ. *Environ Health* 2014;13:10 – hereafter referred to as Bove 2014a]. Benzene was present at concentrations above the U.S. maximum contaminant levels (MCL). Military personnel in the Camp Lejeune cohort had an elevated mortality for kidney cancer (HR 1.35; 95% CI 0.84–2.16). Furthermore, a monotonic cumulative exposure trend was observed for kidney cancer and total contaminants. In the supplemental data, benzene was associated with increased rates of kidney cancer at low (HR 1.31; 95% CI 0.52–3.29), medium (HR 1.38; 95% CI 0.58–3.28), and high (HR 1.36; 95% CI 0.57–3.25) exposure levels.

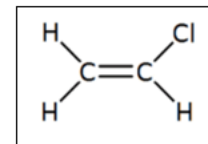
A 2002 study by Hu *et al.* investigated the occurrence of renal cell carcinoma with various occupational chemical exposures in Canada. [Hu J. *Occup Med* 2002;52:157–64]. They obtained data on 1279 (691 male and 588 female) renal cell carcinoma cases and 5370 controls between 1994 and 1997. In order to control for other potential cancer risk factors, they also collected data smoking, alcohol use, diet, residential and occupational histories, and years of exposure to any of the chemicals. The study found an increased risk of renal cell carcinoma in males with occupational exposure to benzene – 1.8 (95% CI 1.2–2.6).

Another occupational study of benzene exposure and kidney cancer was published by Greenland *et al.* [Greenland S. *Int Arch Occup Environ Health* 1994;66:49-54]. Their case-control study of people with benzene and other exposures in transformer factories in Massachusetts found an odds ratio of kidney cancer with benzene exposure of 4.29 (95% CI 1.33-13.8). Finally, a meta-analysis of 29 studies published by Seyyedsalehi *et al.* found an association between occupational benzene exposure and kidney cancer, with a

relative risk of 1.20 (95% CI 1.03-1.39). [Seyedsalehi MS. Eur J Cancer Prev 2024;ahead of print - DOI: 10.1097/CEJ.0000000000000911].

4. 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].

The Hu 2002 study cited above also investigated the occurrence of kidney cancer with exposure to vinyl chloride. They reported an elevated risk with an OR of 2.0 (95% CI 1.2–3.3).

The Camp Lejeune studies cited above also support an association between vinyl chloride and kidney cancer as vinyl chloride was known to exist in the water at Camp Lejeune in significant quantities and there was an increased risk found between exposure to the water at Camp Lejeune and kidney cancer.

C. Mechanisms of toxicity

1. TCE and kidney cancer

TCE has been implicated in the development of kidney cancer through several mechanisms. The primary pathway involves its metabolism via glutathione conjugation, leading to formation of S-(1,2-dichlorovinyl)-L-cysteine (DCVC), a nephrotoxic and mutagenic metabolite. This metabolite is further bioactivated by renal cysteine conjugate beta-lyase (CCBL1), resulting in the production of reactive intermediates that can cause cellular damage and mutations. Additionally, TCE exposure has been associated with specific somatic mutations in the von Hippel-Lindau (VHL) gene, which is critical in the pathogenesis of clear-cell renal cell carcinoma. [Brüning T and Bolt HM. Crit Rev Toxicol 2000;30:253-85; Moore LE. Cancer Res 2010;70:6527-36].

Like other chlorinated hydrocarbons, it is also well-established that TCE causes oxidative stress in various tissues and cell types. For instance, Khan *et al.* reported that TCE administration in rats resulted in increased lipid peroxidation and decreased activities of antioxidant enzymes such as superoxide dismutase (SOD) and catalase in multiple tissues [Khan S. Food Chem Toxicol 2009;47:1562–8]

Toxicokinetic and mechanistic data in both humans and experimental animals provide evidence for a mechanism of action by which TCE causes kidney cancer [NTP 15th Report on Carcinogens, 2015]. The evidence indicates that TCE causes genotoxicity (such as DNA and chromosomal damage) and cytotoxicity as a result of being metabolized into products that can damage DNA or cells [Chiu WA. Environ Health Perspect 2013;121:303-11].

2. PCE and kidney cancer

PCE induces kidney cancer through several mechanisms:

- **Metabolic activation and DNA damage:** PCE is metabolized in the liver to trichloroacetic acid (TCA) and other metabolites, which can be further processed in the kidney. These metabolites can form DNA adducts, leading to mutations and initiating carcinogenesis. This is supported by studies showing DNA damage in the liver and kidney of exposed animals.
- **Oxidative stress:** PCE exposure induces oxidative stress, characterized by increased levels of reactive oxygen species (ROS) and lipid peroxidation. This oxidative damage can lead to DNA strand breaks and mutations, contributing to carcinogenesis. The induction of oxidative stress has been observed in various studies, including those examining the effects of PCE on renal cells.
- **Cellular toxicity and proliferation:** PCE and its metabolites can cause cytotoxicity, leading to cell death and compensatory cell proliferation. This increased cell turnover can enhance the likelihood of mutations and cancer development.

3. Benzene and kidney cancer

The mechanism by which benzene causes kidney cancer involves several pathways, primarily through its metabolites and the resultant oxidative stress and DNA damage. Benzene is metabolized in the liver to various reactive intermediates, including benzene oxide, phenol, hydroquinone, catechol, and benzoquinones. These metabolites can generate reactive oxygen species (ROS) through redox cycling, leading to oxidative DNA damage. The oxidative stress induced by benzene metabolites results in DNA strand breaks, chromosomal aberrations, and mutations. Specifically, hydroquinone and 1,4-benzoquinone are potent inducers of oxidative DNA damage and apoptosis, which can contribute to carcinogenesis. [IARC Monograph 120, 2018].

Additionally, benzene metabolites can inhibit DNA topoisomerase II, leading to DNA double-strand breaks and further genomic instability. Moreover, benzene exposure has been associated with the formation of DNA adducts, which are modifications of DNA that can lead to mutations if not properly repaired. The impaired DNA repair mechanisms, such as base excision repair and nucleotide excision repair, further exacerbate the mutagenic effects of benzene. [Hartwig A. *Chemico-Biol Interact* 2010;184:269-72].

4. Vinyl chloride and kidney cancer

Overall, the carcinogenic mechanism of vinyl chloride in the kidney involves the formation of DNA adducts by its reactive metabolites, leading to genetic mutations, oxidative stress, and disruption of cellular pathways critical for maintaining genomic integrity. Vinyl chloride is metabolized in the body to reactive intermediates, primarily chloroethylene oxide and chloroacetaldehyde, which are implicated in its carcinogenicity. These metabolites form DNA adducts, such as etheno-deoxyadenosine and etheno-deoxycytidine, which can lead to mutations in critical genes involved in cell cycle regulation and DNA repair. [Antweiler H. *Environ Health Perspect* 1976;17:217-9; Bartsch H. *Environ Health Perspect* 1976;17:193-8; Green T and Hathway DE. *Chemico-Biol Interact* 1978;22:211-24].

In the kidney, exposure to vinyl chloride also induces oxidative stress and dysregulation of the TP53 pathway, which are key mechanisms in the development of renal cell carcinoma [Hayes SA. *Toxicol Pathol* 2016;44:71-87].

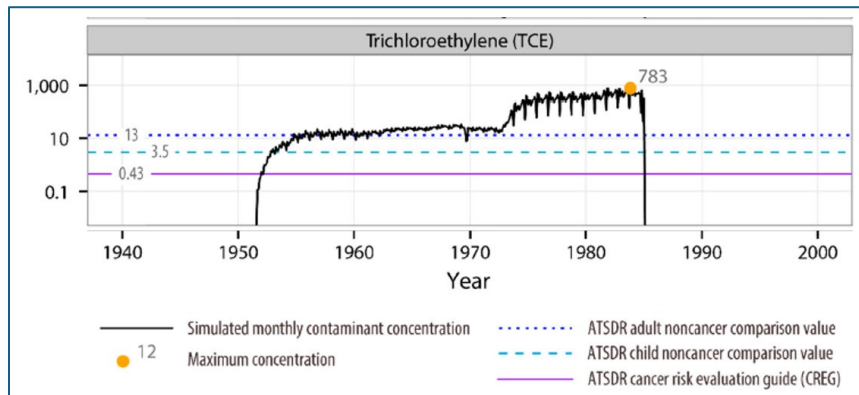
VI. CHEMICAL CONTAMINATION IN THE WATER AT CAMP LEJEUNE SPANNED DECADES

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.

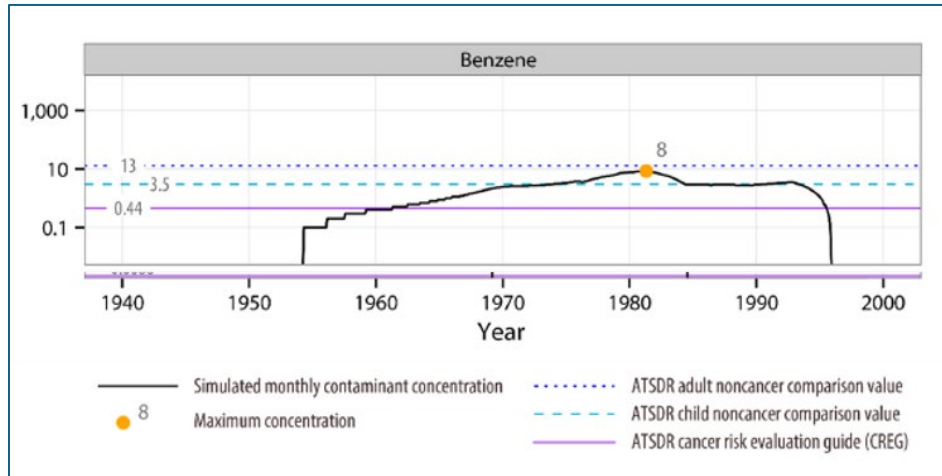


The graph illustrates that TCE concentrations at Hadnot Point consistently exceeded CREG level,¹ defined as the “concentrations of cancer-causing substance [that are] unlikely to result in an increase of cancer risk in an exposed population.” [ATSDR PHA at 7]. For TCE, the CREG limit is 0.43 ppb. With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

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

B. Hadnot Point: Benzene Contamination

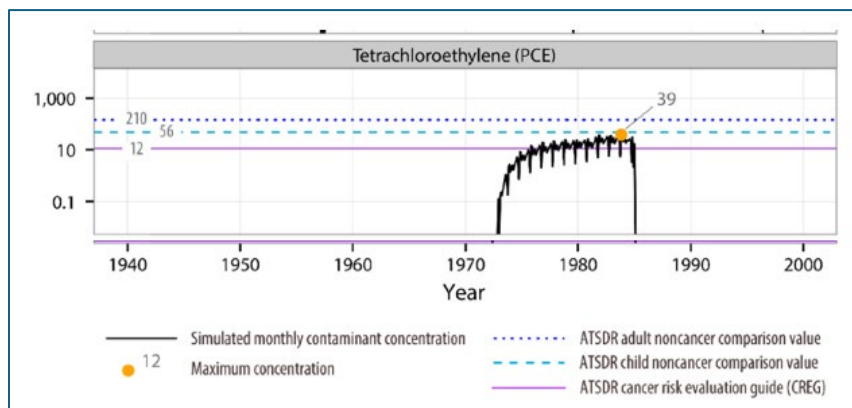
The reconstructed benzene concentrations in the water at Hadnot Point are illustrated in the graph below.



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.

C. Hadnot Point: PCE Contamination

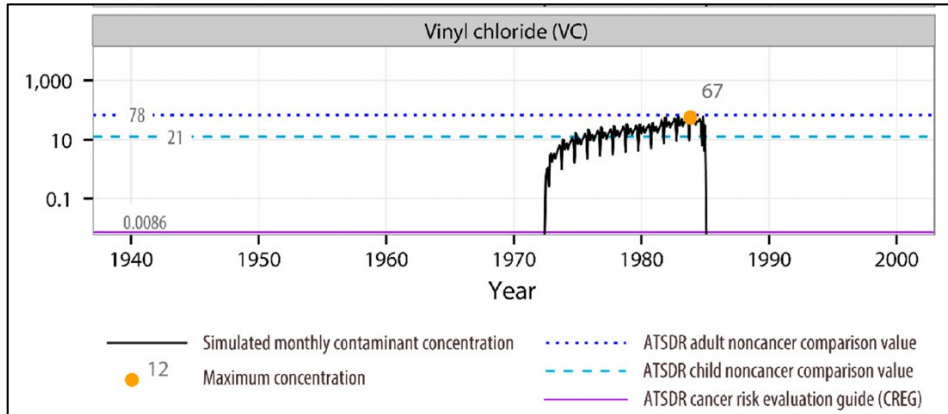
At Hadnot Point, the median monthly PCE contamination was 15 micrograms per liter. [Bove 2014a at 3]. The reconstructed concentrations in the water are illustrated in the graph below.



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.

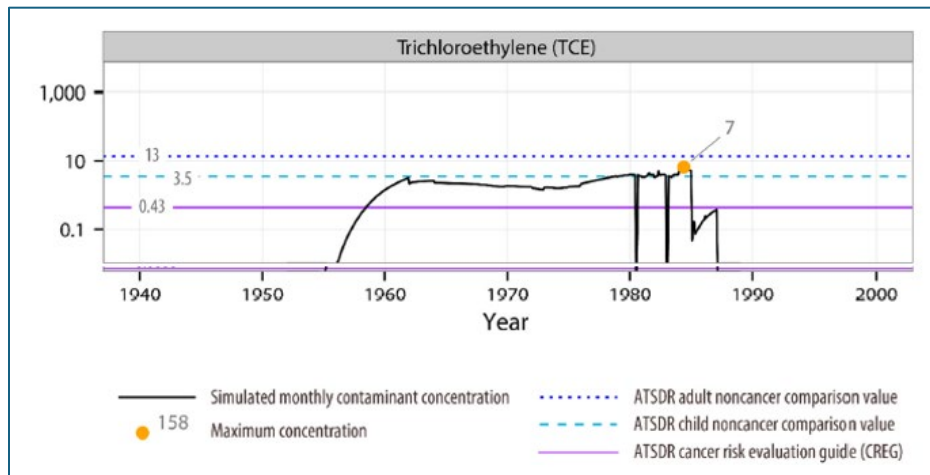
D. Hadnot Point: Vinyl Chloride contamination

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

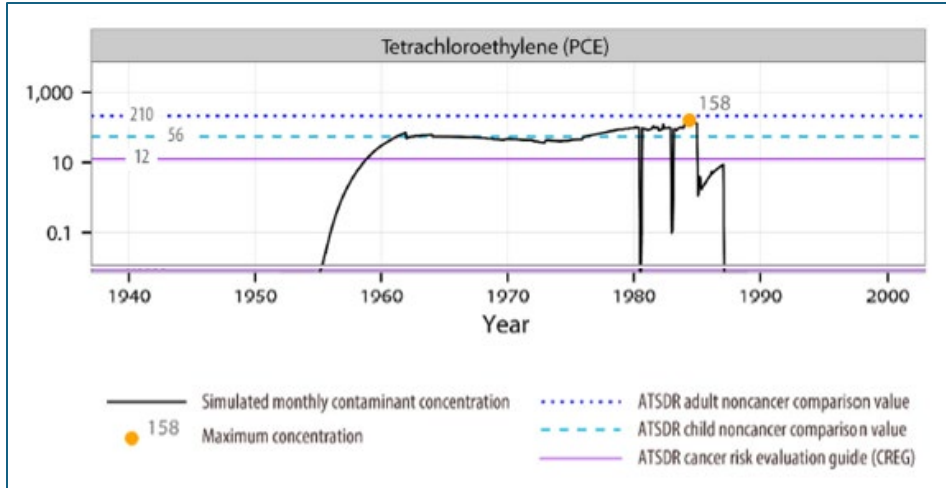
The reconstructed TCE concentrations in the water at Tarawa Terrace are shown below.



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

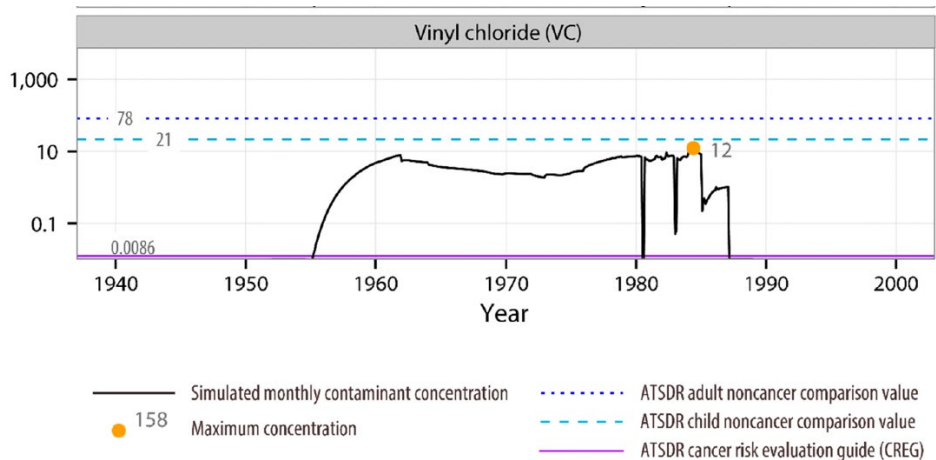
At Tarawa Terrace, concentrations of PCE ranged from 0 to 158 µg/liter, with a median of 85 µg/liter [Bove 2014a at 3]. The reconstructed concentrations in the water are illustrated in the graph below.



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 1×10^{-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 kidney cancer. 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.² Dose-response curves in animal studies may not

² For TCE, the cancer-slope was calculated in part based on a human occupational study by Charbotel [Charbotel B. *Ann Occup Hyg* 2006;50:777-87]. But as with the animal studies, the researchers in that study did not actually

accurately reflect human physiology, and 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.

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].

Further, 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 provides superior evidence

CREG limits should not be relied upon when there are better data available - for example, from human epidemiology dealing with the actual exposure scenario at issue.

Although CREG limits can provide an explanation for identifying environmental hazards, human epidemiological data are highly valuable for assessing cancer risk and identifying the levels of the toxins at issue that are known to cause kidney cancer. Epidemiological studies evaluate real-world exposures and outcomes, providing critical insights into the actual risk posed by contaminants and the actual levels of the contaminants that cause specific cancers. 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 kidney cancer among those exposed to contaminated water. This real-world data highlights the limitations of CREG levels, which calculate risks for individual chemicals in isolation, often underestimating the cumulative risk from multiple exposures. The human epidemiology data, especially that taken directly from Camp Lejeune is more accurate and provides a better analysis of the levels that are hazardous to humans generally and that cause kidney cancer.

4. The limited relevant data from risk assessment in this case supports the conclusion that the toxins at Camp Lejeune are hazardous to human generally and can cause kidney cancer

Rosenfeld *et. al* wrote an article in 2024 relating to the water at Camp Lejeune that, among other things, utilized a risk assessment analysis [PE. Water Air Soil Pollut 2024;235:124]. The authors calculated exposure scenarios using the same slope factors that are used to set the CREG levels.

Rosenfeld and his co-authors calculated increased risks of between 1 and 75 in one million. This may seem to a layperson to be insignificant, however, the authors concluded that these results constituted a serious risk to people present at Camp Lejeune. The authors stated, “it can be reasonably concluded from the results and discussion that Camp Lejeune had significant enough water contamination to threaten the health of

measure risk at lower levels of exposure. That is why the authors of that study stated that “further epidemiological studies are necessary to analyze the effect of lower levels of exposure.”

Marines living and working on the base.” [Rosenfeld 2023 at 13]. They went on to state “kidney cancer” (among other diseases) poses “a high risk to individuals who spent time on the base, especially during the years of greatest contamination in the late 1970s and 1980s.”

This is just one example of the CREG limit of 1×10^{-6} being interpreted by scientists as hazardous to humans generally during the use of risk assessments. Though a 1×10^{-6} risk may seem small, the numbers are not a precise estimate of the actual risk, as described above.

The 2017 ATSDR PHA also performed a risk assessment analysis and similarly concluded that the drinking water from Camp Lejeune posed an increased risk of cancer. [ATSDR PHA, 2017]. Specifically, ATSDR found that using “a 3-year exposure duration, the estimated upper-bound cancer risk exceeds the USEPA’s Superfund target cancer-risk range (1 excess case for every 10,000 exposed persons to 1 excess case for every 1,000,000 exposed) during the years 1964–1985.” Specifically, ATSDR found that:

- “Children living on-base from the early-1970s to the mid-1980s had an estimated, upper-bound cancer risk up to about 45 excess cases of cancer for every 10,000 exposed persons.
- Workers from the mid-1960s to the early-1980s had an estimated, upper-bound cancer risk of about three excess cases of cancer for every 10,000 exposed persons.
- Marines-in-training from the early-1970s to the early-1980s had an estimated, upper-bound cancer risk of about four excess cases of cancer for every 10,000 exposed persons.
- Other adults living on-base from the late-1970s to the early-1980s had an estimated, upper-bound cancer risk of about one excess case of cancer for every 10,000 exposed individuals.”

Again, while these risk estimates may seem to a lay person to be low, understanding their purpose and known flaws, these results are indicative of an increased risk for cancer and provide some support that the water at Camp Lejeune existed at levels that are hazardous to humans generally and are known to cause kidney cancer.

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. This provides additional support for the fact that the levels of toxins in the water at Camp Lejeune were hazardous to humans and were known to cause kidney cancer.

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/l) 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 C¹⁴ 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 μmL [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 Perspect 1975;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 cm², 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/(cm²·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

Occupational literature demonstrate that TCE, PCE, vinyl chloride, and benzene cause kidney cancer. Exposure assessments in the occupational literature are occasionally qualitative in nature. “Many of the causal associations between chemicals and human disease have been developed from epidemiological studies relating a workplace chemical to an increased risk of the specific disease in cohorts of workers, often with only a qualitative assessment of exposure.” [Ref Manual at 657].

However, this constraint in the literature does not undermine the efficacy of its evidence. Similarly, while some occupational studies involved TCE exposure at high levels, “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 could have a daily

exposure “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.

Further, as stated before, the levels at issue in occupational studies do not undermine the fact that lower levels also cause kidney cancer. In fact, these studies provide support for this likelihood, especially when used in conjunction with other epidemiological studies that have exposures at much lower levels.

The occupational studies of these chemicals and their clinical effects have already been discussed in this report and will not be repeated.

B. Water-Contamination Studies

The studies discussed above demonstrate that TCE, benzene, vinyl chloride, and PCE are capable of causing kidney cancer. While the concentrations of these chemicals in the studies were sometimes higher than those at Camp Lejeune, this does not imply that lower exposure levels are not capable of causing kidney cancer. 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 kidney cancer.

However, the occupational studies represent only one part of the body of research on TCE, PCE, vinyl chloride, benzene, and kidney cancer. Beyond the occupational literature, multiple studies have shown that these chemicals can also cause kidney cancer at lower levels of exposure. Specifically, studies on other water contamination incidents in the U.S. have provided evidence that chemical exposures similar to those at Camp Lejeune are sufficient to increase the risk of kidney cancer, 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 kidney cancer among individuals exposed to lower levels of TCE, PCE, vinyl chloride, and benzene.

1. Aschengrau et al., 1993, *Cancer risk and tetrachloroethylene-contaminated drinking water in Massachusetts*

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. [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. As mentioned previously, the relative risk of kidney cancer was 1.23 (95% CI 0.40-3.11), suggesting a 23% increased risk.

Researchers in this study also constructed a measure of Relative Delivered Dose (RDD) to model the total amount of PCE consumed by individuals on Cape Cod. The 90th percentile for cumulative exposure was 27.1- 44.1 milligrams. For comparison these levels are in the same range of 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. A number of other scenarios, where a Marine stationed on Camp Lejeune would have a cumulative PCE exposure equivalent to those seen at the 90th percentile on Cape Cod, are possible.

This study provides evidence that people exposed to comparable levels of PCE as the Camp Lejeune cohort are at an increased risk of kidney cancer.

2. Andrew et al., 2022, *Kidney Cancer Risk Associated with Historic Groundwater Trichloroethylene Contamination*

Water contamination is not limited to Camp Lejeune or Massachusetts [Andrew AS. *Inter J Environ Res Public Health* 2022;19:618]. The Andrew authors identified 292 cases of kidney cancer and 448 age- and gender-matched controls in New Hampshire. They also searched a commercial financial database for address histories of the cases and controls. They then used publicly available data on TCE concentrations in groundwater measured at contaminated sites within the state, and then modeled the spatial dispersion and temporal decay of TCE. The authors lastly overlaid geospatial residential locations of cases and controls with maps of estimated TCE concentrations to estimate median exposures to TCE before the kidney cancer diagnosis. They found that residential exposure to TCE in groundwater was associated with an increased risk of kidney cancer. Specifically, individuals in the 50th-75th percentile of estimated residential TCE exposure over a 15-year period had an adjusted odds ratio of 1.78 (95% CI 1.05-3.03) for developing kidney cancer compared to those in the <50th percentile. The authors found that sustained exposures to 0-25ppb of TCE was causally related to kidney cancer development.

3. Alaneet et al., 2015, *Trichloroethylene Is Associated with Kidney Cancer Mortality: A Population-based Analysis*

This study sought to examine the association between the distribution of TCE exposure and mortality from kidney cancer in 163 counties across the U.S. [Alaneet S. *Anticancer Res* 2015;35: 4009-14] They assessed the association of TCE discharged from industrial sites and the adjusted incidence and mortality rates for kidney cancer in each of the counties.

Compared to counties with low release of TCE, counties with intermediate or high TCE release had higher mortality rates for kidney cancer. The authors highlighted the importance of this finding because the data indicate that TCE exposure is predisposing patients to a more aggressive form of kidney cancer with a resultant higher mortality rate.

C. Evidence from Camp Lejeune Studies Confirms That These Chemicals Cause Kidney Cancer at Detected Concentrations

Extensive research has already shown that TCE, benzene, vinyl chloride, and PCE are capable of causing kidney cancer, 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 of most importance when looking at effects of these exposures, confirming a link between the contaminated water and an increased risk of kidney cancer 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 superior 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 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 kidney cancer. The unique epidemiological focus on Camp Lejeune offers 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.

1. **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. This was a quasi-experimental design: Camp Lejeune and Camp Pendleton are both military bases and likely to be similar populations. The key difference is that people at Camp Lejeune were exposed to the chemicals of interest here (TCE, PCE, benzene, and vinyl chloride) while people at Camp Pendleton were not.³

The study noted, "On average, an individual in the Camp Lejeune cohort resided at the base for 18 months." [Bove 2014a at 3]. Researchers anticipated a "healthy veteran effect" in that the Marines would have better outcomes than the general population by virtue of Marines being typically healthier than the average

³ Camp Pendleton was chosen in these studies as a comparison based on the assumption that the Camp Pendleton cohort was not exposed to these chemicals. But there is some suggestion in the literature that even the Marines and civilians at Camp Pendleton might have been exposed. If so, that does not undermine the signal being generated from these studies. To the contrary, if the Camp Pendleton cohort was also exposed, that suggests that the results comparing Camp Lejeune to Camp Pendleton would be biased toward the null, *i.e.*, it suggests that the risk ratios in these studies are *understated*, and that if a comparison had been made to a population of Marines that was truly unexposed, the risk ratios would have been even higher.

American. [Bove 2014a at 6] Yet, the data showed the opposite for kidney cancer. Compared with even the overall mortality rates in the United States, the Marines and Navy personnel at Camp Lejeune had higher mortality rates from kidney cancer, with a SMR of 1.16 (95% CI 0.84-1.57).⁴

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

TCE: Low exposure (1–3,100 $\mu\text{g/L-month}$), medium exposure (3,100–7,700 $\mu\text{g/L-month}$), and high exposure (7,700–39,745 $\mu\text{g/L-month}$).

PCE: Low exposure (1–155 $\mu\text{g/L-month}$), medium exposure (155–380 $\mu\text{g/L-month}$), and high exposure (380–8,585 $\mu\text{g/L-month}$).

Vinyl Chloride: Low exposure (1-205 $\mu\text{g/L-month}$), medium exposure (205-500 $\mu\text{g/L-month}$), and high exposure (500 – 2800 $\mu\text{g/L-month}$).

Benzene: Low exposure (2–45 $\mu\text{g/L-month}$), medium exposure (45–110 $\mu\text{g/L-month}$), and high exposure (110–601 $\mu\text{g/L-month}$).

TVOC: Low exposure (1–4,600 $\mu\text{g/L-month}$), medium exposure (4,600–12,250 $\mu\text{g/L-month}$), and high exposure (12,250–64,016 $\mu\text{g/L-month}$).

The authors then calculated the risk of kidney cancer for different exposure levels. First, they compared Marines stationed at Camp Lejeune with those at Camp Pendleton who had either “No/very low cumulative exposure” or “low to high cumulative exposure.” This ensured the increased kidney cancer risk was attributable to “cumulative exposures to the contaminants” rather than “due to some other factor.” [Bove 2014a at 9]

The results indicated that the kidney cancer risk was in fact due to the chemicals. For TCE, Marines with No/Very low exposure (less than 1 $\mu\text{g/liter-month}$) did not show an increased risk of kidney cancer (HR = 0.95; CI 0.48-1.86). But for Marines with low to high cumulative exposure (more than 1 $\mu\text{g/liter-month}$), they had a 50% increased risk of kidney cancer compared to Camp Pendleton (HR =1.50; CI 0.91-2.49). [Bove 2014a Addition File 1: Table S3]

Similarly, for PCE, Marines with No/Very low exposure (less than 1 $\mu\text{g/liter-month}$) did not show an increased risk of kidney cancer (HR = 0.91; CI 0.46-1.78). However, those with low to high cumulative exposure (more than 1 $\mu\text{g/liter-month}$) had a 55% increased risk of kidney cancer compared to Camp Pendleton (HR =1.55, CI: 0.94-2.57). [Bove 2014 Addition File 1: Table S3]

For TVOC (a combination of all the chemicals) Marines with No/Very low exposure (less than 1 $\mu\text{g/liter-month}$) did not show an increased risk of kidney cancer (HR 0.92; CI 0.46-1.85). But for Marines with low

⁴ By contrast, for Marines at Camp Pendleton, the Healthy Veteran Effect predominated. Marines at that base (unlike Camp Lejeune) had *lower* rates of kidney cancer versus the general population, with a SMR of 0.89 (0.61-1.25).

to high cumulative exposure (more than 1 µg/liter-month), they had a 50% increased risk of kidney cancer compared to Camp Pendleton (HR 1.50; CI 0.91-2.47). [Bove 2014 Addition File 1: Table S3]

Finally, the study examined the relationship between cumulative exposure at Camp Lejeune itself. For TCE, Marines with low, medium, and high exposures had risks ratios of 1.54, 1.21, and 1.52, respectively. [Bove 2014a Additional file 2: Table S1] For PCE, the risks were 1.40, 1.82, and 1.59. [Bove 2014a Additional file 2: Table S]. And for TVOC, Marines with low, medium, and high exposures had risks of 1.42, 1.44, and 1.55, respectively. [Bove 2014a Additional file 2: Table S1] The authors noted that they “observed a monotonic exposure-response relationship for kidney cancer” and TVOC and a “non-monotonic exposure-response trend for PCE and kidney cancer.” [Bove 2014a at 9]

The findings demonstrated a non-linear exposure-response relationship, with significant increases in mortality risk found in different cumulative exposure levels. Specifically, cumulative exposure within the range of 1 to 4,600 microgram/liter-month (of TCE, PCE, and the combination of the chemicals) is sufficient to cause kidney cancer per Bove *et al.* Additionally, the data show that higher levels of cumulative exposure, such as to PCE of 155-380 µg/liter-months, and to TCE 3,100–7,700 µg/liter-months, is sufficient to cause kidney cancer.

None of these discussed concentrations represent threshold doses. Meaning, these results don’t suggest lower amounts are also not enough to cause kidney cancer. These are simply the cutoffs used in this particular epidemiological study. While the study did not establish clear exposure thresholds, it is clear that the levels of contamination at Camp Lejeune were high enough to be hazardous to humans generally and cause kidney cancer, with no indication that the risk would decrease at lower levels of exposure.

The Bove 2014a study offers strong evidence that the contamination at Camp Lejeune significantly increased the risk of kidney cancer-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.

2. 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 1.92 (95% CI 0.58–6.34) for kidney cancer, representing a 92% increased mortality risk. This finding underscores the potential for Camp Lejeune’s chemical contamination to contribute to kidney cancer, with an average exposure duration of 2.5 years. These findings reinforce the idea that the chemicals at Camp Lejeune were present in sufficient quantities to cause kidney cancer. Given the median employment duration “was about 2.5 years”, the results strongly suggest that 2.5 years of employment at the base is

sufficient to cause kidney cancer. [Bove 2014b at 2]. However, this does not suggest shorter periods of exposure do not also elevate the risk—it merely reflects the median employment length in this study.

There are clear differences between civilians who only worked on base and Marines who lived on base. For instance, Marines would have had daily exposure to contaminated water through activities like showering and eating, while civilians might not all have had this additional exposure, often only being on base during their work hours. Additionally, Marines may have had more exposure to harmful vapors containing chemicals like TCE, PCE, benzene, and vinyl chloride, especially if they slept in the barracks.

This study also compared civilians at Camp Lejeune with below median exposure to those with above median exposure. For TVOC, the hazard ratio was 4.44, indicating a 344% increased risk of dying of kidney cancer. For PCE and TCE, all of the kidney cancers occurred in above-median exposed civilians, theoretically suggesting an infinite increased risk (and practically making the result difficult to evaluate). The median exposure to PCE in the Bove 2014b study was 22.3 µg/L-year, and the median exposure to vinyl chloride was 34.54 µg/L-year (based upon my review of the document, it does not appear that the median exposures for TCE or benzene were reported).

3. 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 ATSDR morbidity study [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] was conducted by the Agency for Toxic Substances and Disease Registry and surveyed over 200,000 Marines stationed at Camp Lejeune between 1972-1985, along with a comparator group of 50,000 Marines stationed at Camp Pendleton during that same period. The survey also included more than 8,000 civilians who worked at Camp Lejeune and a comparator of 7,000 civilians who worked at Camp Pendleton. The study aimed “to evaluate whether exposure to the contaminated drinking water at Camp Lejeune was associated with medically confirmed specific diseases of interest.”

The results showed that Marines at Camp Lejeune had a relative risk of developing kidney cancer of 1.31 (95% CI 0.86-1.99), indicating a 31% increased risk compared to the Marines at Camp Pendleton. Civilians working at Camp Lejeune had an even high relative risk of 1.52 (95% CI 0.69-3.35), reflecting a 52% increased risk. These findings provide compelling evidence that exposure to the water at Camp Lejeune is sufficient to cause kidney cancer.

The study also analyzed kidney cancer risk based on specific degree of chemical exposure, comparing Marines at Camp Pendleton with those at Camp Lejeune who had varying degrees of exposure to the specific chemicals water. Using water distribution models and residential locations and periods of residence at Camp Lejeune, the authors calculated cumulative and average residential exposure to each contaminant. Marines at Camp Lejeune with medium exposure to TCE (defined as between 110 and 11,030 ppb-months) had a relative risk of kidney cancer of 1.33 (95% CI 0.84-2.13) - a 33% increased risk compared with their peers at Camp Pendleton. For Marines with high exposure (more than 11,030 ppb-months), that risk increased to 1.42 (95% CI 0.78-2.58). These findings indicate 110-11,030 ppb-months of exposure to TCE is causally related to kidney cancer.

Marines with medium exposure to PCE (defined as between 36 and 711 ppb-months) had a relative risk of kidney cancer of 1.28 (95% CI 0.79-2.05), a 28% increased risk compared to their peers at Camp Pendleton. For Marines with high exposure to PCE (more than 711 ppb-months), that risk increased to 1.79 (95% CI

1.02-3.12). These findings indicate 36 ppb-months to 711 ppb-months of exposure to PCE is enough to show hazard to human health and a causal connection to kidney cancer.

Civilians with medium combined exposure to TCE and PCE (defined as between 10,868 and 50,563 ppb-months of TCE exposure or between 457 and 2,118 ppb-months of PCE exposure) had a relative risk of 1.80 (95% CI 0.68-4.76), corresponding to an 80% increased risk compared to Camp Pendleton civilians. Civilians with high combined TCE and PCE exposure showed a relative risk of 13.92 (95% CI 5.09-38.1), corresponding to a staggering (and statistically significant) increased risk of 1,292% compared with Camp Pendleton civilians. This civilian exposure and findings make clear that exposure to 10,868 ppb-months to 50,563 ppb-months of TCE or 457 ppb-months to 2,118 ppb-months of PCE is causally related to kidney cancer.

As a final comparative set, study authors looked at Camp Lejeune personnel who were exposed to higher amounts of TCE and PCE and personnel stationed at Camp Lejeune who were exposed to lower amounts. Marines exposed to between 110 and 11,030 ppb-months of TCE had an increased risk of kidney cancer of 1.45 (95% CI 1.05-2.00). The risk increased as levels of exposure increased; those with high levels of exposure had a relative risk of 1.55 (95% CI 0.95-2.54). These results show a dose in the range of 110 to 11,030 ppb-months of TCE exposure is sufficient to be causally related to kidney cancer.

Marines with exposure of between 36 and 711 ppb-months of PCE had a relative risk of 1.43 (95% CI 1.02-2.00) contrasted with Marines exposed to lower amounts. Again, risks increased even further with higher levels of exposure, with odds ratios equaling 2.01 (95% CI 1.20-3.13). The conclusion is that a dose in the range of 36 to 711 ppb-months of PCE exposure is causally related to kidney cancer.

For civilians with medium exposure (defined as between 10,868 and 50,563 ppb-months of TCE exposure or between 457 and 2118 ppb-months of PCE exposure) the relative risk was 5.34, indicating a 434% increase in kidney cancer risk. At even higher levels of exposure, the risk climbed to 41.54 (95% CI 10.2-169.23), indicating an increased risk in the tens of thousands percent. It is clear from these results that being exposed to either 457-2,118 ppb-months of PCE or 10,868-50,563 ppb-months of TCE is causally related to kidney cancer.

4. 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.

Navy/Marine personnel at Camp Lejeune showed a hazard ratio for dying of kidney cancer of 1.21 (95% CI 0.95-1.54) compared against those at Camp Pendleton. Civilian employees at Camp Lejeune showed a hazard ratio for dying of kidney cancer of 1.49 (95% CI 0.76-2.92), corresponding to a 49% increased risk. Subgroup analyses focused on the underlying cause of death from kidney cancer also showed an increased risk of 1.44 (95% CI 0.73-2.84). Consistent with earlier studies, this paper demonstrates the sufficiency of the concentrations of the chemicals present at Camp Lejeune to cause kidney cancer.

Study authors also assessed the risk of kidney cancer based on exposure duration, specifically the time spent on base. For Navy and Marine personnel stationed on base, an increased risk of kidney cancer was observed even at short duration (for instance, just 1-2 quarters on base) – HR 1.33 (95% CI 0.95-1.86). [Bove 2024 Supplemental Table S6]. Similarly, civilians on base also showed an increased risk of kidney cancer at short duration (e.g., 1-2 quarters on base: HR 1.36 (95% 0.48-3.82)). [Bove 2024 Supplemental Table S8]. In

addition, the authors found elevated risks at medium duration (6-22 quarters: HR 1.36 (95% CI 0.54-3.41) and high duration (23-54 quarters: HR 1.68 (95% CI 0.75-3.76). These findings show that even a brief exposure of 1-2 quarters on base between 1972-1985 is associated with an increased risk of kidney cancer. The same risk applies to individuals who were exposed at different times but accumulated a dose equivalent to having spent that amount of time on base during those years. The authors ultimately concluded, “The results of this study are relevant to everyone exposed to the contaminated drinking water at Camp Lejeune” and suggested that “continued follow-up is indicated” for people who might have been exposed to these chemicals.

5. Bove 2024b Study: *Cancer Incidence Among Individuals Exposed to Contaminated Drinking Water at Camp Lejeune*

Like the previous Bove studies, the 2024 cancer incidence study [Bove FJ. *Environ Health Perspect* 2024;132:107008-1 through 15]] compared cancer rates at Camp Lejeune to the similar cohort at Camp Pendleton. The study then examined cancer incidence of cancer among these individuals between 1996 and 2017 in order to determine whether being stationed or employed at Camp Lejeune increased the risk of cancer incidence. Camp Pendleton, which housed a similar population but “was not known to have contaminated drinking water,” was viewed as an ideal comparator to base the experimental design upon. Again, the two populations of Marines/Navy personnel and civilians theoretically are identical in all material respects except for the exposure to hazardous amounts of the chemicals described above experienced by the Camp Lejeune cohort.⁵

In addition to the overall comparison of cancer rates between Camp Lejeune and Camp Pendleton, the study also analyzed cancer risk in relation to the total exposure to the chemicals, using “duration of assignment” (for the Marines/Navy) and “duration of employment” (for the civilians) “as a surrogate for overall cumulative exposure.” For Marines, “low duration” was defined as 1-6 quarters, “medium duration” was defined as 7-10 quarters, and “high duration” was defined as more than 10 quarters on base. For civilian workers, “low/medium duration” was defined as 1-21 quarters on base, and “high duration” was defined as >21 quarters on base.

Again, results found that individuals stationed at Camp Lejeune had a higher incidence of kidney cancer. Overall, Marines and Navy personnel showed a relative risk of 1.06 (95% CI 0.95-1.18) and civilians showed a relative risk of 1.12 (95% CI 0.76-1.67). These findings suggest exposure to the water at Camp Lejeune, particularly during the years 1975-1985, increases the risk of kidney cancer.

For Marines with “low duration” exposure at Camp Lejeune (1-6 quarters on base), the relative risk of kidney cancer was 1.12 (95% CI 0.99-1.27) compared to Marines stationed at Camp Pendleton. This indicates even short term exposure—equivalent to 1-6 quarters on base—during the 1975-1985 period – was sufficient to increase the risk of kidney cancer. For civilians with high duration exposure, the relative risk of kidney cancer was 1.70 (95% CI 0.93–3.13), further supporting the link between prolonged exposure to contaminated water and hazard to human health and a causal relationship to kidney cancer.

Epidemiological studies that do not yield statistically significant results do not negate the validity or importance of studies that do show positive results. This is due to several key factors in the interpretation and evaluation of scientific evidence.

⁵ See page 23 fn. 3.

Statistical significance does not always equate to clinical or practical significance. A study may fail to reach statistical significance but still provide valuable information. Non-significant results can be clinically significant, even with insufficient statistical power.

Furthermore, each epidemiological study has its own limitations and potential biases and confounding, which cannot always be accounted for. Like all sciences, toxicology and epidemiological data build knowledge cumulatively. Individual studies contribute to a broader body of evidence, and their results should be synthesized and evaluated collectively. While the replication of findings in diverse populations and through different study designs is important and the ideal, significant inherent differences in study populations, available data, and study design often leads to imprecision across studies.

Lastly, recognizing and communicating uncertainty is crucial in research. All scientific work, whether observational or experimental, is incomplete and subject to modification as knowledge advances. So the presence of non-significant results in some epidemiological studies do not invalidate the positive findings of others. Instead, they contribute to the overall body of evidence, which must be carefully evaluated and synthesized to draw meaningful conclusions about causal relationships and public health implications.

6. 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 suggests 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.

7. Studies That Did Not Show an Association Between Camp Lejeune Chemicals and Kidney Cancer

In my review of the literature, I also considered studies that did not demonstrate an association between the Camp Lejeune water contaminants and kidney cancer.

For instance, in 1997 McLaughlin and Blot (1997) conducted a review of epidemiological studies and found little evidence of an increased risk of renal cell cancer with exposure to TCE or PCE. [McLaughlin JK and Blot WJ. *Inter Arch Occup Environ Health* 1997;70:222-31]. However, this study was published in 1997, and subsequent studies have reliably found an association with kidney cancer. This is one example of how it takes time for science evidence to accumulate and evolve.

Another publication that did not detect an association between exposure to TCE and kidney cancer was by Vlaanderen *et al.* in their study of occupational exposure in Nordic countries. [Vlaanderen J. *Occ Environ Med* 2013;70:393-401]. They reported a hazard ratio of 1.03 (95% CI 0.97-1.10) for those exposed in the highest tercile of TCE. However, the authors acknowledged that “this study was subject to limitations related to the low prevalence of exposure to PER and TCE in the Nordic population and a limited exposure assessment strategy... .”

Studies have also failed to find an association between benzene and kidney cancer. For instance, a report from the Shanghai Men's Health Study by DeMoulin *et al.* did not find an positive association or a dose-response effect for kidney cancer among men with occupational benzene exposure using a job exposure matrix, [DeMoulin D. *Cancer Epidem Biomarker Prevent* 2024;33:1465–74]

With regards to vinyl chloride and kidney cancer, Bosetti *et al.* reviewed the epidemiologic literature and found inconsistent evidence for an association between vinyl chloride exposure and kidney cancer, with no significant excess mortality from kidney cancer observed in large cohort studies. [Bosetti C. *Euro J Cancer Prevent* 2003;12:427-30] Similarly, Wong *et al.* did not find any excess in kidney cancer mortality among vinyl chloride workers in their industry-wide epidemiologic study [Wong O. *Am J Indust Med* 1991;20:317-34].

Again, while these studies exist, they do not negate the positive findings in the many other studies detailed above.

IX. OTHER RELEVANT CONSIDERATIONS

A. Carcinogenic Latency

The concept of latency is important when discussing adverse health effects, including cancer. In short, latency is the amount of time that elapses between an exposure to a carcinogen and the diagnosis of cancer. However, there are several confounding factors when assessing cancer latency because of exposure, especially as cancer risk increases over one’s lifetime. A significant limitation to much of toxin-induced cancer research is the reliance on mortality from cancer rather than on the diagnosis. This concept is critically important when trying to determine the risk of cancer from a toxic exposure, because mortality studies will only detect the cancer if the person dies of that cancer. However, if someone dies *with* a cancer (rather than because of the cancer), then that person would not be counted as having developed cancer from the exposure, thus severely limiting the ability for mortality studies to detect an association between exposure and cancer. Furthermore, if a person has developed cancer due to an exposure, but their death certificate does not expressly list the cancer as the cause of death (*e.g.*: the person dies of a myocardial infarction or stroke which were unrelated to their cancer), then that patient would also not be counted as having died of their toxin-induced cancer. For these reasons, mortality studies are likely to underestimate this issue.

Important information about cancer latency comes from studies performed in Hiroshima and Nagasaki, Japan. The detonation of the atomic bombs provided a perfectly established exposure time to a known carcinogen (ionizing radiation). A number of study cohorts from Japan have been followed for nearly 80 years, providing information on the increased risk of cancers, as well as latency, and the effect of age of exposure to a carcinogen and cancer development. Preston *et al.* examined members of the Life Span Study of Hiroshima and Nagasaki survivors through 1998. They found a 17% decrease in the risk of cancer for every decade of age at the time of the bombing (Preston DL. *Rad Res* 2007;168:1-64). Preston has followed-up that study with another examining excess risk of cancers in people exposed *in utero* or in childhood to ionizing radiation (Preston DL. *J Natl Cancer Inst* 2008;100:428-36). They found excess absolute rates of

cancer increased markedly with attained age among those exposed in early childhood but exhibited little change in the *in utero* group. At age 50, the estimated excess absolute rates per 10,000 person-years per Sievert (a measure of radiation exposure) were 6.8 for those exposed *in utero*, and 56 for those exposed as young children. This data is important and informative for the people exposed to the carcinogens from water at Camp Lejeune. Firstly, the risk of adverse effects (at least carcinogenicity) is greatest for *in utero* and childhood exposures. Secondly, there is a significant latency to the development of cancer after exposure. Thus, ongoing psychological stress and the need for medical monitoring needs to be considered.

B. 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, vinyl chloride – 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).⁶ 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 exposed to more than one of the relevant chemicals in the 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 vinyl chloride 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.⁷ “Trichloroethylene (TCE) and tetrachloroethylene (PCE) are structurally

⁶ 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.”

⁷ 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.

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 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.⁸ TCOH and related chemicals have been studied for their carcinogenic potential.⁹

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).¹⁰ 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.¹¹ 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.¹²

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.: $2 + 2 = 3$);¹³ 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

⁸ Luo 2018, citing Chiu WA. *Toxicol Sci* 20078;95:23-36.

⁹ 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 cytotoxic, mutagenic, and carcinogenic effects.

¹⁰ Luo 2018, citing Lash LH. *Environ Health Perspect* 2000;108:177-200.

¹¹ *Id.*

¹² Luo 2018, citing Lash LH. *Mutat Res Rev Mutat Res* 2014;762:22-36.

¹³ 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.

combination effect that is greater than the additive effect expected. Synergy can also be called superadditivity.

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 suggest 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.¹⁴

¹⁴ 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

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.¹⁵ The science of additive and synergistic interactions between multiple chemical contaminants such as, e.g., the PCE, TCE, DCE, vinyl chloride and benzene series here, 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.

C. Urothelial carcinoma of the renal pelvis

Urothelial carcinoma of the renal pelvis or upper tract is a cancer located in the kidney. It has some properties that are different from renal cell carcinoma, the most common form of kidney cancer. These cancers are often thought of as having more in common with bladder tumors from a cellular standpoint, however, the majority of epidemiology studies include these cancers with other kidney cancers, such as renal cell carcinoma. In fact, in the studies that analyze urothelial carcinoma of the upper tract separately from renal cell carcinoma or other kidney cancers, the measure of association is very similar between the two kidney cancers. Further, in studies that include upper tract urothelial carcinomas with other kidney cancers, as compared to studies that do not include these cancers with other kidney cancers, the measures of association are closely related. (Lynge 1997; Raaschou-Nielsen 2003).

As a result of the above, kidney cancer epidemiology will be used in any causation analysis involving urothelial carcinoma of the upper tract. Further, TCE, PCE, vinyl chloride, and benzene are all known to cause upper tract urothelial carcinoma, as is explained by the data in this report.

X. BRADFORD HILL ANALYSIS

A. TCE

I generally followed the weight of the evidence approach to investigating and analyzing the data on TCE, PCE, benzene, and vinyl chloride exposure and adverse health effects in the Camp Lejeune cohort. However, I have also evaluated adverse health effects and the Camp Lejeune water through consideration of the Bradford Hill “considerations.” Published as nine viewpoints in 1965, the Bradford Hill considerations are often used to determine if observed epidemiologic associations are causal. Those nine principles are: strength of association; consistency; specificity; temporality; biological gradient;

(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....”).

¹⁵ See Alejandro F. GeoHealth 2022;6 (so stating).

plausibility; coherence; experiment; and analogy. This section is naturally a summary of the evidence on the many pages preceding. Not all of the studies and evidence will be repeated in full in each of the Bradford Hill considerations to which they pertain, but the evidence from the prior sections will be incorporated by reference.

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 TCE water of greater than 1.1. The 1.1 amount is used here given the lower standard at issue, as described earlier, of “as likely than not” or “equipoise.” That is consistent with my education, training and experience and the science as it exists. For example, ATSDR used a threshold of risk of ≥ 1.1 in their assessment of equipoise or greater. 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 individuals exposed to Camp Lejeune water as well as studies of occupational exposure and other environmental pollution, reliably demonstrate risks of greater than 1.1 for exposure to TCE and kidney cancer. For example, the Kelsh study found a summary RR of 1.42, and the Scott and Jinot study found a summary risk of 1.27 for TCE exposure and kidney cancer.

The Bradford Hill term of consistency refers to the concept that studies done in different populations yield similar results. This consideration is also met in that studies utilizing varied *in vitro*, animal studies, and human studies consistently demonstrate kidney cancer after exposure to TCE.

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 consideration is difficult to meet with the chemical contaminants at Camp Lejeune with regards to TCE.

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

The concept of a biological gradient is that a dose-response exists. That is, 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 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 TCE exposure and the occurrence of kidney cancer. Of note, there are several of the studies designed to specifically look at exposures at Camp Lejeune that found a dose response and found that with increased exposure came increased causal relationship to kidney cancer.

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 were detailed. There have been several epidemiological studies performed examining TCE

exposure. Given this abundant evidence, it is my opinion that the biologic plausibility standard has been met with regards to TCE exposure and kidney cancer.

The Bradford Hill consideration 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 contaminant TCE found at Camp Lejeune is a known carcinogen. There are mechanistic, animal, and human studies evaluating the effect of TCE on kidney gene expression and the occurrence of kidney cancer. It is my opinion that the consideration of coherence has also been met.

Bradford Hill also identified experimentation as a consideration 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 expose individuals (particularly children) for any significant length of time to TCE by any method of exposure. However, there are decades of epidemiologic research which demonstrate that TCE causes cancer, and specifically that TCE causes kidney cancer. Therefore, it is my opinion that the experimentation consideration has also been met.

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, PCE, and vinyl chloride) causing various cancers, with TCE specifically causing kidney cancer. With the wide range and varied adverse effects (including carcinogenesis) of the chlorinated solvents, it is my opinion that the analogy consideration has also been met.

When the body of research on TCE is considered in light of the Bradford Hill considerations, I am able to opine that exposure to TCE at Camp Lejeune, including at the levels that existed at Camp Lejeune during the relevant time period, was hazardous to human health and is more likely than not known to cause kidney cancer. This opinion is given to a standard more rigorous than the as likely than not standard that needs to be met according to the statute at issue. However, it is also important to note that the Bradford Hill considerations 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.

Furthermore, under an as likely as not or equipoise standard, it is also my opinion that the TCE water contaminant present at Camp Lejeune causes kidney cancer and is hazardous to humans generally.

B. PCE

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. However, I have also evaluated adverse health effects and the Camp Lejeune water through consideration of the Bradford Hill “considerations.” This section is naturally a summary of the evidence on the many pages preceding. Not all of the studies and evidence will be repeated in full in each of the Bradford Hill considerations to which they pertain, but the evidence from the prior sections will be incorporated by reference.

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 PCE water of greater than 1.1. The 1.1 amount is used here given the lower standard at issue, as described earlier, of “as likely than not” or “equipoise.” That is consistent with my education, training and experience and the science as it exists. For example, ATSDR used a threshold of risk of ≥ 1.1 in their assessment of equipoise or greater. 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 kidney cancer. For instance, Purdue *et al.* found an OR of 3.1 (95% CI 1.3-7.4) for high cumulative exposure to PCE and kidney cancer, indicating a strong association [Purdue MP. *Occup Environ Med* 2017;74:268–74]

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 Vlaanderen 2013 study did not find a significant association between PCE exposure and kidney cancer in a Nordic population, suggesting some inconsistency in the findings. As cited above, there are several studies that did find an association between PCE and kidney cancer, which supports the consistency analysis. Furthermore, the studies that analyzed the specific circumstances at issue here, the epidemiology studies involving Camp Lejeune, had fairly consistent findings with regard to the development of kidney cancer as a result of exposure to the toxic water, which included PCE. Based on the significant evidence that does exist, this consideration is as likely than not met.

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 consideration is difficult to meet with PCE.

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

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 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 PCE exposure and the occurrence of kidney cancer. For instance, Purdue *et al.* [Purdue 2017] reported a higher risk of kidney cancer with increased cumulative hours of PCE exposure, indicating a biological gradient.

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 were detailed. Specifically, Guyton *et al.* discussed the toxicokinetics and toxicodynamics of PCE, providing evidence of its potential to cause kidney toxicity through metabolic pathways. [Guyton KZ. *Environ Health Perspect* 2014;122:325-34]

The Bradford Hill consideration 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 mechanistic, animal, and human studies evaluating the effect of PCE on kidney gene expression [Zhou YH. *Toxicol Sci* 2017;160:95-110] and the occurrence of kidney cancer. It is my opinion that the consideration of coherence has also been met.

Bradford Hill also identified experimentation as a consideration 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 expose individuals (particularly children) for any significant length of time to these chemicals by any method of exposure. However, there are decades of epidemiologic research which demonstrate that PCE causes cancer, and specifically that PCE causes kidney cancer. Therefore, it is my opinion that the experimentation consideration has also been met.

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, PCE, and vinyl chloride) causing various cancers, and specifically causing kidney cancer. With the wide range and varied adverse effects (including carcinogenesis) of the chlorinated solvents, it is my opinion that the analogy consideration has also been met.

When the body of research on PCE exposure is considered in light of the Bradford Hill considerations, I am able to opine that exposure to PCE, including at the levels that existed at Camp Lejeune during the relevant time period, were hazardous to human health and is more likely than not known to cause kidney cancer. This opinion is given to a standard more rigorous than the as likely than not standard that needs to be met according to the statute at issue. However, it is also important to note that the Bradford Hill considerations 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.

Furthermore, under an as likely as not or equipoise standard, it is also my opinion that the PCE water contaminant present at Camp Lejeune causes kidney cancer and is hazardous to humans generally.

C. Vinyl Chloride

I generally followed the weight of the evidence approach to investigating and analyzing the data on and vinyl chloride exposure and adverse health effects in the Camp Lejeune cohort, including kidney cancer. However, I have also evaluated vinyl chloride and kidney cancer through consideration of the Bradford Hill “considerations.” This section is naturally a summary of the evidence on the many pages preceding. Not all of the studies and evidence will be repeated in full in each of the Hill considerations to which they pertain, but the evidence from the prior sections will be incorporated by reference.

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 vinyl chloride in water of greater than 1.1. The 1.1 amount is used here given the lower standard at issue, as described earlier, of “as likely than not” or “equipoise.” That is consistent with my education, training and experience and the science as it exists. For example, ATSDR used a threshold of risk of ≥ 1.1 in their assessment of equipoise or greater. Studies of vinyl chloride exposure often focus on liver angiosarcoma and not kidney cancer. Some studies have not found an association of vinyl chloride with kidney cancer. However, the Hu 2002 study did investigate the occurrence of kidney cancer with exposure to vinyl chloride and found an elevated risk with an OR of 2.0 (95% CI 1.2–3.3). Additionally, the studies relating to Camp Lejeune through Bove and the ATSDR provide further evidence that exposure to vinyl chloride is causally related to kidney cancer.

The Bradford Hill term of consistency refers to the concept that studies done in different populations yield similar results. The majority of epidemiological studies have not reported a significant increase in kidney cancer among vinyl chloride-exposed workers, making the consistency factor difficult to meet. However, the studies that analyzed the specific circumstances at issue here, the epidemiology studies involving Camp

Lejeune, had fairly consistent findings with regard to the development of kidney cancer as a result of exposure to the toxic water, which included VC.

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 vinyl chloride causes other cancers, particularly hepatic angiosarcoma. Therefore, the specificity consideration is difficult to meet with vinyl chloride and kidney cancer.

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

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. Granular dose-response data are not available for the Camp Lejeune cohorts and vinyl chloride. The Hu study provides a dose-response relationship and in conjunction with Bove 2014, there is limited evidence of a dose-response relationship between vinyl chloride exposure and kidney cancer.

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 vinyl chloride exposures were detailed. There have been several epidemiological studies performed for the chemicals at issue here, documenting breakdown of the chemicals and reactive metabolites. Given this abundant evidence, it is my opinion that the biologic plausibility standard has been met with regards to vinyl chloride exposure and kidney cancer.

The Bradford Hill consideration 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 vinyl chloride) are known or probable carcinogens. There are mechanistic, animal, and human studies evaluating the effect of the chemicals on kidney gene expression and the occurrence of kidney cancer. It is my opinion that the consideration of coherence has also been met.

Bradford Hill also identified experimentation as a consideration to evaluate with regards to causation. Put simply, conduct experiments whereby you either purposely expose individuals to a toxin (such as vinyl chloride), or you eliminate such an exposure and determine the effect on adverse health outcome occurrence. Clearly one cannot ethically expose individuals (particularly children) for any significant length of time to vinyl chloride by any method of exposure. However, there are decades of research which demonstrate that vinyl chloride cause cancer (most specifically, hepatic angiosarcoma), and specifically the Hu study shows that vinyl chloride causes kidney cancer. Therefore, it is my opinion that the experimentation consideration has not clearly been met for vinyl chloride and kidney cancer, but this is largely because there are simply not enough studies that exist on this issue. It is not based on negative studies that do exist because they are also few.

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, PCE, and vinyl chloride) causing various cancers, including kidney cancer. With the wide range and varied adverse effects (including carcinogenesis) of the chlorinated solvents, it is my opinion that the analogy consideration has also been met.

When the body of research on vinyl chloride exposure is considered in light of the Bradford Hill considerations, I am able to opine that exposure to vinyl chloride at Camp Lejeune, including at the levels they existed at Camp Lejeune during the relevant time period, were hazardous to human health and is as likely as not known to cause kidney cancer. However, it is also important to note that the Bradford Hill considerations 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.

In sum, under an as likely as not or equipoise standard, it is my opinion that the vinyl chloride water contaminant present at Camp Lejeune causes kidney cancer and is hazardous to humans generally. As evidence to support this conclusion, it is worth reiterating the accepted science for the “as likely as not” or “equipoise” standard and, in particular, the language from ATSDR used to define how that entity classified equipoise and above evidence of causation:

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.

D. Benzene

I generally followed the weight of the evidence approach to investigating and analyzing the data benzene exposure and adverse health effects in the Camp Lejeune cohort, including kidney cancer. However, I have also evaluated adverse health effects and Camp Lejeune water through consideration of the Bradford Hill “considerations.” This section is naturally a summary of the evidence on the many pages preceding. Not all of the studies and evidence will be repeated in full in each of the Hill considerations to which they pertain, but the evidence from the prior sections will be incorporated by reference.

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 in water of greater than 1.1. The 1.1 amount is used here given the lower standard at issue, as described earlier, of “as likely than not” or “equipoise.” That is consistent with my education, training and experience and the science as it exists. For example, ATSDR used a threshold of risk of ≥ 1.1 in their assessment of equipoise or greater. A systematic review and meta-analysis by Seyyedsalehi *et al.* reported a relative risk of 1.20 (95% CI 1.03-1.39) for kidney cancer among those occupationally exposed to benzene.

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. Multiple studies included in the meta-analysis by Seyyedsalehi *et al.* found an association, although the strength of the association varied across studies. Furthermore, in the case-control study from Germany by Pesch [Pesch 2000], an association was found between benzene exposure and an increased risk of kidney cancer - they found that after controlling for age and smoking, an employment duration exceeding the 90th percentile of benzene exposure in the male British cohort were associated with renal cell carcinoma (OR 1.5; 95% CI 1.0-2.1). Furthermore, the studies that analyzed the specific circumstances at issue here, the epidemiology studies involving Camp Lejeune, had fairly consistent findings with regard to the development of kidney cancer as a result of exposure to the toxic water, which included Benzene.

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. Benzene is known to cause hematologic malignancies, particularly acute myelogenous leukemia (AML). Therefore, the specificity consideration is difficult to meet with benzene and kidney cancer.

Temporality is the easiest of the Bradford Hill consideration to understand, and the one consideration that must be met. Simply put, the exposure must precede the development of the disease. This consideration is also met in the issue at hand with regards to benzene exposure and cancer development.

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 mechanisms of benzene exposure and absorption at Camp Lejeune. The Seyyedsalehi meta-analysis did not find a clear dose-response for benzene and kidney cancer. However, evidence of a monotonic biological gradient for benzene exposure and kidney cancer was found by Hu *et al.* (Hu 2002). It is therefore my opinion that the biological gradient consideration has been met.

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 benzene exposures were detailed. Benzene is a well-known carcinogen with established mechanisms of causing DNA damage and cancer. It is therefore my opinion that the biological plausibility factor is met.

The Bradford Hill consideration 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 well known carcinogen. There are mechanistic, animal, and human studies evaluating the effects of benzene. The association

between benzene and kidney cancer does not conflict with the known facts about benzene's carcinogenic properties, although it is less well-established compared to its effects on hematologic cancers.

Bradford Hill also identified experimentation as a consideration 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 expose individuals (particularly children) for any significant length of time to benzene by any method of exposure. There is limited experimental evidence directly linking benzene to kidney cancer in humans. However, there are decades of research which demonstrate the carcinogenicity of benzene. Therefore, it is my opinion that the experimentation consideration has been partially met.

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. With the wide range and varied adverse effects (including carcinogenesis) of the solvents, and considering benzene's established carcinogenic effects on the hematopoietic system providing some analogy, it is my opinion that the analogy consideration has also been met.

When the body of research on benzene exposure is considered in light of the Bradford Hill considerations, I am able to opine that exposure to benzene at Camp Lejeune, including at the levels that existed at Camp Lejeune during the relevant time period, were hazardous to human health and is as likely as not known to cause kidney cancer. However, it is also important to note that the Bradford Hill considerations 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.

In sum, under an as likely as not or equipoise standard, it is my opinion that the benzene water contaminant present at Camp Lejeune causes kidney cancer and is hazardous to humans generally. As evidence to support this conclusion, it is worth reiterating the accepted science for the “as likely as not” or “equipoise” standard and, in particular, the language from ATSDR used to define how that entity classified equipoise and above evidence of causation:

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.

E. TVOC

I generally followed the weight of the evidence approach to investigating and analyzing the data on the TVOC (that is, TCE, PCE, benzene, and vinyl chloride) exposure and adverse health effects in the Camp Lejeune cohort. However, I have also evaluated adverse health effects and Camp Lejeune water through consideration of the Bradford Hill “considerations.” This section is naturally a summary of the evidence on the many pages preceding. Not all of the studies and evidence will be repeated in full in each of the Hill considerations to which they pertain, but the evidence from the prior sections will be incorporated by reference.

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 combined TVOC in water of greater than 1.1. The 1.1 amount is used here given the lower standard at issue, as described earlier, of “as likely than not” or “equipoise.” That is consistent with my education, training and experience and the science as it exists. For example, ATSDR used a threshold of risk of ≥ 1.1 in their assessment of equipoise or greater. 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 demonstrate risks of greater than 1.1 for exposure to total VOCs at Camp Lejeune and kidney cancer in both Marines and civilians [Bove 2014a and Bove 2014b]. Specifically, Marines with No/Very low exposure (less than 1 $\mu\text{g}/\text{liter-month}$) to TVOC did not show an increased risk of kidney cancer (HR 0.92; CI 0.46-1.85). But for Marines with low to high cumulative exposure (more than 1 $\mu\text{g}/\text{liter-month}$), they had a 50% increased risk of kidney cancer compared to Camp Pendleton (HR 1.50; CI 0.91-2.47). [Bove 2014 Addition File 1: Table S3]

The Bradford Hill term of consistency refers to the concept that studies done in different populations yield similar results. This consideration is also met in that studies utilizing varied *in vitro*, animal studies, and human studies consistently demonstrate kidney cancer after exposure to the VOC water contaminants found at Camp Lejeune.

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 consideration is difficult to meet with the chemical contaminants at Camp Lejeune.

Temporality is the easiest of the Bradford Hill consideration to understand, and the one consideration that must be met. Simply put, the exposure must precede the development of the disease. This consideration is also met with regards to the Camp Lejeune water contaminants and kidney cancer.

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 exposure and absorption at Camp Lejeune. The 2014a study by Bove found that military personnel in the Camp Lejeune cohort had an elevated mortality for kidney cancer (HR 1.35; 95% CI 0.84–2.16) and that a monotonic cumulative exposure trend was observed for kidney cancer and TVOCs.

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. There have been several epidemiological studies performed for the chemicals at issue here. Given this abundant evidence, it is my opinion that the biologic plausibility standard has been met with regards to TVOC exposure and kidney cancer.

The Bradford Hill consideration 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, animal, and human studies evaluating the effect of the chemicals and the occurrence of kidney cancer. It is my opinion that the consideration of coherence has also been met.

Bradford Hill also identified experimentation as a consideration 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 expose individuals (particularly children) 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. Therefore, it is my opinion that the experimentation consideration has also been met.

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 TCE, PCE, benzene, and vinyl chloride) causing various cancers, with TCE specifically causing kidney cancer. With the wide range and varied adverse effects (including carcinogenesis) of the solvents, it is my opinion that the analogy consideration has also been met.

When the body of research on TCE, PCE, benzene, and vinyl chloride exposure is considered in light of the Bradford Hill considerations, I am able to opine that exposure to these chemicals at Camp Lejeune, including at the levels they existed at Camp Lejeune during the relevant time period, were hazardous to human health and are more likely than not known to cause kidney cancer. This opinion is given to a standard more rigorous than the as likely than not standard that needs to be met according to the statute at issue. However, it is also important to note that the Bradford Hill considerations 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.

Furthermore, under an as likely as not or equipoise standard, it is also my opinion that the TVOC water contaminants present at Camp Lejeune causes kidney cancer and is hazardous to humans generally.

XI. CONCLUSION

The water at Camp Lejeune was contaminated for decades with TCE, PCE, vinyl chloride, and benzene. It is my opinion that these water contaminants have been shown to cause adverse health effects, including kidney cancer, 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 kidney cancer. 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 kidney cancer.

Respectfully,

A handwritten signature in black ink, appearing to read 'S. Bird', with a stylized flourish at the end.

Steven B. Bird, MD

**DR. BIRD'S
RELIANCE FILES**

IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF NORTH CAROLINA
SOUTHERN DIVISION

IN RE:)	
)	
CAMP LEJEUNE WATER LITIGATION)	
)	
This Document Relates to:)	Case Nos.:
)	
ALL CASES)	7:23-CV-897
)	
DAVID DOWNS)	7:23-CV-01145-BO
)	
DAVID WILLIAM FANCHER)	7:23-CV-00275-BO-BM
)	
ALLAN WAYNE HOWARD)	7:23-CV-00490-BO
)	
FRANK W. MOUSSER)	7:23-CV-00667-BO-RN
)	
JACQUELINE JORDAN TUKES)	7:23-CV-01553-BO-BM

**PLAINTIFFS' DESIGNATION AND DISCLOSURE OF PHASE II EXPERT
WITNESSES WITH RESPECT TO KIDNEY CANCER**

STEVEN B. BIRD, MD'S RELIANCE FILES

Pursuant to Fed. R. Civ. P. 26(a)(2)(B)(ii) and the Stipulated Order Regarding Expert Discovery (Case Management Order No. 17) (D.E. 305), Plaintiffs hereby identify the facts, data, and publications considered by Steven B. Bird, MD ("Dr. Bird") in forming his opinions concerning general causation and kidney cancer.

Dr. Bird's report, produced contemporaneously herewith, contains a thorough statement of the facts, data, and publications that he considered in forming his opinions, and Plaintiffs incorporate all facts, data, and publications referenced in Dr. Bird's report as if fully listed herein. In addition, Plaintiffs identify the following facts, data, and publications considered by Dr. Bird in forming his opinions:

1. 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 Feb 19 (bates number CLJA_HEALTHTHEFFECTS-0000141103);
2. Bove FJ, Ruckart PZ, Maslia M, Larson TC. Mortality study of civilian employees exposed to contaminated drinking water at USMC Base Camp Lejeune: a retrospective cohort study. Environ Health. 2014 Aug 13 (bates number CLJA_VA_RFP_4THSET_0000135084));
3. ATSDR Public Health Assessment, 2017 (bates number CLJA_HEALTHTHEFFECTS-0000000011);
4. ATSDR Assessment of the Evidence for the Drinking Water Contaminants at Camp Lejeune and Specific Cancers and Other Diseases, 2017 (bates number CLJA_VA-RFP11-0000000131);
5. 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 (bates number CLJA_HEALTHTHEFFECTS-0000000214);
6. Bove FJ, Greek A, Gatiba R, Kohler B, Sherman R, Shin GT, Bernstein A. 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 Oct;
7. Bove FJ. Evaluation of cancer incidence among Marines and Navy personnel and civilian workers exposed to contaminated drinking water at USMC Base Camp Lejeune: a cohort study (Unpublished). 2024 Jan 29 (bates number CLJA_ATSDR_BOVE-0000060101);

8. Bove FJ, Greek A, Gatiba R, Boehm RC, Mohnsen MM. Evaluation of mortality among Marines, Navy personnel, and civilian workers exposed to contaminated drinking water at USMC base Camp Lejeune: a cohort study. *Environ Health*. 2024 Jul 3;
9. Andrew AS, Li M, Shi X, Rees JR, Craver KM, Petali JM. Kidney Cancer Risk Associated with Historic Groundwater Trichloroethylene Contamination. *Int J Environ Res Public Health*. 2022 Jan 6;
10. Aschengrau A, Ozonoff D, Paulu C, Coogan P, Vezina R, Heeren T, Zhang Y. Cancer risk and tetrachloroethylene-contaminated drinking water in Massachusetts. *Arch Environ Health*. 1993 Sep-Oct;
11. Webler T, Brown HS. Exposure to tetrachloroethylene via contaminated drinking water pipes in Massachusetts: a predictive model. *Arch Environ Health*. 1993 Sep-Oct;
12. Aschengrau A, Gallagher LE, Webster TF, Heeren TC, Ozonoff DM. Evaluation of the Webler-Brown model for estimating tetrachloroethylene exposure from vinyl-lined asbestos-cement pipes. *Environ Health*. 2008 Jun 2;
13. Alanee S, Clemons J, Zahnd W, Sadowski D, Dynda D. Trichloroethylene Is Associated with Kidney Cancer Mortality: A Population-based Analysis. *Anticancer Res*. 2015 Jul
14. Fagliano J, Berry M, Bove F, Burke T. Drinking water contamination and the incidence of leukemia: an ecologic study. *Am J Public Health*. 1990 Oct;
15. Moore LE, Boffetta P, Karami S, Brennan P, Stewart PS, Hung R, Zaridze D, Matveev V, Janout V, Kollarova H, Bencko V, Navratilova M, Szeszenia-Dabrowska N, Mates D, Gromiec J, Holcatova I, Merino M, Chanock S, Chow WH, Rothman N. Occupational trichloroethylene exposure and renal carcinoma risk: evidence of genetic susceptibility by reductive metabolism gene variants. *Cancer Res*. 2010 Aug 15;

16. Parker S, Rosen S. Woburn: Cancer Incidence and Environmental Hazards 1969-1978. 1981 Jan 23;
17. Rosenfeld P, Spaeth K, McCarthy S, Winter S, Wilson M, Hagemann M. Camp Lejeune Marine Cancer Risk Assessment for Exposure to Contaminated Drinking Water from 1955 to 1987. 2023 Mar 21;
18. Wong O. An industry wide mortality study of chemical workers occupationally exposed to benzene. I. General results. *Br J Ind Med*. 1987 Jun;
19. Wong O. An industry wide mortality study of chemical workers occupationally exposed to benzene. II. Dose response analyses. *Br J Ind Med*. 1987 Jun;
20. Lynge E, Andersen A, Nilsson R, Barlow L, Pukkala E, Nordlinder R, Boffetta P, Grandjean P, Heikkilä P, Hörte LG, Jakobsson R, Lundberg I, Moen B, Partanen T, Riise T. Risk of cancer and exposure to gasoline vapors. *Am J Epidemiol*. 1997 Mar 1;
21. Collins JJ, Anteau SE, Swaen GM, Bodner KM, Bodnar CM. Lymphatic and hematopoietic cancers among benzene-exposed workers. *J Occup Environ Med*. 2015 Feb;
22. Greenland S, Salvan A, Wegman DH, Hallock MF, Smith TJ. A case-control study of cancer mortality at a transformer-assembly facility. *Int Arch Occup Environ Health*. 1994;
23. Gérin M, Siemiatycki J, Déry M, Krewski D. Associations between several sites of cancer and occupational exposure to benzene, toluene, xylene, and styrene: results of a case-control study in Montreal. *Am J Ind Med*. 1998 Aug;
24. Pesch B, Haerting J, Ranft U, Klimpel A, Oelschlägel B, Schill W, MURC Study Group. Occupational risk factors for urothelial carcinoma: agent-specific results from a case-control study in Germany. 2000;

25. Hu J, Mao Y, White K. Renal cell carcinoma and occupational exposure to chemicals in Canada. *Occup Med (Lond)*. 2002 May;
26. Jones P, Purdue, M. Invited Perspective: Insights into Exposure to Industrial Solvents and Cancer Risk at Camp Lejeune. 2024 Oct;
27. Purdue MP, Stewart PA, Friesen MC, Colt JS, Locke SJ, Hein MJ, Waters MA, Graubard BI, Davis F, Ruterbusch J, Schwartz K, Chow WH, Rothman N, Hofmann JN. Occupational exposure to chlorinated solvents and kidney cancer: a case-control study. *Occup Environ Med*. 2017 Mar;
28. Martin O, Martin S, Kortenkamp A. Dispelling urban myths about default uncertainty factors in chemical risk assessment-sufficient protection against mixture effects? 2013;
29. Vandenberg L, et al. Addressing systemic problems with exposure assessments to protect the public's health 2022;
30. Varshavski, J, et al. Current practice and recommendations for advancing how human variability and susceptibility are considered in chemical risk assessment. 2023;
31. EPA. Toxicological Review of Trichloroethylene. 2011 Sep;
32. ATSDR. Toxicological Profile for Trichlorethylene 2019 Jun;
33. Water Modeling Data – Appendices I, J, H1 & K to Morris Malia’s report in the above-captioned matter, dated October 25, 2024;
34. Deposition of Frank Bove;
35. Deposition of Morris Maslia;
36. The Camp Lejeune Justice Act;
37. *Westberry v. Gislaved Gummi AB*, 178 F.3d 257 (4th Cir. 1999);
38. *Nix v. Chemours Co. FC*, 2023 WL 6471690 (E.D.N.C. Oct. 4, 2023);

39. *Lightfoot v. Georgia-Pacific Wood Prods., LLC*, 2018 WL 4517616 (E.D.N.C. Sept. 20, 2018);
40. *Yates v. Ford Motor Co.*, 113 F. Supp. 3d 841 (E.D.N.C. 2015);
41. *Dew v. E.I. Du Pont de Nemours & Co.*, 2024 WL 4349883 (E.D.N.C. Sept. 30, 2024);
42. *In re Lipitor (Atrovastatin Calcium) Mktg., Sales Practices & Prods. Lia. Litig.*, 892 F.3d 624 (4th Cir. 2018);
43. Order, *In re: Camp Lejeune Water Litigation*, No. 7:23-CV-897, Dkt. No. 227 (E.D.N.C. June 5, 2024);
44. Order, *In re: Camp Lejeune Water Litigation*, No. 7:23-CV-897, Dkt. No. 247 (E.D.N.C. June 28, 2024);
45. All facts and data listed herein are either identified by bates number or are publicly available to and accessible by Defendant United States of America;
46. Dr. Bird reserves the right to review and consider additional facts, data and publications;
47. Dr. Bird reserves the right to consider the report of any other witness in this action;
and
48. Dr. Bird reserves the right to supplement this list of reliance files.

DR. BIRD'S CV

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

Home: 6 Laurel Ridge Ln
Shrewsbury, MA 01545

Telephone: (508) 421-1422
Cell: (508) 868-6705
Fax: (508) 421-1490
E-mail: steven.bird@umassmemorial.org

EDUCATION

M.D., *Alpha Omega Alpha* 1991 – 1995
Northwestern University
Chicago, Illinois

B.S. Biology, *cum laude* 1987 – 1991
Yale University
New Haven, Connecticut

POST-GRADUATE TRAINING

Fellow in Toxicology 2002 – 2004
University of Massachusetts Medical School
Worcester, MA

Chief Resident in Emergency Medicine 2001 – 2002
University of Massachusetts Medical School
Worcester, MA

Resident in Emergency Medicine 1999 – 2002
University of Massachusetts Medical School
Worcester, MA

US Naval Flight Surgeon 1996 – 1999
Marine Corps Air Station Futenma
Okinawa, Japan

Resident in Surgery 1995 – 1996
Naval Hospital San Diego
San Diego, CA

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 3/2016 - current
Department of Emergency Medicine
University of Massachusetts Medical School
Worcester, MA

Associate Professor of Emergency Medicine 1/2010 – 3/2016
Department of Emergency Medicine
University of Massachusetts Medical School
Worcester, MA

Assistant Professor of Emergency Medicine 9/2004 – 1/2010
Department of Emergency Medicine
University of Massachusetts Medical School
Worcester, MA

Instructor of Emergency Medicine 8/2002 – 8/2004
Department of Emergency Medicine
University of Massachusetts Medical School
Worcester, MA

DEPARTMENTAL, SCHOOL, and HOSPITAL APPOINTMENTS

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

IT Steering Council 2/2020 – 11/2024
UMassMemorial Health
Worcester, MA

Space Allocation and Utilization Committee 2/2020 – 2022
UMass Medical School & UMassMemorial Health
Worcester, MA

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

Medical Center/Medical Group Leadership Team 9/2019 – 11/2024
UMassMemorial Health
Worcester, MA

Joint Leadership Team 9/2019 – 11/2024
UMass Medical School & UMassMemorial Health

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 Society for Academic Emergency Medicine	2007
Best Resident Basic Science Presentation Society for Academic Emergency Medicine	2002
Excellence in Research Award New England Regional Research Directors	2002
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

Manuscript reviewer for *JAMA*; *Academic Emergency Medicine*; *Annals of Emergency Medicine*; *Pediatrics*; *Journal of Emergency Medicine*; *Journal of Medical Toxicology*; *Clinical Toxicology*; *The Open Toxicology 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. <https://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 Catalyzt.* 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. <https://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](https://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 lethality 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 10.1007/s13181-010-0075-9
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 organophosphorus 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.
62. **Bird SB**, Gaspari R, Dickson EW. "Early death due to acute, severe organophosphate poisoning is a centrally mediated process". *Acad Emerg Med* 2003;10:295-298.
63. **Bird SB**, Gaspari RJ, Lee WJ, Dickson EW. "Diphenhydramine as a protective agent in severe organophosphate poisoning" *Acad Emerg Med* 2002 9:1369-1372.
64. Bonkovsky H, Azar R, **Bird S**, Szabo G, Banner B "Severe cholestatic hepatitis caused by thiazolidinediones: risks associated with substituting rosiglitazone for troglitazone" *Digest Dis Sci* July 2002;44:1632-1637.
65. **Bird SB**, Dickson EW. "Clinically significant Changes in pain along the visual analog scale" *Ann Emerg Med*. 2001;38:639-643.
66. **Bird SB**, Zarum RS, Renzi FP. "Emergency medicine resident procedure documentation using a handheld computerized device" *Acad Emerg Med*. 2001;8:1200-1203

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.
- Bird SB.** "Antipsychotic Poisoning" *Intensive Care Medicine*. Rippe, and Irwin, Eds. 9th edition.
- Bird SB.** "Antiarrhythmic Poisoning" *Intensive Care Medicine*. Rippe, and Irwin, Eds. 9th edition.
- Bird SB.** "Chromium" Goldfrank L. et al., editors. *Goldfrank's Toxicologic Emergencies*, McGraw Hill. 10th edition.
- Bird SB.** "Acetaminophen Poisoning" *Intensive Care Medicine*. Rippe, and Irwin, Eds. 8th edition.
- Bird SB.** "Anticonvulsant Poisoning" *Intensive Care Medicine*. Rippe, and Irwin, Eds. 8th edition.
- Bird SB.** "Antipsychotic Poisoning" *Intensive Care Medicine*. Rippe, and Irwin, Eds. 8th edition.
- Bird SB.** "Antiarrhythmic Poisoning" *Intensive Care Medicine*. Rippe, and Irwin, Eds. 8th edition.
- Bird SB.** "Chromium" Goldfrank L. et al., editors. *Goldfrank's Toxicologic Emergencies*, McGraw Hill. 9th edition.
- Bird SB.** "Organophosphates and Carbamates" Aghababian R. editor. *Emergency Medicine: The Core Curriculum*. Jones & Bartlett, 2nd edition.
- Bird SB.** "Acetaminophen Poisoning" *Intensive Care Medicine*. Rippe, and Irwin, Eds. 7th edition.
- Bird SB.** "Antipsychotic Poisoning" *Intensive Care Medicine*. Rippe, and Irwin, Eds. 7th edition.
- Bird SB.** "Anticonvulsant Poisoning" *Intensive Care Medicine*. Rippe, and Irwin, Eds. 7th edition.
- Bird SB.** "Beta Blockers" Shannon M. et al., editors. *Clinical Management of Poisoning and Drug Overdose*, WB Saunders. 4th Ed.
- Bird SB.** "Organophosphates and Carbamates" Aghababian R. editor. *Emergency Medicine: The Core Curriculum*. Jones & Bartlett, 1st edition.
- Bird SB.** "Chromium" Goldfrank L. et al., editors. *Goldfrank's Toxicologic Emergencies*, McGraw Hill. 8th edition.
- Bird SB.** *Organophosphates and Carbamates*. UpToDate, 2004-present.
- Bird SB.** *Manual of Overdoses and Poisonings*. Linden, Rippe, and Irwin, Eds. 1st edition. Lipincott Williams & Wilkins, Philadelphia, 2005. **Author of 12 chapters.**
- Bird SB.** "Acetaminophen Poisoning" *Intensive Care Medicine*. Rippe, and Irwin, Eds. 6th edition.
- Bird SB.** "Anticonvulsant Poisoning" *Intensive Care Medicine*. Rippe, and Irwin, Eds. 6th edition.

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 Dysrhythmias Associated with Severe Salicylate Toxicity Kent KJ, Cohen JE, Ganetsky M, **Bird SB**. Clin Toxicol 2006; 44.
15. **Bird SB**, Schmidt K, Kulkarni P, Ferris C. M1 Receptor Activation in the rat: a pHMRI Analysis. Society for Neuroscience Annual Meeting 2005, Miami, FL.
16. **Bird SB**, Lo JCY, Dickson EW, Sivilotti MLA. Multiple centrally-acting antidotes protect against severe organophosphate toxicity.,. J Toxicol Clin Toxicol 2005; 43.
17. **Bird SB**, Dickson EW, Gaspari RJ, Boyer EW, Ferris CF. Brain functional MRI after acute organophosphate poisoning. Acad Emerg Med 2004;11:473.
18. Mazzola JL, **Bird SB**, Brush DE, Boyer EW, Aaron CK. Anticholinergic syndrome after isolated olanzapine overdose. J Tox Clin Tox 2003;41:472.

19. Brush DE, **Bird SB**, Boyer EW, Aaron CK. Geriatric Overdose of 1,4-Butanediol Masquerading as Syncope and Seizure. *J Tox Clin Tox* 2003;41:508.
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.
22. Lovesky D, **Bird S**, Restuccia M, Mangolds G, Dickson EW. Effect of a Paramedic Pain Management Training Program on Pre-hospital Analgesic Use. *Acad Emerg Med* 2003;10:450.
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.
29. **Bird SB**, Gaspari RJ, Aaron CK, Boyer EW, Dickson EW. Nebulized Ipratropium Bromide Offers No Protection Against Severe Organophosphate Poisoning. *J Tox Clin Tox* 2002;40:695.
30. Sivilotti MLA, **Bird SB**, Montalvo M, Aaron CK, Brison RJ, Linden CH, "Serum a-Glutathione S-transferase (aGST) Becomes Elevated Shortly After Subtoxic Acetaminophen Overdose" *Acad Emerg Med* 2002;9:534-535.
31. **Bird SB**. Critical Care Toxicology: Organophosphate Poisoning. 2002 North American Congress of Clinical Toxicology, Palm Springs, CA.
32. **Bird SB**, Gaspari RJ, Lee WJ, Dickson EW. Early Death due to Acute, Severe Organophosphate Poisoning is a Centrally Mediated Process. *Acad Emerg Med* 2002;9:485.
33. **Bird SB**, Gaspari RJ, Lee WJ, Dickson EW. Diphenhydramine as a Protective Agent in Severe Organophosphate Poisoning. *Acad Emerg Med* 2002;9:357.
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" Jan 2021-Dec 2021 Massachusetts Digital Health Right Care 4 You Grant Program	\$ 100,000
"RCT of Wellness Coaches to Decrease Burnout" Jan 2020-Dec 2020 Carl Atkins Risk Management Grant UMassMemorial Healthcare	\$ 12,000
"Development of a Peer Support Network" June 2016-May 2017 Carl Atkins Risk Management Grant UMassMemorial Healthcare	\$ 10,000
"Pharmacotherapy to counterACT parathion-induced NMJ dysfunction" Principal Investigator: Steven B. Bird, MD U01 NIH/NINDS Sept 2013 – Aug 2016	\$3,082,749
"Novel Neuromuscular Protection to CounterACT Acute Organophosphate Poisoning" Principal Investigator: Steven B. Bird, MD R21 NIH/NINDS Oct 2011 – Sept 2013	\$ 823,588
"Use of a bacterial OP hydrolase antidote for parathion poisoning" Principal Investigator: Steven B. Bird, MD R21 NIH/NIEHS Aug 2007 – Aug 2009	\$ 446,875
"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

DR. BIRD'S TESTIMONY HISTORY

Steven B. Bird, MD
6 Laurel Ridge Ln
Shrewsbury, Massachusetts 01545

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-2971LEK-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. Stamford 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