Exhibit 98

General Causation Expert Report of Timothy M. Mallon, M.D., M.P.H., MS.

Leukemia

Prepared by

____

Timothy M. Mallon, M.D., M.P.H., M.S.
Occupational and Environmental Medicine
Adjunct Assistant Professor, Preventive Medicine
Uniformed Services University,
Bethesda, MD, 20814

Consultant Address:
6508 Folded Leaf Square,
Columbia, MD, 21044, the USA

Email: mallonti03@gmail.com

Contents

I. Summary of Opinions 3

II. Expert Qualifications 3

III. Causation Standard 4

IV. Methodology Employed 5

V. Discussion 6

A. Leukemia 6

B. Chemicals in Camp Lejeune Water 7

C. Camp Lejeune Specific Studies and Reports 7

D. TCE AND LEUKEMIA 10

E. Benzene & Leukemia 20

F. Perchloroethylene (PCE) and Leukemia 32

VI. Chemical Concentrations Associated with Cancer Causation 40

VII. ADDITIVE Effects of TCE, PCE, and BenzenE ON LEUKEMIA RISK 41

VIII. CONCLUSION: TCE, PCE, and Benzene EXPOSURE AT LEAST AS LIKELY AS NOT CAUSES LEUKEMIA 42

Case 7:23-cv-00897-RJ Document 465-3 Filed 08/24/25 Page 3 of 67

The following is my medical expert opinion on whether there is at least as likely as not a causal relationship between exposure to the chemicals in the water at the Camp Lejeune military base, including trichloroethylene (TCE), tetrachloroethylene (PCE), and benzene, and the development of leukemia. I hold all of my opinions in this report to a reasonable degree of medical and scientific certainty. I reserve the right to amend my report should new information become available.

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

I. SUMMARY OF OPINIONS

In this report, I conclude to a reasonable degree of medical and scientific certainty that there is:

1. More likely than not a causal relationship between exposure to TCE and leukemia.
2. More likely than not a causal relationship between exposure to benzene and leukemia.
3. At least as likely as not a causal relationship between exposure to PCE and leukemia.

It is my opinion, to a reasonable degree of scientific certainty that it is more likely than not that the combination of chemicals in the water would have created an increased risk for leukemia which was greater than if just one of those chemicals was present in the water.

II. EXPERT QUALIFICATIONS

I am board-certified in preventive medicine (occupational medicine). I hold master's degrees in public health, environmental health and Master of Science in natural resource policy and management. I presently hold an adjunct Assistant Professor position in Preventive Medicine at Uniformed Services University in Bethesda, MD. Prior to my retirement from military service in 2016, I was a full professor in Preventive Medicine at the Uniformed Services University.

For over six years (January 2013 – August 2019), I led a team of investigators studying the association between certain diseases and exposures to burn pit smoke in Iraq and Afghanistan. This team included researchers from the University of Rochester, Clarkson University, Emory University, Uniformed Services University, and the Armed Forces Health Surveillance Agency. We completed a health assessment of 200 service members exposed to burn pit smoke in Iraq and Afghanistan which generated over 30 publications in the peer-reviewed literature and won several awards, including grants from NIEHS, and the Department of Defense's Defense Health Agency, and earned recognition by the American College of Occupational and Environmental Medicine.

I was awarded a Lifetime Achievement Award for Leadership in Academic Medicine and Research in 2019 and the Army Surgeon General's Academic Excellence Award "the A-Designator" as the Residency Director in Occupational Medicine at the Uniformed Services University. I currently consult for the Veteran's Evaluation Services and the Health and Human Services Federal Occupational Health Program.

I was the specialty editor for The Textbook of Military Medicine in Occupational and Environmental Medicine, the specialty editor of three supplements to the Journal of Occupational and Environmental

Medicine in Workers Compensation Programs, and editor of two supplements on Burn Pit Exposures in Iraq and Afghanistan in 2016 and 2019.

I have authored or co-authored over 44 journal articles and written 23 book Chapters for the Textbook of Military Medicine and the Clinics of North America. I also served on the American Board of Preventive Medicine and the Accreditation Council for Graduate Medical Education Residency Review Committee in Preventive Medicine.

My training, expertise, and service have included work specific to environmental exposures and associated cancers. I trained specifically in toxicology, environmental health, environmental epidemiology, and cancer epidemiology as part of my master's in public health coursework in occupational health at the Johns Hopkins University School of Public Health and in my master's in environmental health at the CUNY Hunter College. I have collaborated on epidemiologic studies of agent orange exposure and non-Hodgkin's lymphoma and soft tissue sarcoma for my master's in public health research project. I also served on the Advisory Board for several Residencies in Aerospace and Occupational and Environmental Medicine for the Air Force at Brook Air Force Base, Johns Hopkins Occupational and Environmental Medicine Residency Program in Baltimore Maryland, and the Navy School of Aerospace Medicine and Occupational Medicine in Pensacola, Florida.

I have taught over 200 residents in occupational and environmental medicine as the occupational and environmental medicine residency program director at the Uniformed Services University in Bethesda, MD from 2005 to 2016.

Based on my training, expertise, and research, I am qualified to evaluate the scientific literature on TCE, PCE, and benzene, and reach causality opinions regarding exposure to these substances and leukemia.

III. CAUSATION STANDARD

I have reviewed the Camp Lejeune Justice Act of 2022 (CLJA), which I understand to be the governing statute for the causation standard in this case. The CLJA requires marines or family members bringing claims under the Act "show one or more relationships between the water at Camp Lejeune and the harm," by "producing evidence showing that the relationship between exposure to the water at Camp Lejeune and the harm is – (A) sufficient to conclude that a causal relationship exists; or (B) sufficient to conclude that a causal relationship is at least as likely as not."

In addition to reviewing the language of the CLJA, I also reviewed the "ATSDR Assessment of the Evidence for the Drinking Water Contaminants at Camp Lejeune and Specific Cancers and Other Diseases" dated January 13, 2017. The ATSDR classified evidence of a causal relationship between certain diseases and contaminants in the water at Camp Lejeune. The ATSDR noted that there is sufficient evidence to conclude that TCE and Benzene cause leukemia, and I concur with their assessment of the evidence.

The causation standard in this case is lower than the "more likely than not" standard, and the ATSDR proposed that in situations where there is not sufficient evidence to conclude a causal relationship exists, as in the case of PCE causing leukemia, the causation burden could be met if it could be shown that the evidence was equipoise and above for PCE causing leukemia. Under the guidance of the ATSDR

framework, one could show the relationship of "at least as likely as not" or equipoise and above, using any one of the three different pathways below:

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. In this case, the degree of evidence for PCE from human studies is less than sufficient.

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 biases 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.

Based on my years of medical and epidemiological training and expertise, I am familiar with the term "equipoise" and find ATSDR's definitions of "equipoise and above" or "at least as likely as not" to be appropriate in this case. I find the above pathways to be reasonable and appropriate methods to meet the "at least as likely as not" standard. I make clear above and through the rest of the report where my opinions are expressed under the "more likely than not" or "at least as likely as not" standard.

IV. METHODOLOGY EMPLOYED

The methodology I used to form my opinions in this case aligns with the standard practices that I have employed and other experts in the field when conducting similar analyses. Specifically, my approach included the following:

- Conducting PubMed searches of peer-reviewed scientific literature examining associations between TCE, PCE, benzene, and/or vinyl chloride and leukemia.

- Searching the Cochrane database for systematic reviews and meta-analyses.

- Reviewing and analyzing reports from national and international agencies, such as the International Agency for Research on Cancer (IARC), the Agency for Toxic Substances and Disease Registry (ATSDR), the National Toxicology Program (NTP), and the United States Environmental Protection Agency (EPA). This included an evaluation of the studies cited within these reports.

I applied a weight-of-the-evidence approach, assigning varying levels of importance to studies based on their designs, methodologies, and limitations.

To contextualize my findings, I evaluated the studies and reports using the Bradford Hill viewpoints, including strength of association, consistency, specificity, temporality, dose-response, plausibility,

coherence, experiment, and analogy. While not every Bradford Hill viewpoint needs to be satisfied to establish causality, they serve as a valuable framework to assist scientists in causation determinations. In my report, I assess both the presence and strength of each Bradford Hill viewpoint and formulate my causation opinions.

Numerous epidemiologic studies on the association between TCE, PCE, and Benzene and leukemia are available. This section identifies and examines meta-analyses, cohort studies, case-control studies, ecologic/water-contamination studies, reports from national and international agencies, and Camp Lejeune-specific studies related to contaminants and leukemia. It is standard practice among experts in my field to consider data from each category when conducting a causality assessment.

I reserve the right to continue to review medical and scientific literature and other documents that are either made available to me or are newly published, and these materials may result in new opinions.

V. DISCUSSION

A. LEUKEMIA

Leukemia is a blood cancer that develops in white blood cells and develops in the spongy part of bone. Doctors categorize leukemia according to the type of white blood cell involved (lymphocytes or myeloid cells) and whether the illness develops quickly (acute disease) or slowly over time (chronic disease). In acute leukemia, which develops rapidly, malignant cells (called blasts) are immature and incapable of performing immune system functions. Chronic leukemia develops in more-mature cells, which can perform some of their duties but not very well. These abnormal cells usually multiply at a slower rate than acute leukemia.

Lymphocytic leukemia develops from cells that give rise to T lymphocytes (T cells), B lymphocytes (B cells), or natural killer (NK) cells. Each of these cell types plays a specialized role in the immune system; some produce antibodies, whereas others directly fight or direct other immune cells to fight infections.

Acute Lymphocytic Leukemia (ALL) is a rare cancer. It affects approximately 3,000 adults in the United States each year. The incidence of this disease increases with age. It is less common among women and African Americans.

Myeloid leukemia develops from cells that give rise to white blood cells, called granulocytes and monocytes. Granulocytes get their name from the enzyme-packed granules they carry inside them. They release these enzymes when encountering invading bacteria or fungi. Monocytes eventually become macrophages, which engulf and destroy bacteria and fungi.

Acute myeloid leukemia (AML), one of the most common types of leukemia in adults, is diagnosed in approximately 20,000 individuals in the United States each year. The average age at diagnosis was 72 years. The disease affects more men than women.

Chronic Myeloid Leukemia (CML) develops when genetic material is exchanged between chromosomes 9 and 22 to generate the Philadelphia chromosome. The average age at diagnosis is 65 years, and the disease is slightly more common in men than in women.

B. CHEMICALS IN CAMP LEJEUNE WATER

The Hadnot Point treatment plant supplied drinking water to the main part of Camp Lejeune, including most of the barracks and workplaces. Maslia reconstructed TCE concentrations reached a monthly average of 783 ug/L compared with a one-time maximum measured value of 1400 ug/L during the period from August 1953 to December 1984. When HTWTP came on line, the maximum reconstructed TCE concentration was 66 ug/L. Maslia (2011)(2013). The Hadnot Point water treatment plant samples were collected in May and July 1982, December 1984, and throughout 1985. In 1982, TCE levels were as high as 1,400 ppb, and PCE levels reached maximum monthly average of 183 ug/L compared with a one-time maximum measured value of 215 ug/L. The Tarawa Terrace treatment plant provided drinking water to the housing area and was sampled in May and July 1982 and again from February 1985 onward. PCE levels in July 1982 reached 104 ppb and peaked at 215 ug/L in February 1985.

The current U.S. maximum contaminant levels (MCLs) for TCE, PCE, and benzene are 5 ppb, established in 1989 for TCE and benzene and in 1992 for PCE. In October of 2023, the EPA (2023) proposed a complete ban on TCE based upon their determination that TCE presents an unreasonable risk to human health. The adverse effects associated with exposure, and considered by the EPA, included TCE's impact on the immune system, as well as several cancers, including but not limited to, kidney cancer and NHL. It will be discussed in further detail, but Benzene, as well as TCE, has been shown to be both immunotoxic and genotoxic in humans. Historical modeling at Camp Lejeune suggests TCE and PCE levels exceeded these MCL safe limits that were present in the water systems as early as the 1950s. The highly contaminated wells were shut down by February 1985. For the cohort study of Marines and Navy personnel, the exposure period was 1975–January 1985. During this time, the mean monthly concentrations in Hadnot Point's water were 358.7 ppb for TCE, 15.7 ppb for PCE, and 5.4 ppb for benzene. In the Tarawa Terrace system, the median monthly PCE and TCE concentrations were 85 and 3.1 ppb, respectively.

C. CAMP LEJEUNE SPECIFIC STUDIES AND REPORTS

1. BOVE 2014 A MILITARY AND BOVE 2014B CIVILIAN MORTALITY STUDIES

Bove et al. 2014a and Bove et al. 2014b conducted two retrospective cohort mortality studies of Marines/Navy personnel and of civilian workers who worked at Camp Lejeune and compared the results with Navy and Marine personnel at Camp Pendleton. These cohort studies found elevated risks of death from leukemias when compared to similar unexposed cohorts from U.S. Marine Corps Base Camp Pendleton. Bove et al. 2014a conducted a retrospective cohort mortality study of Marine and Naval personnel who began service during 1975-1985 and were stationed at Camp Lejeune or Camp Pendleton, California. Camp Pendleton was used as a control population because there was no documented drinking water contamination during the time of the study. Mortality follow-up was 1979-2008. Standardized Mortality Ratios were calculated using U.S. mortality rates as reference. The authors used survival analysis to compare mortality rates between Camp Lejeune (N = 154,932) and Camp Pendleton (N = 154,969) cohorts and assess effects of cumulative exposures to contaminants within the Camp Lejeune cohort. Models estimated monthly contaminant levels at residences. Confidence intervals (CIs) indicated good precision in the effect estimates. Compared to Camp Pendleton, Camp Lejeune had elevated mortality hazard ratios (HRs) for all cancers (HR = 1.10, 95% CI: 1.00, 1.20), and the risk for leukemia was slightly elevated with an SMR of 1.10 (95% CI: 0.75 1.62). Within the Camp Lejeune cohort, there was no monotonic exposure trends for cumulative exposure to TCE and leukemia. There was a

significantly elevated risk with a risk ratio of 2.0 (95% CI: 1-4) for low exposure category, for the moderate exposure category with a risk ratio of 1.54 (95% CI: 0.71-3.36) and for high cumulative exposure which had a risk ratio of 1.81 (95% CI: 0.85-3.85). The authors concluded that there were elevated hazard ratios for death from leukemia.

Although some of the results from Bove above refer to hazard ratios whose confidence intervals include the null value, it is my professional opinion that this fact, by itself, does not necessarily render the study results as “insignificant.” The analysis of a study that shows a positive association, as above, between TCE and leukemia mortality, but whose confidence interval includes 1, as in the high cumulative risk category above, would suggest that the most consistent risk estimate would be in the middle of the confidence interval range Li et al. (2021).

In addition, Bove et al. (2024) conducted a cancer incidence study and cancer mortality Study (discussed below) that used data from extensive water modeling provided by Maslia et al. (2007), (2013) to reconstruct monthly levels of contaminants in the drinking water.

2. ATSDR 2017 ASSESSMENT OF THE EVIDENCE FOR DRINKING WATER CONTAMINANTS AT CAMP LEJEUNE AND SPECIFIC CANCERS AND OTHER DISEASES

ATSDR completed several epidemiological studies to determine if Marines, Navy personnel, and civilians residing and working on U.S. Marine Corps Base Camp Lejeune were at increased risk for cancer in general, and leukemia in particular, as a result of exposure to water contaminated with TCE, PCE, and benzene. The ATSDR Public Health Assessment published on 1/20/2017, and the ATSDR 2018 Morbidity Study of Camp Lejeune Military and Civilian Personnel found increased risk of leukemia in the Camp Lejeune population.

ATSDR also integrated the findings from its Camp Lejeune studies with findings from studies of other populations exposed occupationally or environmentally to TCE and PCE and Benzene. The purpose was to assess the strength of the evidence supporting causality of leukemia due to exposures to the drinking water contaminants at Camp Lejeune. The ATSDR Assessment of the Evidence report represents ATSDR’s assessment of the state of evidence in 2017. ATSDR did not conduct any new meta-analyses~~.~~ but the ATSDR reviewed the scientific literature on these contaminants and placed high weight on assessments conducted by other agencies mandated to evaluate the health effects of these chemicals: i.e., the U.S. Environmental Protection Agency (EPA 2011, 2012), the National Toxicology Program (NTP 2015) and the International Agency for Research on Cancer (2012), (2014). High weight was also given to meta-analyses. The ATSDR report summarized the evidence for leukemia for which there was some epidemiological evidence for an association with TCE, PCE and Benzene, the primary contaminants in the drinking water systems at Camp Lejeune. In sum, ATSDR concluded that there is “equipoise and above evidence for causation for TCE and all adult leukemias, including AML, ALL, and CML.” For benzene, ATSDR concluded "there is sufficient evidence for causation for benzene and all leukemia types (ALL, AML, and CML)" based on robust meta-analyses, recent cohort studies, and mechanistic evidence showing its effects on both lymphoid and myeloid cell types. Although the ATSDR concluded there was equipoise and below evidence for PCE and risk of leukemia, my opinion is that the evidence that has come out on PCE since 2017 has moved PCE and the risk of leukemia into the at least as likely as not category.

Case 7:23-cv-00897-RJ Document 465-3 Filed 08/24/25 Page 9 of 67

3. ATSDR MORBIDITY STUDY OF THE CAMP LEJEUNE COHORT COMPARED WITH THE CAMP PENDLETON COHORT OF SERVICE MEMBERS AND CIVILIAN EMPLOYEES 2018

The ATSDR (2018)[74] also conducted a morbidity study of Marines and Navy personnel stationed at Camp Lejeune, North Carolina, and Marines and Navy personnel at Camp Pendleton, California between 1972-1985. The study also included civilian workers at Camp Lejeune and Camp Pendleton.

The study, which has some limitations, assessed leukemia risk by examining exposure levels to specific contaminants in the water at Camp Lejeune and Camp Pendleton. Researchers used water distribution models alongside data on residential locations and the duration of residence at Camp Lejeune to estimate cumulative and average exposure to each chemical.

Among civilians with moderate combined exposure to TCE and PCE (defined as 10,868 ppb-months of TCE or 457 ppb-months of PCE), the relative risk was 1.41 (95% CI: 0.38–5.28), representing a 41% higher leukemia risk compared to civilians at Camp Pendleton. Those with higher combined exposure levels showed a relative risk of 1.32 (95% CI: 0.15–11.4) (Table 12), translating to a 32% increased leukemia risk. These findings suggest that cumulative exposure exceeding 15,000 ppb-months of TCE and 2,000 ppb-months of PCE is associated with at least a 32% increase in leukemia risk. The confidence intervals do show the risk estimate is more precise towards the center of the confidence interval, which is well above the null value and reflective of increased risk of leukemia.

The study also compared leukemia rates among Camp Lejeune personnel with medium TCE and PCE exposure to those with lower exposure levels. For individuals with high TCE exposure (over 15,000 ppb-months), the relative risk was 1.58 (95% CI: 0.16–15.3) (Table 13), indicating a 58% higher leukemia risk. These results highlight that TCE exposure at 15,000 ppb-months significantly increased the leukemia risk by at least 58%. Dr. Bove acknowledged the limitations of the study both in the study itself and in his deposition, but explained that the limitations would have biased the results towards the null value.

4. BOVE F., ET AL. (2024) CANCER MORTALITY STUDY

The Bove 2024 cancer mortality study explored cancer mortality by type, utilizing a longer follow-up period than earlier investigations. The study extended the Camp Lejeune Cohort's follow-up from 2008 to 2018, comparing the cancer risks among military and civilian personnel stationed at Camp Lejeune and Camp Pendleton between 1972 and 1985.

The findings revealed that Navy and Marine personnel at Camp Lejeune had a hazard ratio of 1.13 (95% CI: 0.89–1.43), so they had a 13% elevated risk of death from leukemia compared to those at Camp Pendleton. For AML specifically, the risk increased by 21%, with a risk ratio of 1.21 (95% CI: 0.94–1.56) (Supplementary Table 3). For CML, the risk rose to a risk ratio of 1.73 (95% CI: 0.47–6.42) (Supplementary Table 7), indicating a 73% elevated risk compared to Camp Pendleton personnel. These results reinforce the conclusion that chemical exposure levels at Camp Lejeune were linked to a higher risk of death due to leukemia~~,~~ even though the confidence interval contained 1.

The study also analyzed leukemia risk relative to exposure duration, measured by time spent on base. For personnel with short-term exposure (1–6 months or 1–2 quarters), the risk ratio was 1.17 (95% CI: 0.84–1.64) (Supplementary Table 6). For medium-term exposure (7–10 quarters), the risk ratio increased to 1.19 (95% CI: 0.86–1.64). These findings suggest that even short durations on base during the 1972–

1985 period were Linked to a higher risk of death due to leukemia. Similarly, individuals who were on base at different intervals but received a cumulative exposure equivalent to 2–7 quarters during that period faced comparable risks.

5. BOVE, ET AL. (2024) CANCER INCIDENCE STUDY

The Bove et al. (2024) Cancer Incidence Study examined cancer rates among personnel stationed at Camp Lejeune from 1975 to 1985 and compared them to a similar cohort stationed at Camp Pendleton during the same period. By extending the follow-up timeframe, the study evaluated cancer incidence from 1996 to 2017 to determine whether being stationed or employed at Camp Lejeune increased leukemia risk.

Compared with Camp Pendleton, Camp Lejeune Marines/Navy personnel had an elevated risk for all myeloid cancers with a risk ratio of 1.24 (95% CI: 1.03,1.49), specifically the risk for acute myeloid leukemia was elevated at 1.38 and the 95% CI was more precise (95% CI: 1.03,1.85). The risk for myelodysplastic and myeloproliferative syndromes were elevated at 1.68 and the risk estimate was more precise (95%CI: 1.07-2.62). Camp Lejeune civilian workers also had an elevated risk of myeloid cancers with a hazard ratio of 1.40 (95% CI: 0.83-2.36). The wide confidence interval was primarily due to the small numbers of cases in the civilian workers. Even with limitations which would bias the results towards the null value, these findings suggest that individuals exposed to contaminated water at Camp Lejeune during 1975–1985 had a moderate to high elevated risk of developing leukemia and AML specifically.

D. TCE AND LEUKEMIA

1. TCE

Trichloroethylene (TCE) is a volatile, colorless liquid organic chemical. Originally developed as an anesthetic, TCE is used primarily in refrigerants and as a metal degreasing solvent. People can be exposed to TCE through indoor and outdoor inhalation, ingesting contaminated water, or dermal exposure. TCE was frequently used by the U.S. military as an equipment degreaser; thus, military bases have been found to have TCE-contaminated soil and groundwater. TCE also “breaks down slowly and remains in the environment for a long time.” As previously noted, the US EPA has sought a complete ban on TCE given its known health effects on humans, which include, among other things, cancers.

2. SYSTEMATIC REVIEWS/META-ANALYSES

Alexander D., et al. (2006) performed a meta-analysis of epidemiologic studies on occupational TCE exposure and multiple myeloma (MM) or leukemia. They identified a total of eight cohort or case-control studies that examined a TCE-exposed study population and determined relative risk estimates for leukemia (n = 7). The individual studies included aerospace or aircraft workers (n = 3 studies), workers from a transformer manufacturing plant (n = 1 study), and workers from numerous occupations who, based on biomonitoring or extensive industrial hygiene exposure measurements, were likely exposed to TCE (n = 4). They used random-effects models to calculate summary relative risk estimates (SRRE) and examined heterogeneity across studies. The SRRE was 1.11, 95% CI: 0.93–1.32, and the P value for heterogeneity was 0.50 based on the TCE-exposed subgroup meta-analyses. Study-specific RR estimates for leukemia ranged from 1.05 to 1.15 in five studies, whereas one study reported a two-fold

increased RR, and another study reported no association at 0.60. The confidence intervals (CIs) for the study estimates indicated that the findings were less precise and included 1.0. The Alexander meta-analysis indicated that in 5 studies, 4 of the 5 risk levels were above 1 and only 1 study had a risk estimate that was less than 1.

Karami et al (2013) performed a systematic review and meta-analysis of TCE and leukemia risk. The authors reviewed studies published between 1950 and 2011 identified through a PubMed Medline search. The authors targeted those studies that assessed only TCE exposure and leukemia risk. Their results revealed that TCE exposures were modestly associated with an increased risk of leukemia. Even with a summary risk estimate of 1.10 (95% CI: 0.94, 1.28) in 9 cohort studies (3 incidence, 6 mortality) .and 1 case-control mortality study, it is as least as likely as not that TCE increases the risk for leukemia. The wide confidence interval suggests that the risk could range from no effect up to moderately elevated risk of developing leukemia.

Results from the Meta-Analyses above support a conclusion that TCE is at least as likely as not causal of Leukemia. There is consistency in the modest risk demonstrated in both meta-analyses, but under the CLJA standard, the results meet the “at least as likely as not” standard.

3. COHORT STUDIES

Anttila et al. (1995) conducted a retrospective cohort study of exposure to trichloroethylene, tetrachloroethylene, or 1,1,1-trichloroethane and increased carcinogenic risk, following a cohort of 2050 male and 1924 female workers monitored for occupational exposure to these agents that was followed up for cancer incidence from 1967 to 1992. The overall cancer incidence within the cohort was similar to that of the Finnish population. There was an excess risk of leukemia with a risk ratio of 1.1 (95% CI: 0.4-2.5). The study relied on biomarker monitoring for TCE exposure, so the risk of misclassification bias was low. The Anttila study revealed a modest increase in risk of leukemia for those exposed to TCE which was above equipoise at 1.1. The wide confidence interval was due to small numbers of cancer cases in the exposed cohort that results in a less precise risk estimate. Despite the fact that the confidence interval includes the null value, one cannot say that exposure to TCE is health protective. Anttila revealed a modest increase in risk of leukemia to those exposed to TCE and other volatile organic compounds, but the data set included parameters consistent with no effect and up to a 250% increase in leukemia risk.

Bahr et al. (2011) conducted a cancer cohort mortality study and cancer incidence study of TCE exposed workers at the Paducah Kentucky Gaseous Diffusion Plant that became operational in 1952. The authors studied a cohort of 6820 workers at the plant for the period 1953 to 2003; there were a total of 1672 deaths in cohort members. TCE exposure is a specific concern for this workforce primarily in departments that clean the process equipment. A Life Table Analysis System developed by NIOSH was used to calculate the standardized mortality ratios for the worker cohort and standardized rate ratios relative to exposure to TCE (the U.S. population is the referent for age-adjustment). A review of cancers of interest produced high SMRs for leukemia with an elevated risk of death for leukemia of 1.2 (95% CI: 0.7-1.7) for males and the risk was further elevated to 1.47 (95% CI of 0.82 to 2.43) in two highest exposure categories. So, there was an elevated risk of death from leukemia but there was a wide confidence interval, so confounding and chance could not be completely ruled out.

Lipworth L et al. (2011) assessed TCE exposure and leukemia risk among aircraft manufacturing workers in a follow-up study between 1960 to 2008. A job exposure matrix was developed for TCE using work histories, walkthrough surveys, interviews, and industrial hygiene records. The study found an SMR of 1.0 (95% CI: 0.6-1.7) for leukemia. The use of a job exposure matrix that relied on surveys and interviews would result in a higher likelihood of exposure misclassification that would bias the result toward the null. In my opinion, the risk ratio of 1.0 is at Equipoise.

Morgan WR, et al. (1998) conducted a cohort study of TCE exposure among aerospace manufacturing workers. Cancer mortality follow-up was conducted for 44 years between 1950 and 1993. A JEM for TCE exposure was developed for long-term employees using company work histories. The authors noted that there was a slightly elevated risk of dying from leukemia as the SMR was 1.1 (95% CI: 0.5-1.9). In my opinion, the risk ratio of 1.1 noted in the Morgan study reaches the level of equipoise and above.

Ritz et al. (1999) conducted a cohort study of TCE exposure among male uranium workers. The authors examined cancer mortality during a 39-year follow-up period from 1951 to 1989. A job exposure matrix for TCE exposure was developed for long-term employees. Leukemia risk was noted to be slightly elevated with a relative risk of dying of leukemia of 1.1(95% CI:0.6-1.9). In my opinion, the risk ratio of 1.1 noted in the Ritz study reaches the level of equipoise and above.

Boice JD, et al. (2006) conducted a cohort study of TCE exposure in male aircraft workers at a rocket engine testing facility. The authors performed cancer mortality follow-up for 51 years from 1948 to 1999. A job exposure matrix for TCE exposure was developed using company work histories, walkthrough surveys, and interviews. The authors noted that the risk of dying from leukemia generally was elevated and the SMR was 1.1 (95% CI: 0.4-2.5). In my opinion, the risk ratio of 1.1 noted in the Boice study reaches the level of equipoise and above.

Hansen J et al. (2001) performed a cohort study of TCE exposure among workers from 275 Danish companies. Cancer incidence follow-up was done for 30 years, from 1968-1996. Urinary biomonitoring (U-TCA) measurements for individuals or company air measurements used to assign TCE exposure. An elevated risk ratio of leukemia was noted with an SIR of 2.0 (95% CI: 0.7-4.4). In my opinion, the risk ratio of 2.0 noted in the Hansen study reaches the level of equipoise and above, as the degree of consistency of risk values would be the greatest in the center of the two endpoints in the confidence interval as discussed in Savitz (2024).

Radican L, et al. (2008) performed a cohort study of TCE exposure and leukemia outcomes. TCE exposure was evaluated among aircraft maintenance workers. The cancer incidence follow-up was done for 18 years, from 1973-1990. Cancer mortality follow-up was performed for 48 years from 1953-2000. A job exposure matrix for TCE exposure was developed using company work history records, walkthrough surveys, interviews, and industrial hygiene and other company records. Leukemia relative risk was not elevated, and the risk ratio was 0.6 (95% CI: 0.4-1.2). The cancer incidence follow-up was only performed for 18 years, and this limits the studies ability for cancer case attainment and biases the study results towards the null. Also, the use of a job exposure matrix that relied on surveys and interviews would result in a higher likelihood of exposure misclassification that would bias the result toward the null. Although the risk ratio of 0.6 noted in the Radican study is less than equipoise, there is likely case attainment bias and exposure misclassification bias and both these bias the study risk estimates to the null and below.

4. CASE CONTROL STUDIES

Greenland S, et al. (1994) conducted a nested case-control study with histologically confirmed cancer deaths from 1969 to 1984 and evaluated exposures and leukemia outcomes among male, aged 20-90, in a TCE-using transformer assembly plant. Pension workers with non-cancer related deaths were identified as controls. The authors used insurance pension records that provided data on work histories. Industrial hygienists developed job/department/building job exposure matrices based on interviews with long-term workers. The authors noted a slightly elevated risk of developing leukemia with an odds ratio of 1.1(95% CI: 0.5-2.7).

Shu et al. (1999) performed a case-control study of Children's Cancer by examining 1842 acute lymphocytic leukemia (ALL) cases and 1986 matched controls. The study examined the association of self-reported occupational exposure to various hydrocarbons among parents with risk of childhood ALL by exposure time window, immunophenotype of ALL, and age at diagnosis. The authors found that overall, the childhood leukemia rate was elevated with maternal exposure to solvents at 1.8 (95% CI: 1.3-2.5); during the preconception period the risk was elevated at 1.6 (95% CI: 1.1-2.3) and exposure during pregnancy increased the childhood leukemia risk to 1.7 (95% CI: 1.2-2.3). The ALL risk associated with parental exposures to hydrocarbons did not vary greatly with immunophenotype of ALL. The study showed that parental exposures to hydrocarbons, including TCE, greatly increases the risk for leukemias in the parent's offspring.

Anderson et al. (2009) conducted an evaluation to assess the risk of myeloid malignancies using US Surveillance Epidemiology and End Results (SEER)-Medicare data that included 13 486 myeloid leukemia cases and 160 086 controls. Logistic regression analysis adjusted for gender, age, race, and calendar year to estimate odds ratios (ORs) for myeloid malignancies. Autoimmune conditions, overall, were associated with an increased risk of acute myeloid leukaemia (AML) (OR 1.29) and myelodysplastic syndrome (MDS, OR 1.50). The authors noted that medications used to treat autoimmune conditions, genetic predisposition and/or direct infiltration of bone marrow could explain these excess risks. This study emphasizes the link between the immune system and blood cancers. This is of particular relevance at Camp Lejeune, as drinking water was contaminated with TCE and Benzene, two chemicals which are known to cause immune dysfunction and cancer.

5. ECOLOGIC/WATER CONTAMINATION STUDIES

New Jersey: Fagliano et al. (1990) and Cohn et al. (1994) multiple studies to evaluate the relationship between groundwater contamination with trichloroethylene (TCE) and tetrachloroethylene (PCE) in 75 towns in New Jersey and the incidence of leukemia. The authors highlighted that TCE and PCE have been demonstrated to be carcinogenic in experimental animal studies, suggesting their potential carcinogenicity in humans. Using water modeling, they assigned concentrations of TCE and PCE to various areas, with the highest assigned levels being 67 parts per billion (ppb) for TCE, 14 ppb for PCE, and 92.9 ppb for total non-trihalomethane VOCs. These levels are comparable to, and in some cases lower than, the contaminant levels found at Camp Lejeune. The study employed geographic data aggregated by exposure, approximating actual exposure levels across populations.

Leukemia rates in towns with the highest concentrations of these chemicals were compared to towns with the lowest concentrations. The study found a statistically significant association between leukemia incidence in females and residence in towns with the highest exposure stratum, defined as total VOC

levels exceeding 20 ppb. This finding suggests that exposure to drinking water with at least 20 ppb of VOCs can cause leukemia. Given that total VOC levels at Camp Lejeune often exceeded 20 ppb, this study provides strong evidence linking Camp Lejeune's water contamination levels to leukemia. Bove et al. (2014) supported this conclusion, noting that the maximum detected level of TCE in the Hadnot Point drinking water at Camp Lejeune was significantly higher than the levels detected in the New Jersey towns.

Cohn et al. (1994) assessed specific risks associated with TCE and PCE exposure. For TCE exposure at or above 5 ppb, females had a relative risk of 1.43 (95% CI: 1.07–1.9), while males had a relative risk of 1.10 (95% CI: 0.84–1.43). These results indicate that exposure to 5 ppb of TCE can cause leukemia in females. For PCE exposure at or above 5 ppb, females experienced a 20% increased risk of developing leukemia. The authors noted that joint exposure to TCE and PCE could increase the carcinogenic effects over what might be expected by adding their individual effects. Both TCE and PCE undergo the same metabolic pathways and produce different metabolic byproducts that when combined may produce more harmful effects than what would be expected if the two effects were added.

I did note that Frank Bove, who was the primary author of the Camp Lejeune health studies, was a contributing author to the New Jersey-studies cited above. It is also worthwhile pointing out that the Cohn study, like Camp Lejeune, yet distinct from nearly all of the other published studies, was a water ingestion study. While the ecologic studies above do have limitations,-these two studies certainly help inform us of the relationships between both TCE and PCE and the increased risk of leukemia due to ingestion of water contaminated with TCE and PCE at levels comparable to those found at Camp Lejeune.

Woburn, Massachusetts: Cuttler (1986) and Lagakos (1986) investigated a cancer cluster in Woburn, Massachusetts, where industrial processes contaminated public water supply wells G and H with TCE at 267 ppb and PCE at 21 ppb. These contaminant levels are comparable to those at Camp Lejeune. After the discovery of contamination, the two Massachusetts studies observed a significantly higher cancer mortality rate in Woburn compared to state averages and nearby communities. Epidemiological studies linked TCE and PCE exposure to a cluster of childhood leukemia cases. Specifically, Lagakos (1986) found that cumulative exposure to the contaminated wells was positively associated with leukemia rates, and adverse outcomes declined after the wells were shut down. These results would suggest that TCE and PCE levels in the range of 10–100 ppb is sufficient to cause leukemia.

Woburn Follow-Up: Costas et al. (2002) conducted a follow-up evaluation of the Woburn cancer cluster. Their study demonstrated a dose-response relationship between exposure to contaminated drinking water during pregnancy and childhood leukemia. Children whose mothers consumed the most water from wells G and H during pregnancy had a 14-fold increased risk of developing leukemia compared to those whose mothers consumed less contaminated water. This study underscores the hazardous nature of the chemicals present in Woburn's water, showing that these exposures were sufficient to induce leukemia. While this study focused on maternal exposure leading to childhood leukemia, it reinforces the conclusion that these contaminant levels pose significant risks to human health, supporting the findings at Camp Lejeune.

6. NATIONAL AND INTERNATIONAL AGENCY REPORTS

The International Agency for Research on Cancer (IARC), the cancer research arm of the World Health Organization, is a vital resource for scientists and experts like me. IARC monographs and carcinogen classifications are widely used in research to assess the carcinogenicity of various agents. IARC categorizes agents into four groups: Group 1 ("carcinogenic to humans"), Group 2A ("probably carcinogenic to humans"), Group 2B ("possibly carcinogenic to humans"), and Group 3 ("not classifiable as to its carcinogenicity to humans").

IARC Monograph 106 specifically addresses TCE and evaluates its carcinogenicity. The IARC Working Groups based their classifications on human epidemiological evidence, animal evidence, and mechanistic data. TCE was classified as a Group 1 carcinogen, meaning it is "carcinogenic to humans." In Monograph 106, the IARC Working Group made the following key determination regarding TCE:

- Human evidence related to TCE was classified as "sufficient," the highest level of evidence under IARC's framework.
- Animal evidence related to TCE's carcinogenicity was also classified as "sufficient."
- TCE metabolites were identified as genotoxic.
- TCE was found to be immunotoxic.

Overall, IARC concluded that epidemiologic, animal, and mechanistic evidence is sufficient to cause cancer. I agree with the conclusions of IARC regarding TCE and its carcinogenicity.

The National Toxicology Program (NTP) Monographs, like those from IARC, are another trusted resource used by experts to evaluate the causal relationships between toxic exposures and disease. In its monograph relevant to leukemia, NTP (2015) concluded, similar to IARC, that there was sufficient evidence to classify TCE as a carcinogen. Specific to leukemia, the NTP noted:

- Inhalation or gavage exposure to TCE caused leukemia in rats.
- TCE has a detrimental effect on the immune system in both humans and animals, and these effects are linked to the development of leukemia.

The NTP highlighted the strongest epidemiological evidence of leukemia in the study by Costas et al. (2002). This study revealed positive associations between TCE exposure and leukemia, reinforcing the link between TCE and hematologic malignancies.

7. ANIMAL STUDIES EVIDENCE FOR AN ASSOCIATION BETWEEN TCE AND LEUKEMIA

The National Toxicology Program 15th Report on Carcinogens (ROC) published in 2021 noted that Trichloroethylene was noted to cause tumors in mice and rats at several different tissue sites by two different routes of exposure. In rats, exposure to TCE by both oral lavage and inhalation, caused kidney cancer and testicular tumors in males. In mice, exposure to trichloroethylene by inhalation oral lavage caused benign and malignant liver tumors in both sexes. The NTP 15th ROC also noted that inhalation

exposure caused lung tumors in both sexes and lymphoma in females. NTP reported on prior EPA studies that found TCE causes autoimmune disorders (EPA 2011). In turn, immune system dysregulation, including autoimmune disorders have been associated with an increased risk of developing leukemia. It is my opinion that the animal studies do provide modest evidence of an association between TCE exposure and increased leukemia risk.

8. MECHANISTIC EVIDENCE FOR AN ASSOCIATION BETWEEN TCE AND LEUKEMIA

According to the ATSDR 2017 Assessment, evidence from human studies indicated that TCE was noted to cause systemic sclerosis, an immune system disorder (EPA 2011). Onishi et al. (2013) observed that systemic sclerosis was associated with leukemia in 2 studies. The SIR was elevated at 2.75 (95% CI: 1.32, 5.73). In general, there is consistency among the three pillars of science as to the immunotoxic effects of TCE, which provide a link with hematopoietic cancers such as leukemias EPA (2011), NTP (2015).

Bassig et al. (2016) conducted a study of factory workers in China exposed to TCE and observed declines in the number of lymphoid cells. This finding supports the association between TCE and lymphoid leukemias, including ALL. There is also strong evidence that autoimmune disorders are associated with myeloid leukemia, myelodysplastic syndrome, and lymphoid leukemia, as reported by Anderson et al (2009), Kristinsson et al (2011), and Gunnarsson et al (2016). It is my opinion that mechanistic studies on TCE (both in humans and animals, and in vitro). Support the biological plausibility of TCE and shed light on the causal relationship between the effects of TCE on the immune system and leukemia development.

Immune Dysfunction: Zhang et al. (2013) investigated immune function in 80 workers exposed to TCE compared to 45 unexposed controls. Their results showed significant declines in immune markers, with a 17.5% reduction in IgG levels ($P = 0.0002$) and a 38% reduction in IgM levels ($P < 0.0001$) among exposed workers. Immune system dysregulation observed even at TCE concentrations below 12 ppm, emphasizing the chemical's ability to impair immune defenses-thus increasing the risk of developing leukemia.

Genotoxicity: Varshney et al. (2014) studied the genotoxic effects of trichloroacetic acid (TCA), a metabolite of TCE, in lymphocytes from healthy donors. Exposure to TCA resulted in chromosomal anomalies, including chromatid breaks, chromosome breaks, and fragments, in a dose-dependent manner. This study highlights TCA's potential to directly damage DNA and contribute to cancer development.

MicroRNA Changes: Lee et al. (2019) examined the effects of TCE on microRNAs (miRNAs), which regulate gene activity. In workers exposed to TCE, seven miRNAs showed significant changes (FDR < 0.20). Among these, miR-150–5p and let-7b-5p displayed inverse exposure-response relationships with TCE (P trend = 0.002 and 0.03, respectively). These miRNAs-help regulate the immune system, including B-cell receptor pathways and innate immune responses, which are critical to the development of leukemias and other hematopoietic cancers.

Epigenetic Alterations: Phillips et al. (2019) conducted an epigenome-wide association study (EWAS) on DNA methylation in TCE-exposed workers. Their findings revealed widespread alterations in methylation variability and specific hypomethylation in a region of the TRIM68 gene promoter. These epigenetic

changes were linked to cancer-related biological pathways, further connecting TCE exposure to mechanisms involved in leukemia development.

The mechanistic evidence clearly establishes the negative impacts that TCE has on immune function, shows how it damages DNA, and alters key biological pathways through epigenetic and molecular changes. These mechanisms provide strong support for the conclusion that TCE exposure contributes to the development of leukemia. The results of the mechanistic studies strengthen the biological plausibility of TCE as a cause of leukemia, complementing the results from the epidemiological findings.

9. APPLYING THE BRADFORD HILL VIEWPOINTS IN THIS CASE

After reviewing the evidence regarding the association between TCE and leukemia, I also used an accepted methodology, known as the Bradford Hill viewpoints, that provides nine considerations to evaluate whether causation specific to blood cancers can be deduced.

It should be noted that BH considerations are not mandatory and are not intended to be a checklist or a rigid set of rules; rather, they are intended to serve as a guide for evaluating the strength of the evidence for a causal relationship. An analysis does not need to satisfy all factors to demonstrate causation; rather, the weight of the evidence applied across these factors should be considered.

a. Strength of the association

This viewpoint is met in this case because meta-analyses and epidemiological studies provide consistent evidence supporting a strong association between TCE exposure and leukemia. Alexander et al. (2006), conducted a meta-analysis of occupational TCE exposure and leukemia, finding subgroup RR estimates for leukemia ranging from 1.05 to 1.15 across five studies. One study reported a two-fold increased RR, while another reported no association (RR = 0.60). Several cohort studies further support this association. Anttila et al. (1995), Morgan WR, et al. (1998), Ritz B. (1999), and Boice JD, et al. (2006) reported excess leukemia risks with RRs around 1.1 (95% CI: 0.4–2.5). Bahr et al. (2011) found elevated SMRs for leukemia, with an RR of 1.2 (95% CI: 0.7–1.7) in males, which increased to 1.47 (95% CI: 0.82–2.43) in the two highest exposure categories. Cocco et al. (2013) conducted a multicenter case-control study and observed that the incidence of CLL increased with the probability of TCE exposure, with ORs ranging from 1.1 (95% CI: 0.7–1.8) for low probability to 2.0 (95% CI: 1.0–4.0) for high probability of exposure. The risk also increased with exposure duration, increasing from an OR of 0.9 (95% CI: 0.3–3.2) for 1–14 years, to 2.3 (95% CI: 0.6–8.7) for 15–29 years, and to 3.8 (95% CI: 1.0–14.0) for 30–39 years. Similarly, Greenland et al. (1994) noted elevated leukemia risk in a nested case-control study (OR = 1.1, 95% CI: 0.5–2.7), while Purdue et al. (2011) detected an elevated risk for CLL of 2.7 (95% CI: 1.2–5.8).

Constantini et al. (2008) conducted a case-control study and found that for low exposure levels, the SRR for AML was 1.0 (95% CI: 0.5–1.8) and for CLL was 1.0 (95% CI: 0.4–2.5). For medium/high exposures, SRRs were 0.7 (95% CI: 0.4–1.8) for AML and 1.1 (95% CI: 0.5–2.9) for CLL. Additionally, with longer exposure durations of 4–15 years, the SRR for CLL rose to 1.2 (95% CI: 0.2–6.2).

Drinking water studies also contribute to the strength of the evidence for an association between TCE and leukemia. Cohn (1994) reported that females exposed to at least 5 ppb of TCE had an elevated risk of leukemia (RR = 1.43, 95% CI: 1.07–1.9), while males had an RR of 1.10 (95% CI: 0.84–1.43). These results demonstrate that exposure to 5 ppb of TCE is sufficient to cause leukemia.

The ATSDR (2017) report concluded that the epidemiological evidence for TCE and leukemia from occupational and drinking water studies was sufficient to at least reach equipoise. The two meta-analyses indicated a risk of about 1.10. Positive findings in human studies have been observed for each leukemia type. Elevated risks have been observed for AML by Constantini et al. (2008) and Talibov et al. (2014). Cohn et al. also found an elevated risk for ALL and CML (1994). In addition, the Silver et al. (2014) study observed an elevated risk for non-CLL leukemias which were predominantly myeloid leukemias and observed an elevated hazard ratio for the group with 5-year cumulative exposure of 1.31 (95% CI: 0.98, 1.75). The ATSDR (2018) study of Marines and Navy personnel did not observe an increased risk in military personnel but did find increased risks in civilian workers who had a slightly increased relative of risk of 1.10 (95% CI: 0.36-3.38).[Table 11]

The Bove (2024) cancer incidence study on Camp Lejeune personnel indicated an 8% increased leukemia risk overall (RR = 1.08, 95% CI: 0.96-1.22),[Table 3] with a 35% increased risk of AML among civilian employees (RR = 1.35, 95% CI: 0.59–3.09).[Table 4] For marines with "low duration" exposure (1-2 quarters on base), the relative risk of leukemia was 1.11 (0.92-1.33) [Table5] for low exposures and this risk was increased to 15% with the longest duration of exposure with a risk ratio of 1.15 (95% CI: 0.86-1.55). [Table5] The risk was increased from 1.04 (95% CI: 0.77-1.40) to 1.10(95% CI: 0.67-1.12) [Table5] for CLL and the risk was increased from 1.36 (95% CI: 0.97-1.90) to 1.9 (95% CI: 1.12-3.21) for the AML subtype. [Table5] These results indicate that going from 1-2 quarters on base for low exposures during 1975-1985 to the longest duration exposures for 10 or more quarters would significantly increase the risk of leukemia. For civilians with "high duration" exposure (>21 quarters on base), there was an increased Chronic myeloid leukemia risk of 61% with an increased risk ratio of 1.61 (95% CI: 0.29, 8.91).[Table 6] In addition, for civilians with "medium duration" exposure (5-21 quarters on base), there was an increased AML risk of 52% with an elevated risk ratio of 1.52 (95% CI: 0.62-1.89).[Table7] These results demonstrate that medium and high duration exposures from 5 to 21 quarters working as a civilian on base increase the risk of CML and AML by 20 to 60%.

Using a weight of the evidence approach in considering the scientific data above, and considering the Bradford Hill considerations above, it is my professional opinion, that TCE, more likely than not, causes Leukemia. Furthermore, based upon the data above, specifically the Bove studies and the New Jersey studies, that TCE, at levels that were modeled to be present at Camp Lejeune, can cause Leukemia. The Bove et al. 2014a study demonstrates that the levels of TCE in the drinking water at Camp Lejeune can cause leukemia.

b. Consistency

The consistency viewpoint is supported by findings across multiple meta-analyses and individual studies. This consistency in findings across various study designs supports the causal relationship between TCE and leukemia.

c. Specificity

The specificity viewpoint is not met in this case as TCE is causally linked to multiple cancers. The temporality viewpoint is unequivocally satisfied in this case, as all studies demonstrating an association between TCE exposure and leukemia confirm that the exposure occurred prior to the onset of disease. This criterion is foundational to causal inference because, as Bradford Hill emphasized, the cause must precede the effect.

Case 7:23-cv-00897-RJ Document 465-3 Filed 08/24/25 Page 19 of 67

d. Exposure-Response

As noted in the systematic review and meta-analysis conducted by Karami et al. (2013), several studies demonstrated an exposed dose and effect related leukemia risk. In my opinion, the evidence in support of this consideration is present, but modest.

e. Biological Plausibility

TCE's genotoxicity, immunotoxicity, and its ability to induce chromosomal aberrations, miRNA changes, and epigenetic modifications strongly support biological plausibility. Animal studies demonstrate that TCE and its metabolites cause immune disruption and DNA damage consistent with leukemia development. In addition, the results of mechanistic studies strengthen the biological plausibility of TCE as a cause of leukemia, complementing the results from the epidemiological findings. Thus, it is my opinion the evidence for this consideration is strong.

f. Coherence

The coherence criterion evaluates whether epidemiological findings align with biological and toxicological knowledge. Studies consistently show an association between TCE exposure and leukemia. Mechanistic and animal studies confirm that TCE's genotoxicity, immunotoxicity, and chromosomal damage align with these risks. Both IARC and NTP have noted this alignment, reinforcing the coherence between the evidence and causal inference.

g. Experimental Evidence

While human experimental evidence is unethical to obtain, NTP 2015 notes that animal studies robustly demonstrate that TCE induces genotoxic and immunotoxic effects. This supports the role of TCE in carcinogenesis and leukemogenesis.

h. Analogy

As noted in Lash (2019), TCE causes the production of toxic intermediates in the metabolism of the chemical that works to cause altered proteins and DNA structure and function that results in the development of leukemia

10. CONCLUSION: TCE EXPOSURE MORE LIKELY THAN NOT CAUSES LEUKEMIA

In conclusion, the analysis of the Bradford Hill viewpoints demonstrates that TCE exposure is causally linked to leukemia. Evidence supporting key considerations-including strength of association, consistency, dose-response, plausibility, and coherence which are moderate to strong, leading to the conclusion that the association between TCE and leukemia is more likely than not, which exceeds the at least as likely as not standard of the CLJA. The analysis of the Bradford Hill considerations demonstrates that TCE exposure is causally linked to leukemia. Evidence supporting key considerations—including strength of association, consistency, dose-response, plausibility, and coherence—is moderate to strong, leading to the conclusion that the association between TCE and leukemia is more likely than not, which exceeds the at least as likely as not standard of the CLJA. at least "equipoise and above."

E. BENZENE & LEUKEMIA

1. BENZENE

Benzene, an aromatic hydrocarbon, is a ubiquitous air pollutant, arising mostly from combustion. It is a component of gasoline, vehicle exhaust, industrial emissions, and tobacco smoke, and was used historically as a solvent in industry and consumer products. The uses of benzene as a solvent are now restricted in many countries, but it is still produced in high volumes for use primarily as a chemical intermediate.

2. IARC's Assessment of Benzene

a. Carcinogenicity Assessment

In October 2017, a Working Group of 27 scientists met at the International Agency for Research on Cancer (IARC) in Lyon, France, to evaluate the carcinogenicity of benzene. This assessment was published in Volume 120 of the IARC Monographs. Benzene has been classified as carcinogenic to humans (IARC Group 1) since 1979, based on sufficient evidence that it causes leukemia. This classification was reaffirmed in 2009, specifically for acute myeloid leukemia (AML) and acute lymphocytic leukemia (ALL), with positive associations for ALL, and multiple myeloma (MM).

The 2017 IARC evaluation reviewed epidemiological and mechanistic evidence and explored the potential to characterize quantitative relationships for cancer risk and biological endpoints related to cancer mechanisms. The IARC working group noted new evidence came from several large occupational cohort studies. In adult humans, benzene was confirmed to cause AML. More recent studies showed positive associations between AML in children and environmental exposure to benzene. Benzene exposure was also associated with chronic myeloid leukemia.

b. Exposure Levels Corresponding to Cancer Development

The IARC 2017 Working Group investigated whether benzene causes AML in meta-regression analyses of six published occupational cohort studies with suitable data. In the majority of human studies that reported exposure-response information for benzene and relevant endpoints for carcinogens (i.e., micronuclei changes, chromosomal aberrations, and altered leukocyte counts), an exposure-response gradient was reported.

3. SYSTEMATIC REVIEWS AND META-ANALYSES

Khalade, et al. (2010) conducted a systematic review of prior epidemiologic studies examining the relationship between benzene exposure and the risk of leukemia, noting that the results across studies were heterogeneous. The authors aggregated existing evidence on the relationship between occupational benzene exposure and leukemia risk, including all types combined and the four main subgroups: acute myeloid leukemia (AML), acute lymphocytic leukemia (ALL), chronic lymphocytic leukemia (CLL), and chronic myeloid leukemia (CML). They conducted a systematic literature review using the Medline and Embase databases, covering studies from 1950 through July 2009. Articles were selected based on their ability to provide quantitative estimates of the relationship between benzene

exposure and cancer risk. A total of 15 studies were identified, providing 16 estimates of effect size for analysis.

The summary effect size for any leukemia from the fixed-effects model was 1.40 (95% CI, 1.23-1.57), but the study-specific estimates were strongly heterogeneous (I2 = 56.5%, Q stat = 34.47, p = 0.003). The random-effects model yielded a summary-effect size estimate of 1.72 (95% CI, 1.37-2.17). Effect estimates from 9 studies were based on cumulative exposures. In these studies, the risk of leukemia increased with a dose-response pattern with a summary-effect estimate of 1.64 (95% CI, 1.13-2.39) for low (< 40 ppm-years), 1.90 (95% CI, 1.26-2.89) for medium (40-99.9 ppm-years), and 2.62 (95% CI, 1.57-4.39) for high exposure category (> 100 ppm-years). In a meta-regression, the trend was statistically significant (P = 0.015). Use of cumulative exposure eliminated heterogeneity between studies. The risk of AML also increased from low (1.94, 95% CI, 0.95-3.95), medium (2.32, 95% CI, 0.91-5.94), to high exposure category (3.20, 95% CI, 1.09-9.45). The study provides evidence that exposure to benzene at work increases the risk of leukemia in a dose-response pattern. There was strong evidence of an increased risk for leukemia in general and AML in particular.

Savitz et al. (1997) performed a systematic review and meta-analysis reviewing the epidemiologic research to assess the association between benzene exposure and lymphatic and hematopoietic cancer. Eighteen relevant case-control and 16 industry-based cohort studies were located. Studies of leukemia showed 2 studies with relative risk greater than 2 in two community-based studies and four industry-based studies as well as two studies with relative risks between 1.5 and 2.0., but several studies showed a relative risk at or near 1.0 or below. An exposure-response analysis noted that the highest exposed individuals with 720 ppm-months had the greatest risk of leukemia with a risk ratio of 2.8 (95% CI: 0.6-8.1). The authors found an elevated risk for leukemia overall and for subtypes including AML and other sub-types that were equivalent in terms of magnitude of the risk.

4. COHORT STUDIES

Stenehjem JS et al. (2015) performed a nested case-control study in a cohort of 25,000 Norwegian offshore petroleum workers with the aim to examine the risk of hematopoietic cancer in benzene-exposed offshore workers. They used cancer registry data to identify 112 cancer cases diagnosed during with leukemia between 1999 to 2011 in a cohort of 24,917 Norwegian men reporting offshore work between 1965 and 1999. Analyses were conducted using a stratified case-cohort design with a reference sub-cohort of 1661 workers. Cox regression was used to estimate hazard ratios with 95% confidence intervals, adjusted for other benzene exposure and smoking. Most workers were exposed to benzene for 0 to 15 years. The upper range values of average intensity and cumulative exposure were estimated to 0.040 ppm-years and 0.948 ppm-years, respectively. The study found that leukemia risk was consistently elevated among exposed workers for the leukemia subtypes combined and for most subgroups, although case numbers were small and yielded imprecise risk estimates. There were three AML cumulative exposure tertiles (T1 to T3) measured as parts per million-years or (ppm-yr). The T1 < 0.001–0.037 exposure tertile had a risk estimate of 1.40 (95%CI: 0.18–11.00); the T2 exposure tertile > 0.037–0.123 ppm-yrs had a risk estimate of 0.85 (95%CI: 0.08–9.29). The T3 exposure tertile 0.124-0.948 ppm-yrs had a risk estimate of 4.85 (95%CI: 0.88–27.00). The test for trends P-value was 0.052, so there was evidence of a significant dose-response pattern for cumulative exposure for acute myeloid leukaemia. The T1 tertile for CLL < 0.001–0.037 had an elevated risk estimate of 6.23 (95%CI: 0.71–54.00); the T2 tertile was 0.037–0.123 ppm-yrs and the risk estimate were elevated at 3.08 (95% CI: 0.28–34.00). The T3 exposure tertile was 0.124 - 0.948 ppm-yrs and the risk estimate were also elevated

Case 7:23-cv-00897-RJ Document 465-3 Filed 08/24/25 Page 22 of 67

at 6.74 (95% ci: 0.75–60.00). The test for trends P-value was 0.094, so there was some suggestive evidence of a dose-response pattern for benzene exposure and cumulative exposure for chronic lymphocytic leukemia. The paper results support a causal association between cumulative exposure with low-level benzene exposure and risk for leukemia.

Linet et al. (2015) examined cancer incidence and mortality in the lymphatic and haematopoietic system in a large cohort of Chinese workers in rubber and chemical manufacturing, shoemaking, and printing industries that made up a large cohort of 74,828 benzene-exposed workers and 35,504 unexposed workers. The workers were dichotomized (benzene exposed/unexposed) based on job titles and factory records on use of benzene-containing materials. The initial follow-up period from 1972 to 1987 was extended to 1999. The risk for leukemia was elevated in exposed workers with a risk ratio of 4.5 (95% CI: 0.8–83.9). Although the null value was included in the confidence interval, the study supports the strong association between benzene and leukemia as exposure to benzene could not be considered to be health protective. The study's strengths include: it was a very large cohort and there were few losses to follow-up; there was a long follow-up (28 yr); and there was very careful ascertainment of hematolymphopoietic malignancies. There were some limitations in that there was no quantitative assessment of exposure, and there were a wide range of industrial processes and co-exposures that were not addressed in the analyses.

Schnatter et al. (2012) performed an update to the study of a cohort of petroleum distribution workers who had lymphatic and hematopoietic system cancers diagnosed until December 2006 in Australia, 1994 in Canada, and 2005 in the United Kingdom, and were pooled for re-analysis using a nested case-control study design. Only male cases and matched controls were included in the analysis. Six exposure metrics were derived: cumulative exposure (ppm-years), average intensity (ppm), maximum intensity (ppm, i.e., the highest job-specific exposure estimate), duration of employment (years), peak exposure (yes/no, when employed in a particular job for at least 1 year and having experienced >3 ppm exposure for 15–60 minutes at least weekly), and dermal exposure (no, low, medium, high; defined as the highest job-specific probability of skin contact for at least 1 year). It was not surprising that conditional logistic odds ratios for AML were above unity for most exposure metrics, highest vs. lowest cumulative exposure tertiles OR, 1.39 (95% CI: 0.68–2.85); average exposure intensity risk was 1.90 (95% CI: 0.86–4.18); maximum exposure risk intensity was 1.65 (95% CI: 0.75–3.73); duration of employment risk intensity was 1.70 (95% CI: 0.75–3.87); peak exposure risk intensity risk ratio was 1.50 (95% CI: 0.82–2.75); dermal exposure risk estimate was 1.15 (95% CI: 0.60–2.22). Although the confidence intervals included the null value, this study is one of many that demonstrate consistent positive associations between benzene and leukemia.

In a subsequent analysis of the same AML data, these associations were found to be more consistent in the subgroup of terminal workers who experienced higher exposure levels. Finally, myelodysplastic syndrome (MDS) showed a consistent monotonic trend for all benzene exposure metrics (e.g., for cumulative exposure, highest vs. lowest tertile with a risk ratio of 4.33 (95% CI: 1.31–14.3), and the P-test for trend was 0.01 based on 29 cases). Although MDS is different from leukemia, it is a disease that originates in the bone marrow and can progress to leukemia over time. The strengths of this study included the high quality of the assessment of benzene exposure and of diagnostic classification. The size of the study was relatively large, but small numbers were available in some subgroup analyses. The confidence intervals did not include one which adds to the precision of the risk estimate.

Collins et al. (2015) updated the Dow Chemical workers, Midland, Michigan retrospective cohort mortality study of 2,266 workers exposed to benzene at the Dow Chemical plant in Michigan. Vital status and cause of death were derived from the company's research database, regularly updated from several sources, including the National Death Index. The average exposure duration of cohort members was 4.9 years (range, 30 days–44.7 years), and cumulative exposure of the subjects was divided into three categories (0–3.9, 4.0–24.9, and ≥25 ppm-years). There were five deaths from AML in the cohort of 2,266 workers exposed to benzene at the Dow Chemical plant, giving a standardized mortality ratio (SMR) of 1.11 (95% CI, 0.36–2.58) in the total population (P for trend, 0.88). The strengths of this study included its long and complete follow-up and comprehensive exposure assessment. The authors noted in conclusion that this study demonstrates a potential for an elevated risk of death due to leukemia.

Rhomberg et al. (2016) did a reassessment of the Pliofilm cohort study. The cohort of workers at three Pliofilm (rubber hydrochloride) manufacturing plants in Ohio (USA) consisted of 1,696 workers followed up for mortality between 1940 and 1996, included in IARC Monographs Volume 100F (available at: http://publications.iarc.fr/123). Methods of exposure assessment differed between investigators, leading to different distributions of benzene exposure in the cohort and different risk values depending on the exposure levels assigned to the cases. In a recent publication, Rhomberg reassessed exposure to benzene using a probabilistic approach based on air sampling data and assumptions about how workplace concentrations decreased over time. The uptake of benzene from dermal exposures was also estimated, and new exposure information was obtained through additional interviews with former workers. Using these new estimates, the authors divided cohort members according to quantiles of benzene exposure distribution; about 20% of the cohort members had the highest cumulative exposures of more than 80.11 ppm-years. Previous investigators (Wong, 1995; Rinsky et al., 2002) had both used fixed cut-offs of 40, 200, and 400 ppm-years. After reassessment of exposure to benzene in the Pliofilm cohort study, all six deaths from AML were observed in the highest quintile of benzene exposure (SMR, 10.11; 95% CI, 3.71–22.01). In the analysis using lag times of 0, 5, 10, 15, or 20 years, the authors found that the highest risk of AML mortality was in the highest exposure category and included a 10-year lag period. There were some notable weaknesses to this study, but the results do provide consistency and strength of association to the link between benzene and leukemia.

5. CASE CONTROL STUDIES

Crosignani et al. (2004) conducted a small study of leukemia incidence in Varese, Italy. There was a total of 120 incident cases that were identified from the population-based Lombardy Cancer Registry, and 480 population controls, matched to cases by age and sex, who were selected from the population-based Health Service Archives. Benzene concentration at the address at diagnosis was calculated on the basis of traffic density on surrounding roads and distances from the home address to roads with heavy traffic. When comparing children exposed to high concentrations of benzene (estimated annual average benzene at >10 μg/m³) with children not exposed to road traffic emissions (estimated annual average benzene at <0.1 μg/m³), the relative risk was 3.9 (95% CI, 1.4–11.3) based on 7 exposed cases, and 4.3 (95% CI, 1.5–12.6) after adjustment for socioeconomic status of the municipality. There was a trend across the three exposure categories (P for trend < 0.005). The strengths of the study included the population-based design and the objective, model-based exposure assessment method. The limitations included the small number of cases, the use of only the address at diagnosis for exposure assessment, and the non-differential misclassification of exposure.

Talibov et al. (2014) conducted a very large case–control study nested within the Nordic Occupational Cancer Study cohort. The study in Finland, Iceland, Norway, and Sweden comprised 15,332 AML cases and 76,660 control subjects. While the authors noted risk ratios at the null and below, the risk ratios were subject to exposure mis-classification bias due to incomplete work histories and a less precise job exposure matrix. The study included its very large cohort and had a nested design, making selection bias less of an issue.

A low-level benzene study conducted by Glass et al. (2003) looked at the association between blood cancers and benzene exposures in a cohort of Australian petroleum workers. The authors found that exposure intensity to be highly related to leukemia risk but even at cumulative exposure levels between a and 2 ppm-years of cumulative lifetime exposure, a significantly elevated risk of leukemia was noted. (OR, 3.9 95% CI .9-17.1). For those exposed to 2-4 ppm-years of benzene, the risk of leukemia was even greater. (OR, 6.1 95% CI 1.4-26). The authors found an increased risk of leukemia at all cumulative exposures above 1 ppm-year with a strong dose-response relationship noted.

6. COMMUNITY/CHILDHOOD CANCER STUDIES

Vinceti et al. (2012) identified 83 incident cases of acute leukemia among children (age 0–14 years) in the population-based Italian Association of Pediatric Hematology and Oncology cancer registry located in the Emilia-Romagna region of northern Italy. A total of 332 population controls, individually matched to cases by sex, year of birth, and province of residence during the diagnosis year, were selected. Modeled benzene concentrations were validated against those measured at fixed-site monitoring stations, showing a correlation coefficient of 0.43 (95% CI, −0.48–0.89) for annual mean values. The odds ratio for acute leukemia was 1.7 (95% CI, 0.8–3.6) for the highest (≥0.50 μg/m³) compared with the lowest (<0.10 μg/m³) category of benzene exposure, after adjustment for PM_{10}. Linear analyses adjusted for PM_{10} showed odds ratios of 0.97 (95% CI, 0.49–1.93; 64 cases) and 1.92 (95% CI, 0.64–5.78; 19 cases) for ALL and AML, respectively, in association with a 1 μg/m³ increase in average benzene concentration. Restricting the linear analyses to children diagnosed when aged 0–4 years yielded odds ratios of 1.95 (95% CI, 0.58–6.50; 27 cases) and 5.46 (95% CI, 1.12–26.51; 11 cases) for ALL and AML, respectively. A strength of this study was the population-based design and the objective exposure assessment by use of a validated exposure model, although the correlation between calculated and measured benzene was relatively low. Limitations included the small sample size resulting in wide confidence intervals, the use of only the address at the time of diagnosis for exposure assessment, and non-differential misclassification of exposure.

Houot et al. (2015) estimated benzene concentrations at the addresses at the time of diagnosis of 517 incident acute leukemia cases (age 0–14 years) and 6,147 control children living in the Île-de-France region in France. Cases were identified from the National Registry of Childhood Hematopoietic Malignancies , and control children were selected from a population-based tax database. The benzene modeling took into account contributions from both urban background pollution and local traffic. The subjects were classified on the basis of the benzene exposure estimate at their home being either less than 1.3 μg/m³ (median exposure for the controls) or 1.3 μg/m³ or more. When comparing the two groups, the odds ratio for ALL was 0.9 (95% CI, 0.7–1.0; based on 210 exposed cases) and for AML was 1.6 (95% CI, 1.0–2.4; $P < 0.05$, based on 59 exposed cases). Strengths included the population-based design and the objective and model-based exposure assessment method. Limitations included the limited adjustment for potential confounders, the use of only the address at the time of diagnosis for exposure assessment, the non-differential misclassification of exposure, and the limited contrast in the

analysis of exposures to above versus below the median.

Janitz et al. (2017) studied benzene and acute leukemia, including 228 cases of ALL and 79 of AML (age 0–19 years) from the Oklahoma Central Cancer Registry, USA. A total of 28% of identified cases were excluded, however, because they could not be linked to birth certificates. Population controls (n = 1,013) were selected from birth certificates, matched by week of birth. Address at birth was allocated to the census tract, and benzene concentrations for 2005 for each census tract were extracted from the NATA database. Children were divided into quartiles of exposure and, in a secondary analysis, the cut-off points at the 40th (0.53 $\mu g/m^3$), 60th (0.78 $\mu g/m^3$), and 95th (1.33 $\mu g/m^3$) percentiles were used to form exposure categories. The two corresponding odds ratios for AML were 2.42 (95% CI, 0.98–5.96) and 1.58 (95% CI, 0.53–4.69), with an indication of an exposure–response relationship over quartiles. The analyses adjusted for time of birth, race/ethnicity, age at diagnosis, sex, birth order, exposure to electromagnetic fields, urbanization, and maternal education, and smoking during pregnancy. The strengths included the population-based design and the objective, model-based exposure assessment method. Limitations included the limited sample size, the lack of information about address history, the exposure assessment being based on only 1 year, and the non-differential misclassification of exposure. The exclusion of cases that could not be linked to a birth certificate was a potential source of selection bias.

7. ANIMAL EXPERIMENTS

Farris, et al. (1993) performed a study in male and female mice of whole-body inhalation and reported the induction of tumours of the hematopoietic and lymphoid tissues, as well as other cancers. The National Toxicology Program (1986) initiated four oral-administration studies by gavage; and Maltoni et al. (1989) conducted two intraperitoneal-injection studies in male and female mice. The oral administration studies reported the induction of tumors of the hematopoietic and lymphoid tissues. The ATSDR Toxicology Profile for Benzene noted one study of intraperitoneal injection where the offspring of injected dams developed liver tumors and tumors of the hematopoietic and lymphoid tissues.

Four oral administration studies (by gavage) in male and female rats, and one whole-body inhalation study in pregnant female rats and their male and female offspring have been published. Benzene caused tumors of the hematopoietic and lymphoid tissues and in the offspring after inhalation. In several studies using three different genetically modified mouse models of different genetic backgrounds, benzene induced tumors of the hematopoietic and lymphoid tissues by oral administration, whole-body inhalation, or skin application; benzene also caused sarcomas of the subcutis in one oral administration study and skin papilloma in two skin application studies. In a study evaluating the potential for wheat grass as an anti-cancer remedy, leukemia was induced in Wister rats by injection after only several weeks. Khan (2015).[107a]

The 2021 National Toxicology Program Assessment on Benzene reported studies in experimental animals that demonstrated benzene causes cancer at numerous tissue sites in rodents. Oral exposure to benzene caused numerous cancers including malignant lymphoma and lung cancer (alveolar/ bronchiolar carcinoma) in mice of both sexes (NTP (1986), Huff et al. (1989). Inhalation exposure to benzene caused tumors at many tissue sites in rats and a tendency towards induction of lymphoid tumors in mice. Benzene is easily absorbed, widely distributed, and extensively metabolised, and thus yielding a complexity of Benzene administered by intraperitoneal injection caused benign lung tumors in male mice IARC (1987). Dermal application of benzene caused benign skin tumors in transgenic mice

carrying the v-Ha-ras oncogene, which increases their susceptibility to carcinogens. Blanchard et al. (1998), Spalding et al. (1999), French et al. (2000). In heterozygous p53-deficient mice (with only one functional copy of the p53 tumor-suppressor gene), benzene administered by stomach tube caused cancer (sarcoma) of head and neck, thoracic cavity, and subcutaneous tissue Hulla et al. (2001).

8. MECHANISTIC EFFECTS

Benzene is absorbed, distributed, and metabolizedinto reactive intermediate species that are reactive electrophiles that work via multiple metabolic pathways in various tissues, including bone marrow. It exhibits many of the key characteristics of carcinogens. In humans, benzene is metabolically active, causes oxidative stress, is genotoxic, and like TCE, causes immune system dysregulation. In addition, evidence from experimental studies shows that benzene causes genomic instability, inhibits topoisomerase II, modulates receptor-mediated effects relevant to the aryl hydrocarbon receptor, and induces apoptosis. NTP (2021).

In benzene-exposed humans, epoxide- and benzoquinone-protein adducts are formed in blood. Additionally, benzene induces oxidative stress in exposed humans, in human cells, and mouse bone marrow. Oxidative stress can result in chronic inflammation, which is linked to cancer. In studies of workers, benzene was noted to cause oxidative DNA damage, DNA strand breaks, gene mutations, and chromosomal aberrations. In the bone marrow of experimental animals exposed in vivo, benzene induces DNA adducts, and chromosomal aberrations. Similarly, in human cells in vitro, benzene or its metabolites induce DNA adducts, and chromosomal aberrations. Many studies in exposed humans have demonstrated hematotoxicity, ranging from decreased white blood cell counts at lower exposures to aplastic anemia and pancytopenia at higher exposure levels. NTP (2021). Benzene-induced hematotoxicity is associated with future risk of developing hematological malignancies, including leukemia.

Benzene is absorbed via inhalation, through oral and dermal exposure in all species studied, including humans and rodents. Benzene is widely circulated by the blood and is largely excreted through the lungs, with small amounts excreted in the urine. Benzene is metabolized by cytochrome P450. Major urinary metabolites include phenol, hydroquinone, and catechol. There is strong evidence, including in exposed humans, that benzene is metabolically activated to electrophilic metabolites. Exposure to benzene causes oxidative stress, which can cause chronic inflammation, thus increasing the risk for cancer. In addition, Benzene exposure causes decreased serum glutathione levels, increased lipid peroxidation, and reactive oxygen species, along with protein and DNA damage. NTP (2021) Benzene or its metabolites induced oxidative stress in both human and other mammalian cells in vitro, and in various tissues, including bone marrow, in mice. The fact that Benzene causes oxidative stress in the bone marrow of mice proves biological plausibility for a leukemia pathway.

There is evidence that benzene is genotoxic due to DNA damage and chromosome strand breaks and gene mutations in exposed humans. Benzene has been noted to cause DNA damage in human cells in vitro and in animals exposed in vivo. Benzene exposure caused DNA adduct formation in bone marrow and leukocytes, which happens to be the site of origin for leukemia. Benzene metabolites have induced DNA adducts in several studies in human hematopoietic cells. People exposed to benzene were also noted to have chromosomal damage to include aneuploidy, translocations, and other chromosome changes. Studies of human cells in vitro, with benzene exposure causes metabolic activation and benzene metabolites that induce chromosomal changes.

Benzene alters DNA repair mechanisms, causes genomic instability, and inhibits topoisomerase II, which interferes with DNA replication. By inhibiting DNA repair mechanisms, Benzene increases the risk of cancer by limiting the body's ability to deal with DNA changes caused by toxic exposure and which occur in the absence of toxic exposure.

Benzene causes immune suppression in exposed humans. Studies in exposed humans have demonstrated hematotoxicity including decreased leukocyte counts, aplastic anemia and pancytopenia at higher exposure levels. More recently, a study has shown that Benzene caused immunosuppression of the adaptive immune system as well as activation of the innate immune system resulting in inflammation. Guo et al. (2022). Specifically, reduced B-lymphocytes and CD4+ T-lymphocytes have been reported in multiple studies in exposed humans. Animal studies have shown consistent immune-suppression in assays of humoral and cell-mediated immunity consistent with similar studies in exposed humans. In addition, several studies have found benzene exposure is linked to future risk of hematological malignancy.

Thus, benzene exposure in humans and experimental animals provides evidence that benzene exposure leads to alterations of cell proliferation and cell death. In human cells in vitro, benzene or its metabolites induced apoptosis consistently across multiple hematopoietic cell types. In addition, in mice, benzene depressed bone marrow cells/progenitor cells mediated by Trp53, and induced apoptosis in various mouse hematopoietic cells in vivo and in vitro. After cessation of benzene exposure, dynamic recovery of bone marrow cells/progenitor cells was observed.

Overall, the mechanistic data provides strong evidence of Benzene's genotoxic and immunotoxic effects, both of which may act together or independently to increase the risk of leukemia. Multiple studies show that benzene causes cell death, and induces apoptosis, modulates receptor-mediated effects with respect to the aryl hydrocarbon receptor and exposure–response gradients were noted for micronucleus formation, chromosomal aberrations, and altered leukocyte counts in the majority of studies examined. The mechanistic data provides biological plausibility for the link between Benzene exposure and leukemia.

9. NTP'S 2021 ASSESSMENT OF BENZENE

When evaluating cancer risks, the NTP uses a thorough, methodology based on established criteria. This approach incorporates evidence from all three pillars of science, including human studies, animal experiments, and mechanistic research. Draft monographs are reviewed by external experts before being finalized and released. In my assessment, NTP monographs, similar to those from the International Agency for Research on Cancer (IARC), are regarded as highly credible and influential, with conclusions that hold significant authority. In 2015, the NTP released a monograph on benzene, which was subsequently updated in 2021 as part of its *Reports on Carcinogens.*

Based on its evaluation, the NTP concluded that there is sufficient evidence to classify benzene as a human carcinogen. This determination was supported by evidence from all three pillars of science and involved epidemiological research, along with toxicological, toxicokinetic, and mechanistic studies that demonstrated the biological plausibility of benzene's carcinogenic effects in humans. Regarding leukemia specifically, the NTP noted that experimental animal studies revealed that benzene exposure through inhalation or oral administration induced leukemia in rats and mice. Moreover, benzene was shown to cause immunomodulation in both humans and animals, with immunomodulation being linked

to leukemia development. The NTP identified the study by Khalade et al. (2010) as providing the strongest epidemiological evidence of the association between benzene exposure and leukemia.

10. RECENT STUDIES PUBLISHED SINCE THE IARC AND NTP REPORTS EXAMINING THE LINK BETWEEN BENZENE EXPOSURE AND LEUKEMIA

Yoon et al. (2018) reviewed evidence for benzene causing types of cancer and exposure levels associated with hematopoietic cancers. The authors noted that benzene was associated with hematopoietic cancers. More recent studies confirm that even low exposure levels are related to cancer risk. Prior studies demonstrated workers exposed to more than 200 ppm-years were at increased cancer risk. However, more recent studies, show significant risk at exposure levels from 0.5 to 1 ppm-year. Although relatively low exposure levels of 0.5–1 ppm-year increase the risk of hematopoietic cancer, further research is needed on exposure response relationships. The levels found by Yoon are in line with the levels found in the drinking water at Camp Lejeune, as the.5 ppm-year relates to a 1.37 ppb/day level in the drinking water at Camp Lejeune which is actually lower than the average contaminant levels found at Camp Lejeune noted in Bove 2014a.

Linet, et al. (2019) performed a case-cohort study of benzene exposure and leukemia. While there is international consensus that benzene exposure is causally related to acute myeloid leukemia (AML), uncertainties remain regarding the exposure-response relationship. In a case-cohort study of 110,631 Chinese workers followed between 1972 and 1999, the authors evaluated combined MDS/AML (n = 44) and CML (n = 18). Benzene exposures were estimated using hierarchical modeling of occupational factors calibrated with historical routine measurements. Exposure-response relationships for cumulative exposure and average intensity were evaluated using Cox regression, with two-sided p-values. Increased MDS/AML risk with rising cumulative exposure in the predefined time window (2 to <10 years before the time at risk) was suggested (Ptrend = .08). For first exposure within the 2 to <10-year window before age 30, the exposure-response relationship was stronger (P = .004), with rate ratios of 1.12 (95% CI, 0.27–4.29), 5.58 (95% CI, 1.65–19.68), and 4.50 (95% CI, 1.22–16.68) for cumulative exposures of >0 to <40, 40 to <100, and ≥100 ppm-years, respectively, compared with no exposure. There was little evidence of exposure response after at least 10 years (Ptrend = .94), regardless of age at first exposure. Chronic myeloid leukemia risk was higher in exposed versus unexposed workers. For myeloid neoplasms, the strongest effects were observed for MDS/AML within 10 years of benzene exposure and for first exposure in the 2 to <10-year window before age 30.

DeMoulin, et al. (2024) investigated associations between occupational benzene exposure and leukemia risk in a population-based cohort of 61,377 men aged 40 to 74 years. A job-exposure matrix constructed by industrial hygienists for the study population was used to calculate cumulative benzene exposure across all jobs held. Cox regression models were used to estimate adjusted hazard ratios (aHR) and 95% confidence intervals (CI) for benzene-leukemia risk associations, with adjustments for potential confounders. Over 15 years of follow-up, 100 leukemia cases were identified. Benzene exposure >550 mg/m^3 was associated with an increased leukemia risk (aHR = 2.3; 95% CI, 1.1–4.5), and benzene exposure was linked to earlier cancer diagnosis age. The benzene-leukemia relationship followed a linear dose-response pattern (Plinear = .016).

11. BRADFORD HILL CONSIDERATIONS

a. Strength of association

The strength of the association is supported by both meta-analyses previously discussed, which shows a significant link between benzene exposure and leukemia. Furthermore, numerous individual cohort and case-control studies contribute additional evidence demonstrating a strong correlation between benzene and leukemia. Khalade et al. (2010) pulled together the existing epidemiologic evidence on the relation between occupational exposure to benzene and the risk of leukemia, including AML, ALL, CLL, and CML. The authors did a systematic review and identified 15 studies that provided 16 estimates of effect size. The random-effects model yielded a summary-effect size estimate of 1.72 (95% CI, 1.37–2.17). Effect estimates from nine studies were based on cumulative exposures. In these studies, the risk of leukemia increased with a dose-response pattern with a summary-effect estimate of 1.64 (95% CI, 1.13–2.39) for low (<40 ppm-years), 1.90 (95% CI, 1.26–2.89) for medium (40–99.9 ppm-years), and 2.62 (95% CI, 1.57–4.39) for high exposure category (>100 ppm-years). In a meta-regression, the trend was statistically significant (P = 0.015). Use of cumulative exposure eliminated heterogeneity between studies. The risk of AML also increased from low (1.94, 95% CI, 0.95–3.95), medium (2.32, 95% CI, 0.91–5.94), to high exposure category (3.20, 95% CI, 1.09–9.45), but the trend was not statistically significant. The study provides evidence that exposure to benzene at work increases the risk of leukemia in a dose-response pattern. There was substantial evidence of an increased risk for leukemia in general and AML in particular. The random-effects model yielded a summary- effect size estimate of 1.72 (95% CI, 1.37-2.17). Effect estimates from 9 studies were based on cumulative exposures. In these studies the risk of leukemia increased with a dose-response pattern with a summary-effect estimate of 1.64 (95% CI, 1.13-2.39) for low (< 40 ppm-years), 1.90 (95% CI, 1.26-2.89) for medium (40-99.9 ppm-years), and 2.62 (95% CI, 1.57-4.39) for high exposure category (> 100 ppm-years). In a meta-regression, the trend was statistically significant (P = 0.015).

Stenehjem JS et al. (2015) performed a nested case-control study in a cohort of 25,000 Norwegian offshore petroleum workers with the aim to examine the risk of hematopoietic cancer in benzene-exposed offshore workers. Most workers were exposed to benzene for 0 to 15 years. The upper range values of average intensity and cumulative exposure were estimated to 0.040 ppm-years and 0.948 ppm-years, respectively. Risks were consistently elevated among exposed workers for the leukemia subtypes combined. AML cumulative exposure tertiles (ppm-years) T1 < 0.001–0.037 risk estimate 1.40 (95% CI: 0.18–11.00); cumulative estimate T2 > 0.037–0.123 ppm-years risk estimates 0.85 (95% CI: 0.08–9.29), and T3 exposure 0.124–0.948 ppm-years risk estimate 4.85 (95% CI: 0.88–27.00). The test for trends P-value was 0.052, so there was evidence of a dose-related risk pattern for cumulative exposure for acute myeloid leukemia. The results for CLL show T1 < 0.001–0.037 risk estimate 6.23 (95% CI: 0.71–54.00); cumulative estimate T2 > 0.037–0.123 ppm-years risk estimate 3.08 (95% CI: 0.28–34.00), and T3 exposure 0.124–0.948 ppm-years risk estimate 6.74 (95% CI: 0.75–60.00). The test for trends P-value was 0.094, so there was suggestive evidence of a dose-related risk pattern for cumulative exposure for chronic lymphocytic leukemia.

Linet et al. (2015) examined cancer incidence and mortality in the lymphatic and hematopoietic system in a large cohort of Chinese workers comprising 74,828 benzene-exposed workers and 35,504 unexposed Chinese workers. Spray and brush painting (coatings), rubber, chemical (including pharmaceutical manufacturing), shoemaking, and other (including printing and insulation) industries were considered. Exposure assessment methods included records; workers were dichotomized

(benzene-exposed/unexposed) based on job titles and factory records on the use of benzene-containing materials. The initial follow-up period from 1972 to 1987, which had a quantitative assessment for exposure to benzene, was extended to 1999 using factory records, hospital records, and death certificates. Benzene exposure assessment was based on factory and job-specific information on the use of material containing benzene and was limited to classification as ever (for at least six months) versus never exposed. The risk for leukemia was elevated with a risk ratio of 4.5 (0.8–83.9) in exposed compared to unexposed workers.

Linet, et al. (2019) performed a multi-center case-cohort study of benzene exposed Chinese workers followed up during 1972–1999 to assess the risk of leukemia and MDS. There were 44 MDS/AML and 18 CML cases. The authors estimated benzene exposures using hierarchical modeling of occupational factors and historical benzene measurements and evaluated cumulative exposure and average exposure intensity using Cox regression. Increased MDS/AML risk with increasing cumulative exposure in their a priori defined time window of from 2 to <10 years (P trend = 0.08). For first exposure in the 2 to <10-year window before age 30 years, the exposure response was stronger (P = 0.004) with rate ratios of 1.12 (95% CI = 0.27–4.29), 5.58 (95% CI = 1.65–19.68), and 4.50 (95% CI = 1.22–16.68) for cumulative exposures of more than 0 to <40, 40 to <100, and > 100 ppm-years, respectively, compared with no exposure.

DeMoulin, et al. (2024) investigated occupational benzene exposure and leukemia risk in a cohort of 61,377 men, ages 40 to 74 years. A job-exposure matrix, constructed by industrial hygienists specifically for the study population, was used to derive cumulative benzene exposure for all jobs held. Cox regressions were performed to estimate adjusted hazard ratios (aHR) and 95% confidence intervals (CI) for benzene–cancer risk associations and the results were adjusted for confounders. During 15 years of follow-up, 100 cases of leukemia were identified. Benzene exposure >550 mg/m^3 was associated with an increased risk of leukemia (aHR = 2.3; 95% CI, 1.1–4.5); and increased risk of leukemia was associated with early cancer diagnosis age.

b. Consistency

As can be seen in the most recent meta-analysis conducted by Khalade et al. (2010), the findings of the cohort and case-control studies demonstrate statistically elevated risks of leukemia and AML in particular in relation to benzene exposure. The random-effects model yielded a summary- effect size estimate of 1.72 (95% CI, 1.37-2.17). Effect estimates from 9 studies were based on cumulative exposures. In these studies the risk of leukemia increased with a dose-response pattern with a summary-effect estimate of 1.64 (95% CI, 1.13-2.39) for low (< 40 ppm-years), 1.90 (95% CI, 1.26-2.89) for medium (40-99.9 ppm-years), and 2.62 (95% CI, 1.57-4.39) for high exposure category (> 100 ppm-years). In a meta-regression, the trend was statistically significant (P = 0.015). In my view, this provides compelling evidence in support of this consideration.

c. Specificity

Benzene is associated with a number of cancers including kidney cancer so this makes the specificity consideration not met.

Case 7:23-cv-00897-RJ Document 465-3 Filed 08/24/25 Page 31 of 67

d. *Temporality*

Studies examining benzene exposure and leukemia found a notable link, and in those reviewed in the meta-analyses mentioned earlier, exposure occurred before the onset of leukemia, thereby establishing a temporal relationship. Research that has taken into account a delay in cancer onset has discovered a more significant link between benzene and leukemia, consistent with the typical latency period seen between exposure and the onset of a cancer like leukemia. In my view, there is substantial evidence backing up this consideration.

e. *Dose-Response*

Consistent with a biological gradient, several studies, as detailed in the systematic review and meta analysis conducted by Khalade et al. (2010), showed a dose-response relationship between the duration of benzene exposure and leukemia. In my opinion, the evidence in support of this consideration is present and strong.

f. *Biological Plausibility*

The mechanistic, experimental and animal evidence are supportive the mechanistic, experimental, and animal evidence are supportive based on evidence of genotoxicity, immunosuppression, autoimmunity, and biomarkers consistent with cancer changes related to miRNA, epigenetics, and chromosomal aberrations. Thus, in my opinion, the evidence in support of this consideration is strong.

g. *Coherence*

The correspondence between the epidemiological evidence and the experimental toxicological evidence noted by IARC and NTP, and confirmed by my review, is consistent with coherence.

h. *Experimental Evidence*

There is a lack of experimental epidemiological data on human exposure to benzene, and conducting such research would be unethical. It is worth noting that the available toxicological evidence on benzene's genotoxic and immunotoxic mechanisms stems from a substantial body of well-conducted animal experiments.

i. *Analogy*

There is similarity between the likely mechanisms of action of benzene with other immunotoxic agents like TCE and the reactive metabolites that are known to induce leukemia, which supports this consideration.

12. CONCLUSION: BENZENE EXPOSURE MORE LIKELY THAN NOT CAUSES LEUKEMIA

In conclusion, the epidemiological evidence of the association between benzene and leukemia is sufficient. There are many tools (e.g., biological markers, DNA adducts) with which to assess historical and/or cumulative exposures to benzene, as well as biological benzene breakdown products that are available. These tools help disentangle exposure to benzene from other solvents. These factors help explain the conclusions reached by the IARC and NTP reports with regards to benzene and leukemia.

There is substantial epidemiological and mechanistic evidence available that benzene causes leukemia, as per IARC and NTP deliberations, including (a) systematic reviews and meta-analyses conducted by Khalade (2010), Bove (2014), and Bove (2024), as well as the recent biomarker epidemiology studies of benzene's genotoxicity, immunotoxicity, autoimmunity, chromosomal aberrations, miRNA perturbations, and epigenetic changes consistent with carcinogenesis. While AML has long been linked to benzene exposures, scientific evidence linking benzene exposures to other subtypes of leukemia has been described as no less persuasively than the evidence for AML. Savitz et al. (1997).

In my opinion, the analysis of the currently available evidence using the Bradford Hill framework makes it more likely than not that benzene is a cause of leukemia to a reasonable degree of medical certainty (and therefore also exceeds the "standard of at least as likely as not" standard prescribed by the Camp Lejeune Justice Act).

F. PERCHLOROETHYLENE (PCE) AND LEUKEMIA

1. PERCHLOROETHYLENE (PCE)

Tetrachloroethylene (PCE) is a non-flammable colorless liquid. Other names for tetrachloroethylene besides perchloroethylene and PCE include PERC, tetrachloroethene, and perchlor. Tetrachloroethylene is one of the most widely used chlorinated solvents. From the 1950s to 1980s, about 80% of PCE was used in dry-cleaning, and 15% in metal-cleaning and vapour degreasing. By the 1980's, the pattern of usage was changing, with about 50% of PCE used for dry-cleaning, 28% for chemical intermediates, and 10-15% for metal cleaning and degreasing. With the continuing decline of its use for dry-cleaning, PCE is now used primarily for producing fluorocarbons ATSDR (2019).[1]

2. IARC'S ASSESSMENT OF PERCHLOROETHYLENE AND CANCER RISK

The 2014 monograph that IARC published on the deliberations of a working group of experts that met from October 2-9, 2012, to address the case of PCE. The Working Group did not find strong evidence for associations of exposure to PCE and cancer. Although the associations found for these cancers in specific studies may reflect true increases in risk, the findings were inconsistent between studies, no clear exposure–response relationships were found, the numbers of observed/expected cases were small and there was contradictory evidence that exposure to PCE is associated with malignant neoplasms.

3. SYSTEMATIC REVIEWS AND META-ANALYSES

Mundt et al. (2003) performed a systematic review of the epidemiological literature regarding the carcinogenic effects of PCE and leukemia. They included forty-four papers that were critically reviewed on 17 cancer sites being assessed for risk of association with PCE exposure. Each paper was assessed on the basis of methodological and scientific quality criteria. The authors did not find epidemiological evidence to support the conclusion that occupational exposure to PCE is a risk factor for cancer at any site, though the authors did not specifically mention that leukemia was an outcome of interest. There was some evidence of a non-significant increased risk between PCE exposure and cancer of the oral

cavity, liver, pancreas, cervix lung, esophagus and bladder.

4. COHORT STUDIES

CAMP LEJEUNE SPECIFIC STUDIES AND REPORTS

Bove et al. 2014a and Bove et al. 2014b conducted two retrospective cohort mortality studies of Marines/Navy personnel and of civilian workers who worked at Camp Lejeune and compared the results with Navy and Marine personnel at Camp Pendleton. Bove et al. 2014a conducted a retrospective cohort mortality study of Marine and Naval personnel who began service during 1975-1985 and were stationed at Camp Lejeune or Camp Pendleton, California. Mortality follow-up was 1979-2008. Standardized Mortality Ratios were calculated using U.S. mortality rates as reference. The authors used survival analysis to compare mortality rates between Camp Lejeune (N = 154,932) and Camp Pendleton (N = 154,969) cohorts and assess effects of cumulative exposures to contaminants within the Camp Lejeune cohort. Confidence intervals (CIs) indicated good precision in the effect estimates. Compared to Camp Pendleton, Camp Lejeune had elevated mortality hazard ratios (HRs) for all cancers (HR = 1.10, 95% CI: 1.00, 1.20), and the risk for leukemia was slightly elevated for TVOC exposure with risk ratios of 2.50 (95% CI:1.24, 5.03) for low exposure duration, for medium exposure the risk was 1.33 (95% CI: 0.56, 3.14) and for high risk exposure, the risk was 2.33 (95% CI 1.08, 5.03). (TVOCs consist of PCE, TCE, VC, and Benzene). The authors concluded that there were elevated hazard ratios for death from leukemia.

Following the Bove 2014 studies, the ATSDR 2017 Public Health Assessment determined for PCE that the risk of leukemia was below equipoise. The ATSDR 2018 Morbidity Study of Camp Lejeune Military and Civilian Personnel used data from extensive water modeling (Maslia et al. (2007), (2013) to reconstruct monthly levels of contaminants in drinking water. These cohort studies found elevated risks of death from leukemias when compared to similar unexposed cohorts from U.S. Marine Corps Base Camp Pendleton.

The Bove 2024 cancer mortality study explored cancer mortality by type, utilizing a longer follow-up period than earlier investigations. The study extended the Camp Lejeune Cohort's follow-up from 2008 to 2018, comparing the cancer risks among military and civilian personnel stationed at Camp Lejeune and Camp Pendleton between 1972 and 1985. The findings revealed that Navy and Marine personnel at Camp Lejeune had a hazard ratio of 1.13 (95% CI: 0.89–1.43), so they had a 13% elevated risk of death from leukemia compared to those at Camp Pendleton. For AML specifically, the risk increased by 21%, with a risk ratio of 1.21 (95% CI: 0.94–1.56) (Supplementary Table 3). For CML, the risk rose to a risk ratio of 1.73 (95% CI: 0.47–6.42) (Supplementary Table 7), indicating a 73% elevated risk compared to Camp Pendleton personnel. These results reinforce the conclusion that chemical exposure levels at Camp Lejeune were linked to a higher risk of death due to leukemia~~,~~ even though the risk estimate was less precise and the confidence interval contained 1. The study also analyzed leukemia risk relative to exposure duration, measured by time spent on base. For personnel with short-term exposure (1–6 months or 1–2 quarters), the risk ratio was 1.17 (95% CI: 0.84–1.64) (Supplementary Table 6). For medium-term exposure (7–10 quarters), the risk ratio increased to 1.19 (95% CI: 0.86–1.64). These findings suggest that even short durations on base during the 1972–1985 period were linked to a higher risk of death due to leukemia. Similarly, individuals who were on base at different intervals but received a cumulative exposure equivalent to 2–7 quarters during that period faced comparable risks.

The Bove et al. (2024) Cancer Incidence Study examined cancer rates among personnel stationed at Camp Lejeune from 1975 to 1985 and compared them to a similar cohort stationed at Camp Pendleton during the same period. By extending the follow-up timeframe, the study evaluated cancer incidence from 1996 to 2017 to determine whether being stationed or employed at Camp Lejeune increased leukemia risk. Camp Pendleton served as the comparison population because it housed a similar demographic but was not believed to have contaminated drinking water during the relevant timeframe. Demographic analysis confirmed no significant differences between the two populations.

Compared with Camp Pendleton, Camp Lejeune Marines/Navy personnel had an elevated risk for all myeloid cancers with a risk ratio of 1.24 (95% CI: 1.03,1.49). Specifically, the risk for acute myeloid leukemia was elevated at 1.38, and the 95% CI was more precise since the CI did not include 1 (95% CI: 1.03,1.85). The risk of myelodysplastic and myeloproliferative syndromes was elevated at 1.68 and was more precise since the CI did not include 1. (95%CI: 1.07-2.62). The Camp Lejeune civilian workers also had an elevated risk of myeloid cancer, with a hazard ratio of 1.40 (95% CI: 0.83-2.36). The wide confidence interval is primarily due to the small number of cases involving civilian workers. Even with limitations which would bias the results towards the null value, these findings suggest that individuals exposed to contaminated water at Camp Lejeune during 1975–1985 had a moderate to high elevated risk of developing leukemia and AML specifically.

Anttila et al. (1995) conducted a retrospective cohort study of exposure to trichloroethylene, tetrachloroethylene, or 1,1,1-trichloroethane and increased carcinogenic risk, following a cohort of 2050 male and 1924 female workers monitored for occupational exposure to these agents that was followed up for cancer incidence from 1967 to 1992. The overall cancer incidence within the cohort was similar to that of the Finnish population. There was an excess risk of leukemia with a risk ratio of 1.1 (95% ci: 0.4-2.5). The study relied on biomarker monitoring for TCE and PCE exposure, so the risk of misclassification bias was low. The Anttila study revealed a modest increase in risk of leukemia for those exposed to TCE and PCE which was above equipoise at 1.1. The wide confidence interval was due to small numbers of cancer cases in the exposed cohort that results in a less precise risk
estimate.

5. CASE CONTROL STUDIES

New Jersey Towns

Fagliano et al. (1990) and Cohn et al. (1994) conducted case-control studies to evaluate the relationship between groundwater contamination with trichloroethylene (TCE) and tetrachloroethylene (PCE) in 75 towns in New Jersey and the incidence of leukemia. The authors highlighted that TCE and PCE have been demonstrated to be carcinogenic in experimental animal studies, suggesting their potential carcinogenicity in humans. Using water modeling, they assigned concentrations of TCE and PCE to various areas, with the highest assigned levels being 67 parts per billion (ppb) for TCE, 14 ppb for PCE, and 92.9 ppb for total non-trihalomethane VOCS. These levels are comparable to, and in some cases lower than, the contaminant levels found at Camp Lejeune. The study employed geographic data aggregated by exposure, approximating actual exposure levels across populations.

Leukemia rates in towns with the highest concentrations of these chemicals were compared to towns with the lowest concentrations. The study found a statistically significant association between leukemia incidence in females and residence in towns with the highest exposure stratum, defined as total VOC

levels exceeding 20 ppb. This finding suggests that exposure to drinking water with at least 20 ppb of VOCS can cause leukemia. Given that total VOC levels at Camp Lejeune often exceeded 20 ppb, this study provides strong evidence linking Camp Lejeune's water contamination levels to leukemia. Bove et al. (2014) supported this conclusion, noting that the maximum detected level of TCE and PCE in the Hadnot Point drinking water at Camp Lejeune was significantly higher than the levels detected in the New Jersey towns.

Cohn et al. (1994) assessed specific risks associated with TCE and PCE exposure. For TCE exposure at or above 5 ppb, females had a relative risk of 1.43 (95% ci: 1.07–1.9), while males had a relative risk of 1.10 (95% ci: 0.84–1.43). These results indicate that exposure to 5 ppb of TCE can cause leukemia in females. For PCE exposure at or above 5 ppb, females experienced a 20% increased risk of developing leukemia. The authors noted that joint exposure to TCE and PCE might increase the carcinogenic effects over what might be expected by adding their individual effects. This is particularly relevant to Camp Lejeune, where many individuals were exposed to both chemicals

Woburn, Massachusetts: Cuttler (1986) and Lagakos (1986) investigated a cancer cluster in Woburn, Massachusetts, where industrial processes contaminated public water supply wells G and H with TCE at 267 ppb and PCE at 21 ppb. These contaminant levels are comparable to those at Camp Lejeune. After the discovery of contamination, the two Massachusetts studies observed a significantly higher cancer mortality rate in Woburn compared to state averages and nearby communities. Epidemiological studies linked TCE and PCE exposure to a cluster of childhood leukemia cases. Specifically, Lagakos (1986) found that cumulative exposure to the contaminated wells was positively associated with leukemia rates, and adverse outcomes declined after the wells were shut down. These results indicate that TCE and PCE levels in the range of 10–100 ppb is sufficient to cause leukemia.

Woburn follow-up:

Aschengrau et al. (1993) conducted a case-control study to assess leukemia risk in the people who had PCE contaminated drinking water in Woburn, MA. The authors noted a markedly increased risk of leukemia in cases compared to controls. The relative risk of leukemia was observed among ever exposed with an adjusted odds ratio of 1.96 (95% Cl = 0.71-5.37) with latency. The relative risk was increased to 2.13 (95% Cl = 0.88-5.19) without latency. People who were exposed above the 90%ile had an adjusted odds ratio of 5.84 (95% Cl = 1.37-24.91) with latency. And the risk was 8.33 (95% Cl = 1.53-45.29) without latency. This study is important to the PCE-Leukemia relationship as it was a water contamination study that had levels of PCE contamination and exposures which were comparable to those at Camp Lejeune. The study demonstrates a rather strong association between PCE and Leukemia.

Costas et al. (2002) conducted follow-up evaluations of the Woburn cancer cluster. Their study demonstrated a dose-response relationship between exposure to contaminated drinking water during pregnancy and childhood leukemia. Children whose mothers consumed the most water from wells G and H during pregnancy had a 14-fold increased risk of developing leukemia compared to those whose mothers consumed less contaminated water. This study underscores the hazardous nature of the chemicals present in Woburn's water, showing that these exposures were sufficient to induce leukemia. While this study focused on maternal exposure leading to childhood leukemia, it reinforces the conclusion that these contaminant levels pose significant risks to human health, supporting the findings at Camp Lejeune on leukemia risk.

6. ANIMAL EXPERIMENTAL DATA

Carcinogenicity animal studies note there is limited data from studies investigating immunotoxicity that suggest PCE exposure can alter white cell counts and immune system markers in humans and in mice U.S. EPA, 2012c). A more recent in vitro study showed that PCE exposure increased changes in mRNA expression of cytokines in macrophages (Kido et al., 2013). The EPA (2012c) noted evidence for effects of PCE on hemolysis and bone marrow function in mice that provides some support for a leukemogenic effect in rodents, but the data were inadequate to establish a mode of action for mononuclear cell leukemia in rats exposed to PCE. A variety of in vitro, and in vivo data on human immune cells provides mixed evidence on genotoxicity due to blood cell toxicity and carcinogenesis. The EPA, 2012c report noted that evidence for effects of PCE on hemolysis and bone marrow function in mice provides some support for a leukemogenic effect in mice but the data were inadequate to establish a mechanism for mononuclear cell leukemia in rats exposed to PCE. A dose-related increase in the incidence and severity of Mononuclear Cell Leukemia (MCL) was observed in male and female F344/N rats exposed to PCE by inhalation at concentrations up to 400 ppm for 103 weeks (NTP, 1986a). The incidence of advanced stage MCL was significantly increased in both sexes at 400 ppm (NTP, 1986a). (Jisa, 1993) also observed a positive dose-related trend in the incidence of MCL in male and female F344/DuCrj rats exposed by inhalation for 2 years, reaching statistical significance in males at 600 ppm. The time to first occurrence of MCL was reduced in exposed female rats, relative to controls (Jisa, 1993). Very high background incidences (36-56%) were observed in both sexes in (NTP, 1986a). The NYT published an article 12/9/2024 noting that the EPA banned all uses of TCE and consumer uses of PCE.

7. MECHANISTIC EFFECTS

PCE is metabolized through oxidative metabolism via the cytochrome P450 pathway and glutathione conjugation followed by subsequent biotransformation to the cystine conjugate which can be cleaved by β-lyase or oxidized by flavin-containing monooxygenase to form metabolites. The same metabolites as TCE that are known to be genotoxic to humans are also produced when PCE is metabolized through the two metabolic pathways. The metabolites include a shared PCA metabolite that has the same toxicity of the TCE metabolite. (Bois et al., 1996). There is some uncertainty regarding the relative contribution of the glutathione conjugation pathway to PCE metabolism, in part, due to the potential for the reactive metabolites of PCE to bind to cellular macromolecules (Cichocki et al., 2016). A more recent study by Luo et al. (2018a) found that, following treatment with both TCE and PCE, the glutathione conjugation

pathway was more reactive for PCE than it was for TCE which may explain the higher potency of TCE and cancer versus PCE as the glutathione conjugation pathway may be responsible for a greater proportion of metabolism for PCE compared to TCE.

8. NTP'S 2021 ASSESSMENT OF TETRACHLOROETHYLENE

The U.S. Department of Health and Human Services released the 15th Report on Carcinogens (ROC) January 2021. The ROC is a congressionally mandated, science-based, public health document that the national Toxicology program (NTP) prepares for the HHS secretary. This cumulative report currently includes 256 listings of agents, substances, mixtures, and exposure circumstances that are known or reasonably anticipated to cause cancer in humans. In the 15th report, the NTP stated that PCE "…is reasonably anticipated to be a Human carcinogen based on sufficient evidence of carcinogenicity from studies in experimental animals and limited studies in humans." With regards to the dose-response

relationship for PCE and cancer, the EPA noted that there were few human studies of leukemia that noted an exposure-response relationship between PCE and leukemia.

9. LITERATURE PUBLISHED AFTER IARC / NTP REPORTS ON PCE CAUSING LEUKEMIA

The EPA PCE Risk Assessment 2020 determined that PCE is characterized as "likely to be carcinogenic in humans by all routes of exposure," based on conclusive evidence in mice and rats and suggestive evidence in humans. No available human studies of cancer were found to be suitable for dose-response assessment. Therefore, the following dose response assessment is based on data from rodent bioassays. Multiple tumor type-specific MOAs for PCE carcinogenicity were considered (Section 3.2.3.3). As discussed in Section 3.2.3.2.3, three chronic exposure studies in rats and mice include an oral gavage study in mice and female rats by the National Cancer Institute (Nci, 1977) and two inhalation studies in mice and rats (Jisa, 1993; NTP, 1986b) established that PCE administration, either by ingestion or by inhalation to sexually mature rats and mice, results in increased incidence of tumors. Mouse liver tumors (hepatocellular adenomas and carcinomas) and rat mononuclear cell leukemia (MCL) were reported in both sexes in two lifetime inhalation bioassays employing different rodent strains (Jisa, 1993; NTP, 1986b), and mouse liver tumors were also reported in both sexes in an oral bioassay (Nci, 1977). Overall, the tumors reported in rodent bioassays are considered relevant to humans and human cancer risks are estimated from the rodent dose-response data using the linear non-threshold model.

10. BRADFORD HILL CONSIDERATIONS

a. *Strength of Association:*

This viewpoint is partially met in this case because a review of the epidemiological studies provides mixed evidence supporting a moderate association between PCE exposure and leukemia. Mundt et al. (2003) performed a systematic review of PCE and cancer. The authors did not find epidemiological evidence to support the as association between occupational exposure to PCE and cancer but did not address leukemia, but this study was done prior to the ATSDR and Bove studies at Camp Lejeune, and the follow-up Woburn, MA studies that demonstrated an exposure-response relationship between PCE and leukemia.

ATSDR completed several epidemiological studies to determine if Marines, Navy personnel, and civilians residing and working on U.S. Marine Corps Base Camp Lejeune were at increased risk for cancer in general, and leukemia in particular, as a result of exposure to water contaminated with TCE, PCE, benzene, and vinyl chloride. The ATSDR 2017 Public Health Assessment, and ATSDR 2018 Morbidity Study of Camp Lejeune Military and Civilian Personnel along with two retrospective cohort mortality studies of Marines/Navy personnel and of civilian workers (Bove et al. 2014a[39], Bove et al. 2014b[40]), as well as the Bove 2024 Cancer Incidence Study and Bove 2024 Cohort Mortality Study used data from extensive water modeling (Maslia et al. 2007, 2013) (Citation) to reconstruct monthly levels of contaminants in drinking water. These cohort studies found elevated risks of death from leukemias when compared to similar unexposed cohorts from U.S. Marine Corps Base Camp Pendleton. Ruckart et al. (2013) conducted a case control study to determine if children born during 1968-1985 to mothers with residential exposure to contaminated drinking water at Camp Lejeune during pregnancy were more likely to have childhood hematopoietic cancers. ORs for any TCE exposure and any vinyl chloride exposure were 1.6 (95% CI: 0.5-4.8), and 1.6 (95% CI: 0.5-4.7), respectively. Although CIs were wide, ORs suggested an association between TCE and childhood hematopoietic cancers.

The Anttila study revealed a modest increase in risk of leukemia for those exposed to TCE and PCE which was above equipoise at 1.1. The wide confidence interval was due to small numbers of cancer cases in the exposed cohort that results in a less precise risk estimate.

Gagliano et al. (1990) and Cohn et al. (1994)[40] conducted case-control studies to evaluate the relationship between groundwater contamination with trichloroethylene (TCE) and tetrachloroethylene (PCE) in 75 towns in New Jersey and the incidence of leukemia. The study found a statistically significant association between leukemia incidence in females and residence in towns with the highest exposure stratum, defined as total VOC levels exceeding 20 ppb which suggests that exposure to 20 ppb of VOCS can cause leukemia. Bove et al. (2014) supported this conclusion, noting that the maximum detected level of TCE and PCE in the Hadnot Point drinking water at Camp Lejeune was significantly higher than the levels detected in the New Jersey towns.

Cuttler (1986)[43] and Lagakos (1986)[44] investigated a cancer cluster in Woburn, Massachusetts, where water was contaminated with PCE at 21 ppb. The two Massachusetts studies observed a cluster of childhood leukemia cases. Lagakos (1986) found that cumulative exposure to the contaminated wells was positively associated with leukemia rates. These results indicate that TCE and PCE levels in the range of 10–100 ppb is sufficient to cause leukemia. Aschengrau et al. (1993) performed a follow-up case-control study in Woburn, MA and noted relative risk of leukemia was 1.96 (95% Cl = 0.71-5.37) after adjustment for latency. People exposed above the 90%ile had an adjusted odds ratio of 5.84 (95% Cl = 1.37-24.91) with latency. Costas et al. (2002)[45] conducted a further follow-up of the Woburn cancer cluster, and their study documented an exposure-response relationship between exposure during pregnancy and childhood leukemia. Children whose mothers consumed the most contaminated water during pregnancy had a 14-fold increased risk of developing leukemia compared to those whose mothers who had consumed less. These studies underscore the hazardous nature of the PCE in drinking water at Camp Lejeune, New Jersey, and Woburn, MA, and demonstrate that these exposures were sufficient to induce leukemia.

Thus, in my opinion, the evidence supports the association reaching at least equipoise and above, for the risk of leukemia following PCE exposure.

b. Consistency:

The consistency viewpoint is supported by findings across several case control and cohort studies in Woburn, MA, New Jersey Towns, and Camp Lejeune. This consistency in findings across various study designs supports the causal relationship between PCE and leukemia.

c. Specificity:

PCE has been linked with causing bladder cancer, so the BH consideration of specificity is not met.

d. Temporality:

In the Cohen and Aschengrau Case control studies and ATSDR and Bove cohort studies that found a significant association between TCE and PCE exposure and leukemia, including those discussed above, exposure preceded disease, providing evidence of temporality. Additionally, studies that have adjusted for a lag period in the onset of cancer have found a stronger association between PCE and Leukemia,

which aligns with the latency period one would expect between exposure and the onset of a cancer such as Leukemia. Thus, in my opinion, the evidence in support of this criterion is strong.

e. Biological Gradient:

a review of the ATSDR Studies 2017, 2018, Bove 2014, and 2024 cohort studies and the Cohen and Aschengrau Case control studies indicates that only Costas found an exposure response relationship with respect to level or duration of PCE exposure and leukemia risk. Thus, in my opinion, the evidence suggests that evidence in support of this criterion is present but is modest.

f. Biological Plausibility:

The mechanistic, experimental and animal evidence are supportive based on evidence of genotoxicity, immunosuppression, autoimmunity, and biomarkers consistent with cancer changes related to miRNA, epigenetics, and chromosomal aberrations. PCE is metabolized in animals and in humans through oxidative metabolism via the cytochrome P450 (CYP) and Glutathione conjugation followed by subsequent biotransformation to the cystine conjugate which can be cleaved by β-lyase or oxidized by flavin-containing monooxygenase to form reactive metabolites that can cause alterations in miRNAs in terms of epigenetics as well as genetic changes including chromosomal aberrations. Thus, in my opinion, the evidence in support of this criterion is strong.

g. Coherence:

The correspondence between the epidemiological evidence and the experimental toxicological evidence noted by IARC and NTP and EPA HRA 2022 [and confirmed by my review,] is consistent with coherence.

h. Experimental Evidence:

Experimental epidemiological evidence is not available for human exposures to PCE (and would be unethical to accomplish). However, it is important to note that the toxicological evidence regarding PCE'S genotoxic and immunotoxic mechanisms are rooted in numerous sound experimental studies.

i. Analogy:

There is similarity between the likely mechanisms of action of PCE with other immunotoxic agents known to induce leukemia e.g., TCE which is a breakdown product of PCE and is known to be genotoxic through its metabolites, some of which are shared with PCE which supports this viewpoint.

11. CONCLUSION: PCE EXPOSURE AT LEAST AS LIKELY AS NOT CAUSES LEUKEMIA

In conclusion, the epidemiological evidence of the association between PCE and leukemia is limited, due, in part, to the fact that leukemia is a relatively rare disease and that other than history, there are no tools (e.g., biological markers) with which to assess historical and/or cumulative exposures to TCE; and even if histories are available, the ability to disentangle exposure to TCE from other solvents is typically limited. These factors account for the limited conclusions reached by the IARC and NTP reports with regards to TCE and NHL. On the other hand, substantial epidemiological and mechanistic evidence has appeared subsequent to the IARC and NTP deliberations that generated their reports, including, (a)

the systematic review and meta-analyses conducted by Karami et al. (2013) and Odutola et al. (2021), and (b) the recent biomarker epidemiology studies of TCE's genotoxicity, immunotoxicity, autoimmunity, and chromosomal aberrations, miRNA perturbations, and epigenetic changes consistent with carcinogenesis. In my opinion, the analysis of the currently assembled evidence using the Bradford Hill framework, makes it at least as likely as not that PCE is a cause of leukemia.

VI. CHEMICAL CONCENTRATIONS ASSOCIATED WITH CANCER CAUSATION

I was also asked to assess the levels of exposure to TCE, PCE, and benzene that have been shown to be hazardous to humans generally. Evidence from the scientific literature highlights several exposure levels identified as harmful to human health, including those capable of causing leukemia. These studies, conducted at Camp Lejeune, New Jersey, and Woburn, MA, outline a range of exposures linked to increased risk:

> **Aschengrau (1993)** demonstrated that cumulative TCE concentrations of 267 ppb and PCE concentrations of 27–44 milligrams exposure in the drinking water in Woburn, MA posed significant health risks for leukemia.
>
> **Cohn (1994)** identified that leukemia risk increased in Jew Jersey towns with exposure to water containing 20 ppb of total VOCs, 5 ppb of TCE, or 5 ppb of PCE, highlighting the dangers of even relatively low contaminant concentrations.
>
> **Fagliano (1990)** reported increased cancer risks from exposure to water with 37–72 ppb of total VOCs, underscoring the risks associated with higher contaminant concentrations.
>
> **Glass (2003)** found an increased risk of leukemia at all cumulative lifetime benzene exposures above 1ppm-year with a strong dose-response relationship noted.
>
> The **Bove (2014a)** Marine study showed that leukemia risk correlated with cumulative exposures as low as 1-3,100 µg/L-month of TCE, 2-45 µg/L-month of benzene, 1-155 µg/L-month of PC, 1-4,600 µg/L-month of TVOCs, or more than 18 months of residence on base from 1975–1985.
>
> The **Bove (2024)** cancer incidence study found that even brief exposure durations, such as 1–6 quarters on base from 1975–1985, were sufficient to cause leukemia.

These studies consistently demonstrate that varying durations and levels of exposure to TCE, PCE, and benzene—whether measured in concentrations, cumulative exposure, or time spent on base—are sufficient to increase leukemia risk. These findings reinforce that even brief exposures at relatively low levels can be harmful. Importantly, these levels are hazardous to humans generally and not specific to any one individual or population. It is crucial to note that these levels are not the "floor" or definitive thresholds below which exposure is harmless. It is plausible, and likely, that lower levels of exposure also carry risks.

This information also helps establish exposure levels which can generally cause leukemia. When studies identify an increased leukemia risk at specific exposure levels—whether measured by concentration, cumulative exposure, or time—those levels are sufficient to demonstrate causation, even if lower levels might also pose a risk.

Randomized human controlled trials, which could definitively answer what levels of exposure cause cancer, are both unethical and impractical in this context. Instead, researchers rely on real-world observational data to estimate exposure levels and assess whether they correlate with higher leukemia rates. Fortunately, the contamination at Camp Lejeune provides high-quality epidemiological data detailing how varying levels and durations of chemical exposure affected cancer risk.

It is important to recognize that the exposure levels examined in human studies are limited by the specific circumstances observed in each case. While an increased risk at a given level suggests that it is harmful, it does not mean lower levels are safe; they may simply not have been evaluated or detected due to limited study power or bias toward the null.

VII. ADDITIVE EFFECTS OF TCE, PCE, AND BENZENE ON LEUKEMIA RISK

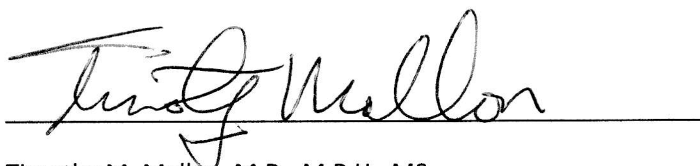
As far as I'm aware, there are no epidemiological, toxicological, or mechanistic studies that specificallyassess the risk of leukemia in individuals who are exposed to TCE, PCE, benzene and vinyl chloride (i.e., alone, but not in mixtures with the other chemicals). When considering the carcinogenic potential of simultaneous exposure to two or more known carcinogens, one may anticipate that the carcinogens may increase risk of cancer in an additive fashion—which is typically the default assumption when regulators assess chemicals that act through a common mode of action. It is theoretically possible, as has been demonstrated by the example of asbestos and smoking in the causation of lung cancer that these chemicals may interact in some way to increase the risk of leukemia beyond what would be expected by summing the individual risks (i.e., a supra-additive or multiplicative risk, also known as "synergy"); on the other hand, it is also possible that these chemicals may interact in some way that results in an overall reduction in the risk of leukemia that is less than the sum of the individual risks, perhaps by interference. However, there are no studies that I found that would suggest that a combination of contamination due to TCE, PCE, VC and Benzene would be health protective, or somehow decrease the risks below what would be experienced if only a single contaminant was ingested. The lack of research and peer reviewed studies that provides substantive evidence regarding the risks posed by "mixtures" of carcinogens has been acknowledged for a long time, with recent initiatives begun to advance a common framework for research in the laboratory as well as in epidemiological studies.

On the other hand, Cohn et al. (1994) noted that joint exposure to TCE and PCE might increase the carcinogenic effects over what might be expected by adding their individual effects.

What can be appreciated is that, as discussed above, the mechanisms of action by which these chemicals are likely to cause cancer to have substantial overlap. The chemicals, including their metabolites have been shown to be genotoxic by causing damage to DNA and to cause chromosomal malformations. Both DNA damage and chromosomal aberrations are well known risk factors for cancers. TCE, PCE, and benzene are also known to suppress the immune system which includes surveillance for and destroying cancerous cells. Having a weakened immune system is well known to be a risk factor for cancer, including, specifically, leukemia. As such, in my opinion, it is reasonable to apply the regulatory approach to carcinogens with a common mode of action (as discussed above) and conclude that the combined risk of simultaneous exposure to TCE, PCE, vinyl chloride and benzene is more likely than not to be at least additive.

VIII. CONCLUSION: TCE, PCE, AND BENZENE EXPOSURE AT LEAST AS LIKELY AS NOT CAUSES LEUKEMIA

In conclusion, there is epidemiological, animal data and mechanistic evidence in the literature that supports a causal relationship between TCE, PCE, Benzene, and exposure and the development of leukemia. In consideration of the epidemiological evidence, animal studies and mechanistic data, it is my professional opinion, to a reasonable degree of medical and scientific certainty, that TCE is more likely a cause of leukemia at the levels of exposure that were known to exist at Camp Lejeune; that Benzene is more likely a cause of leukemia at the levels of exposure that were known to exist at Camp Lejeune; that PCE is at least as likely as not a cause of leukemia at the levels of exposure that were known to exist at Camp Lejeune; that while Vinyl Chloride by itself is not causally related to leukemia, its presence in the drinking water contributed to the additive effects of TCE, Benzene, and PCE on leukemia risk at Camp Lejeune.



Timothy M. Mallon, M.D., M.P.H., MS.

Attachments and Other Requested Information

Dr. Mallon's Curriculum Vitae includes a list of publications for the past 10 years.

I have been deposed one time in the last four years. I was deposed in one EEO case in the last four years for the Federal Occupational Health Program of HHS."

My hourly rate for writing this report was $650 per hour.

IX. REFERENCES

1. Camp Lejeune Justice Act of 2022, https://www.congress.gov/117/plaws/publ168/PLAW-117publ168.pdf.

2. Agency for Toxic Substances and Disease Registry, Centers for Disease Control and Prevention. ATSDR Summary of the Evidence for the Drinking Water Contaminants at Camp Lejeune and Specific Cancers and Other Diseases. ATSDR, January 13, 2017.pp. 6-7

3. IARC. Trichloroethylene, Tetrachloroethylene, and Some Other Chlorinated Agents. Volume 106, IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. 2014. International Agency for Research on Cancer, Lyons, France. WHO Press, World Health Organization.

4. Memorial Sloan Kettering Research Center. Leukemia Fact sheet.

5. Maslia ML, Sautner JB, Faye RE, Suárez-Soto RJ, Aral MM, Grayman WM, Jang W, Wang J, Bove FJ, Ruckart PZ, Valenzuela C, Green JW Jr, Krueger AL: Analyses of Groundwater Flow, Contaminant Fate and Transport, and Distribution of Drinking Water at Tarawa Terrace and Vicinity, U.S. Marine Corps Base Camp Lejeune, North Carolina: Historical Reconstruction and Present-Day Conditions— Executive Summary. Atlanta, GA: Agency for Toxic Substances and Disease Registry; 2007.
http://www.atsdr.cdc.gov/sites/lejeune/tarawaterrace.html

6. Maslia ML, Suárez-Soto RJ, Sautner JB, Anderson BA, Jones LE, Faye RE, Aral MM, Guan J, Jang W, Telci IT, Grayman WM, Bove FJ, Ruckart PZ, Moore SM: Analyses and Historical Reconstruction of Groundwater Flow, Contaminant Fate and Transport, and Distribution of Drinking Water Within the Service Areas of the Hadnot Point and Holcomb Boulevard Water Treatment Plants and Vicinities, U.S. Marine Corps Base Camp Lejeune, North Carolina—Chapter A: Summary and Findings. Atlanta, GA: Agency for Toxic Substances and Disease Registry; 2013. http://www.atsdr.cdc.gov/sites/lejeune/hadnotpoint.html.

7. Environmental Protection Agency Notice of Proposed Rulemaking 40 CFR Part 751 EPA-HQ-OPPT-2020-0642; FRL-8317-01-OCSPP- RIN 2070-AK83 Environmental Protection Agency (EPA). The Environmental Protection Agency (EPA) is proposing to address the unreasonable risk of injury to human health presented by trichloroethylene (TCE) under its conditions of use as documented in EPA's November 2020 Risk Evaluation for TCE and January 2023 revised risk determination for TCE pursuant to the Toxic Substances Control Act (TSCA).

8. Bove FJ. Mortality Study of Service Members exposed to contaminated drinking water at USMC base Camp Lejeune: A retrospective study. Env. Health. 2014a; 13:68 .

9. 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 2014b;13:68.

10. Guowei Li, Stephen D Walter, Lehana Thabane, Shifting the focus away from binary thinking of statistical significance and towards education for key stakeholders: revisiting the debate on whether it's time to de-emphasize or get rid of statistical significance, Journal of Clinical Epidemiology, Volume 137, 2021, Pages 104-112, ISSN 0895-4356

11. Bove F., April Greek, Ruth Gatiba, Betsy Kohler, Recinda Sherman, Gene T. Shin, and Aaron Bernstein

(2024). 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. Environmental Health Perspectives 132:10 CID: 107008 https://doi.org/10.1289/EHP14966.12. ATSDR. 2018. Morbidity study of former marines, employees, and dependents potentially exposed to contaminated drinking water at U.S. Marine Corps Base Camp Lejeune. Agency for Toxic Substances and Disease Registry. https://www.atsdr.cdc.gov/sites/lejeune/docs/health_survey_report-508.pdf. December 7, 2018.

12. EPA Toxicological Review of TCE, September 2011. http://www.epa.gov/iris/toxreviews/0199tr/0199tr.pdf

13. EPA Toxicological Review of PCE, February 2012. http://www.epa.gov/iris/toxreviews/0106tr.pdf

14. NTP. Report on Carcinogens: Monograph on Trichloroethylene. National Toxicology Program, National Institute of Environmental Health Sciences, U.S. Department of Health and Human Services, January, 2015. Available at: https://ntp.niehs.nih.gov/sites/default/files/ntp/roc/monographs/finaltce _508.pdf

15. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Vol 100F. Chemical Agents and Related Occupations. A Review of Human Carcinogens. Lyon, France 2012.

16. 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. ATSDR, DHHS, PHS, Division of Toxicology and Human Health Sciences.

17. ATSDR Camp Lejeune Drinking Water Public Health Assessment-1-20-2017, ATSDR, DHHS, PHS, Division of Toxicology and Human Health Sciences, Environmental Toxicology Branch,1600 Clifton Road NE, Atlanta, Georgia 30333.

18. Bove, F.J., Greek, A., Gatiba, R. et al. 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 23, 61 (2024). https://doi.org/10.1186/s12940-024-01099-7.

19. Alexander, D. D., Mink, P. J., Mandel, J. H., & Kelsh, M. A. (2006). A meta-analysis of occupational trichloroethylene exposure and multiple myeloma or leukaemia. Occup Med (Lond), 56(7), 485-493. doi:10.1093/occmed/kql083.

20. Karami S, Bassig B, Stewart PA, Lee KM, Rothman N, Moore LE, Lan Q. (2013) Occupational trichloroethylene exposure and risk of lymphatic and hematopoietic cancers: a meta-analysis. Occup Environ Med. 2013 Aug;70(8):591-9. doi: 10.1136/oemed-2012-101212. Epub 2013 May 30. PMID: 23723297.

21. Anttila A, Pukkala E, Sallmén M, Hernberg S, Hemminki K. (1994) Cancer incidence among Finnish workers exposed to halogenated hydrocarbons. J Occup Environ Med. 1995 Jul;37(7):797-806. doi: 10.1097/00043764-199507000-00008. PMID: 7552463.

22. Bahr E., Aldrich TE., Seidu D., Brion GM., Tollerud DJ. Muldoon S., Reinhart N., Youseefagha A., Mckinney P., Hughes T., Chan C., Rice C., Brewer DE., Freyberg RW. Mohlenkamp AM., Hahn K., Hornung R., Ho M., Dastidar A., Freitas S., Saman D., Ravdal H., Scutchfield D., Eger KJ. (2011) Occupational Exposure to Trichloroethylene and Cancer Risk for Workers at the Paducah Gaseous Diffusion Plant. Int J Occup Med

Environ Health. 2011 March ; 24(1): 67–77. doi:10.2478/s13382-011-0007-1.

23. Lipworth L, Sonderman J, Mumma MT, et al. Cancer mortality among aircraft manufacturing workers: an extended follow-up. J Occup Environ Med 2011;53:992–1007.

24. Morgan WR, Kelsh MA, Zhao K, et al. Mortality of aerospace workers exposed to trichloroethylene. Epidemiology 1998;9:424–31.

25. Ritz B. Cancer mortality among workers exposed to chemicals during uranium processing. J Occup Environ Med 1999;41:556–66.

26. Boice JD, et al. Boice JD Jr, Marano DE, Cohen SS, et al. Mortality among Rocketdyne workers who tested rocket engines, 1948–1999. J Occup Environ Med 2006;48:1070–92.

27. Hansen J, Raaschou-Nielsen O, Christensen JM, et al. Cancer incidence among Danish workers exposed to trichloroethylene. J Occup Environ Med 2001;43:133–9.

28. Savitz D.. Wise LA., Bond JC., Hatch EE., Ncube CN., Wesselink AK., Willis MD., Rothman KJ. (2024) Responding to Reviewers and Editors About Statistical Significance Testing, Annals of Internal Medicine.,

29. Radican L, Blair A, Stewart P, et al. Mortality of aircraft maintenance workers exposed to trichloroethylene and other hydrocarbons and chemicals: extended follow up. J Occup Environ Med 2008;50:1306–19.

30. Greenland S, Salvan A, Wegman DH, et al. A case-control study of cancer mortality at a transformer-assembly facility. Int Arch Occup Environ Health 1994;66:49–54.

31. Shu XO, Stewart P, Wen WQ, Han D, Potter JD, Buckley JD, Heineman E, Robison LL. (1999) Parental occupational exposure to hydrocarbons and risk of acute lymphocytic leukemia in offspring. Cancer Epidemiol Biomarkers Prev. 1999 Sep;8(9):783-91. PMID: 10498397.

32. Anderson LA, Pfeiffer RM, Landgren O, Gadalla S, Berndt SI, Engels EA. Risks of myeloid malignancies in patients with autoimmune conditions. Br J Cancer. 2009 Mar 10;100(5):822-8. doi: 10.1038/sj.bjc.6604935. PMID: 19259097; PMCID: PMC2653768.

33. Fagliano JA, Berry MK, Bove FB, Burke TA: (1990) Drinking water contamination and the incidence of leukemia: an ecologic study. Am J Public Health 1990;80(10):1209-12.

34. Cohn P, Klotz J, Bove F, Berkowitz M, Fagliano J: Drinking water contamination and the incidence of leukemias and lymphomas. Environ Health Perspec 1994;102(6-7):556-61..

35. Cutler JJ, Parker GS, Rosen S, Prenney B, Healey R, Caldwell GG (1986). Childhood leukemia in Woburn, Massachusetts. Public Health Rep. 1986;101(2):201-205.

36. Lagakos, S.W., Wessen, B.J., & Zelen, M. (1986). An Analysis of Contaminated Well Water and Health Effects in Woburn, Massachusetts. Journal of the American Statistical Association, 81, 583-596.

37. Costas K, Knorr RS, Condon SK (2002) : A case-control study of childhood leukemia in Woburn,

Massachusetts: the relationship between leukemia incidence and exposure to public drinking water. Sci Total Environ 2002, Dec 2; 300 (1-3) 23-35.

38. NTP (National Toxicology Program). 2021. Report on Carcinogens, Fifteenth Edition. Research Triangle Park, NC: U.S. Department of Health and Human Services, Public Health Service. https://ntp.niehs.nih.gov/go/roc15.

39. Under the NTP classification scheme the main categories are: 1. Known to be a Human Carcinogen: This classification is used when there is sufficient evidence from human studies that a substance causes cancer; 2. Reasonably Anticipated to be a Human Carcinogen: This category is used when there is limited evidence from human studies and/or sufficient evidence from animal studies. It suggests that a substance may cause cancer in humans, but the evidence is not as strong as for the first category; 3. Not Classifiable as to its Carcinogenicity to Humans: This is used when the evidence is inadequate to make a determination about the substance's potential to cause cancer. Source: NTP (National Toxicology Program). 2021. Report on Carcinogens, Fifteenth Edition. Research Triangle Park, NC: U.S. Department of Health and Human Services, Public Health Service. https://ntp.niehs.nih.gov/go/roc15 (EndNote XML) DOI: https://doi.org/10.22427/NTP-OTHER-1003

40. Onishi A et al. Cancer incidence in systemic sclerosis: meta-analysis of population-based cohort studies. Arthritis Rheum 2013;65:1913-1921.

41. Bassig BA et al. Comparison of hematological alterations and markers of B-cell activation in workers exposed to benzene, formaldehyde and trichloroethylene. Carcinogenesis 2016;37:692-700.

42. Kristinsson SY et al. Chronic immune stimulation might act as a trigger for the development of acute myeloid leukemia or myelodysplastic syndromes. J Clin Oncol 2011;29:2897-2903.

43. Gunnarsson N et al. Increased prevalence of prior malignancies and autoimmune diseases in patients diagnosed with chronic myeloid leukemia. Leukemia 2016;30:1562-1567.

44. Zhang L, Bassig BA, Mora JL, Vermeulen R, Ge Y, Curry JD, Hu W, Shen M, Qiu C, Ji Z, Reiss B, McHale CM, Liu S, Guo W, Purdue MP, Yue F, Li L, Smith MT, Huang H, Tang X, Rothman N, Lan Q. Alterations in serum immunoglobulin levels in workers occupationally exposed to trichloroethylene. Carcinogenesis. 2013 Apr;34(4):799-802. doi: 10.1093/carcin/bgs403. Epub 2012 Dec 30. PMID: 23276795; PMCID: PMC3616671.

45. Varshney M, Chandra A, Chauhan LK, Goel SK. In vitro cytogenetic assessment of trichloroacetic acid in human peripheral blood lymphocytes. Environ Sci Pollut Res Int. 2014 Jan;21(2):843-50. doi: 10.1007/s11356-013-1949-6. Epub 2013 Jun 30. PMID: 23812791.

46. Lee KM, Bassig BA, Zhang L, Vermeulen RC, Hu W, Wong JYY, Qiu C, Wen C, Huang Y, Purdue MP, Ji BT, Li L, Tang X, Rothman N, Smith MT, Lan Q. Association between occupational exposure to trichloroethylene and serum levels of microRNAs: a cross-sectional molecular epidemiology study in China. Int Arch Occup Environ Health. 2019 Nov;92(8):1077-1085. doi: 10.1007/s00420-019-01448-x. Epub 2019 Jun 3. PMID: 31161417; PMCID: PMC6953905.

47. Phillips RV, Rieswijk L, Hubbard AE, Vermeulen R, Zhang J, Hu W, Li L, Bassig BA, Wong JYY, Reiss B, Huang Y, Wen C, Purdue M, Tang X, Zhang L, Smith MT, Rothman N, Lan Q. Human exposure to trichloroethylene is

associated with increased variability of blood DNA methylation that is enriched in genes and pathways related to autoimmune disease and cancer. Epigenetics. 2019 Nov;14(11):1112-1124. doi: 10.1080/15592294.2019.1633866. Epub 2019 Jun 26. PMID: 31241004; PMCID: PMC6773405.

48. Cocco P, Vermeulen R, Flore V, Nonne T, Campagna M, Purdue M, Blair A, Monnereau A, Orsi L, Clavel J, Becker N, de Sanjosé S, Foretova L, Staines A, Maynadié M, Nieters A, Miligi L, 't Mannetje A, Kricker A, Brennan P, Boffetta P, Lan Q, Rothman N. Occupational exposure to trichloroethylene and risk of non-Hodgkin lymphoma and its major subtypes: a pooled InterLymph [correction of IinterLlymph] analysis. Occup Environ Med. 2013 Nov;70(11):795-802. doi: 10.1136/oemed-2013-101551. Epub 2013 Jul 23. PMID: 23881218.

49. Talibov M et al. Occupational exposure to solvents and acute myeloid leukemia: a population-based, case–control study in four Nordic countries. Scand J Work Environ Health. 2014;40:511–517.

50. Silver SR et al. Retrospective cohort study of microelectronics and business machine facility. Am J Ind Med 2014;57:412-424.

51. Lash, L.H. and Parker, J.C. (2001) Hepatic and renal toxicities associated with trichloroethylene. Pharmacological Reviews, 53, 177-208.

52. IARC. A review of human carcinogens Part F: chemical agents and related occupations. IARC Monograph Evaluating Carcinogenic Risks in Humans 2012; 100F: 249–94.

53. IARC 2018 Monograph Volume 120 on Benzene and The Evaluation Of Carcinogenic Risks To Humans.

54. Khalade A et al. Exposure to benzene at work and the risk of leukemia: a systematic review and meta-analysis. Environ Health 2010;9:31.

55. Savitz DA, Andrews KW. Review of epidemiologic evidence on benzene and lymphatic and hematopoietic cancers. Am J Ind Med. 1997 Mar;31(3):287-95. doi: 10.1002/(sici)1097-0274(199703)31:3<287::aid-ajim4>3.0.co;2-v. PMID: 9055951.

56. Stenehjem JS, Kjærheim K, Bråtveit M, et al. Benzene exposure and risk of lymphohematopoietic cancers in 25 000 offshore oil industry workers. Br J Cancer. 2015; 112: 1603–12.

57. Linet MS, Yin SN, Gilbert ES, et al. A retrospective cohort study of cause-specific mortality and incidence of hematopoietic malignancies in Chinese benzene-exposed workers. Int J Cancer 2015; 137: 2184–97.

58. Schnatter AR, Glass DC, Tang G, Irons RD, Rushton L. Myelodysplastic syndrome and benzene exposure among petroleum workers: an international pooled analysis. J Natl Cancer Inst 2012; 104: 1724–37.90. IARC. 1982. Benzene. In Some Industrial Chemicals and Dyestuffs. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, vol. 29. Lyon, France: International Agency for Research on Cancer. pp. 93-148.

59. Collins JJ, Anteau SE, Swaen GM, Bodner KM, Bodnar CM (2015). Lymphatic and hematopoietic cancers among benzene-exposed workers. J Occup Environ Med, 57(2):159–63. doi:10.1097/JOM.0000000000000324 PMID:25654516

Case 7:23-cv-00897-RJ Document 465-3 Filed 08/24/25 Page 48 of 67

60. Rhomberg L, Goodman J, Tao G, Zu K, Chandalia J, Williams PR, et al. (2016). Evaluation of acute nonlymphocytic leukemia and its subtypes with updated benzene exposure and mortality estimates: a lifetable analysis of the Pliofilm cohort. J Occup Environ Med, 58(4):414–20. doi:10.1097/JOM.0000000000000689 PMID:27058483 Richardson DB (2009).

61. Crosignani P, Tittarelli A, Borgini A, Codazzi T, Rovelli A, Porro E, et al. (2004). Childhood leukemia and road traffic: a population-based case-control study. Int J Cancer, 108(4):596–9. doi:10.1002/ijc.11597 PMID:14696126.

62. Vinceti M, Rothman KJ, Crespi CM, Sterni A, Cherubini A, Guerra L, et al. (2012). Leukemia risk in children exposed to benzene and PM10 from vehicular traffic: a case-control study in an Italian population. Eur J Epidemiol, 27(10):781–90. doi:10.1007/s10654-012-9727-1 PMID:22892901.

63. Houot J, Marquant F, Goujon S, et al. Residential proximity to heavy-traffic roads, benzene exposure, and childhood leukemia the GEOCAP study, 2002–2007. Am J Epid. 2015; 182: 685–93.

64. Janitz AE, Campbell JE, Magzamen S, Pate A, Stoner JA, Peck JD. Benzene and childhood acute leukemia in Oklahoma. Environ Res 2017; 158: 167–73.

65. Farris GM, Everitt JI, Irons RD, Popp JA. Carcinogenicity of inhaled benzene in CBA mice. Fundam Appl Toxicol 1993; 20: 503–07.

66. National Toxicology Program. NTP toxicology and carcinogenesis studies of benzene (CAS no. 71–43–2) in F344/N rats and B6C3F1 mice (Gavage studies). Natl Toxicol Program Tech Rep Ser 1986; 289: 1–277.

67. Maltoni C, Ciliberti A, Cotti G, Conti B, Belpoggi F. Benzene, an experimental multipotential carcinogen: results of the long-term bioassays performed at the Bologna Institute of Oncology. Environ Health Perspect 1989; 82: 109–24.

68. Khan N, Ganeshpurkar A, Dubey N, Bansal D. Immunoprophylactic potential of wheat grass extract on benzene-induced leukemia: An in vivo study on murine model. Indian J Pharmacol. 2015 Jul-Aug;47(4):394-7. doi: 10.4103/0253-7613.161261. PMID: 26288471; PMCID: PMC4527060.

69. Huff JE, Haseman JK, DeMarini DM, Eustis S, Maronpot RR, Peters AC, Persing RL, Chrisp CE, Jacobs AC.1989. Multiple-site carcinogenicity of benzene in Fischer 344 rats and B6C3F1 mice. Environ Health Perspect 82: 125-163.

70. IARC. 1987. Benzene. In Overall Evaluations of Carcinogenicity. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, suppl 7. Lyon, France: International Agency for Research on Cancer. pp. 120-122.

71. Blanchard KT, Ball DJ, Holden HE, Furst SM, Stoltz JH, Stoll RE. 1998. Dermal carcinogenicity in transgenic mice: relative responsiveness of male and female hemizygous and homozygous Tg.AC mice to 12-O-tetradecanoylphorbol 13-acetate (TPA) and benzene. Toxicol Pathol 26(4): 541-547.

72. Spalding JW, French JE, Tice RR, Furedi-Machacek M, Haseman JK, Tennant RW. 1999. Development of a transgenic mouse model for carcinogenesis.

73. French JE, Lacks GD, Trempus C, Dunnick JK, Foley J, Mahler J, Tice RR, Tennant RW. 2001. Loss of heterozygosity frequency at the Trp53 locus in p53-deficient (+/–) mouse tumors is carcinogen-and tissue-dependent. Carcinogenesis 22(1): 99-106.

74. Hulla JE, French JE, Dunnick JK. 2001. Chromosome 11 allelotypes reflect a mechanism of chemical carcinogenesis in heterozygous p53-deficient mice. Carcinogenesis 22(1): 89-98.

75. Guo H, Ahn S, Zhang L. Benzene-associated immunosuppression and chronic inflammation in humans: a systematic review. Occup Environ Med. 2020 Sep 16:oemed-2020-106517. doi: 10.1136/oemed-2020-106517. Epub ahead of print. PMID: 32938756; PMCID: PMC7960562.

76. Yoon, JH., Kwak, W.S. & Ahn, YS. A brief review of relationship between occupational benzene exposure and hematopoietic cancer. Ann of Occup and Environ Med 30, 33 (2018). https://doi.org/10.1186/s40557-018-0245-9.

77. Martha S Linet, Ethel S Gilbert, Roel Vermeulen, Graça M Dores, Song-Nian Yin, Lutzen Portengen, Richard B Hayes, Bu-Tian Ji, Qing Lan, Gui-Lan Li, Nathaniel Rothman, Chinese Center for Disease Control and Prevention–US National Cancer Institute Benzene Study Group , Benzene Exposure Response and Risk of Myeloid Neoplasms in Chinese Workers: A Multicenter Case–Cohort Study, JNCI: Journal of the National Cancer Institute, Volume 111, Issue 5, May 2019, Pages 465–474, https://doi.org/10.1093/jnci/djy143.

78. Douglas DeMoulin, Hui Cai, Roel Vermeulen, Wei Zheng, Loren Lipworth, Xiao-Ou Shu; Occupational Benzene Exposure and Cancer Risk among Chinese Men: A Report from the Shanghai Men's Health Study. Cancer Epidemiol Biomarkers Prev 1 November 2024; 33 (11): 1465–1474.

79. Mundt, K.A., Birk, T. & Burch, M.T. Critical Review of The Epidemiological Literature On Occupational Exposure To Perchloroethylene And Cancer. Int Arch Occup Environ Health 76, 473–491 (2003). https://doi.org/10.1007/s00420-003-0457-2

80. Aschengrau A, Ozonoff D, Paulu C et al. (1993). Cancer risk and tetrachloroethylene-contaminated drinking water in Massachusetts. Arch Environ Health, 48: 284–292. doi:10.1080/00039896. 1993.9936715 PMID:8215591.

81. Japan Industrial Safety Association Technical Report 1993 Carcinogenicity study of tetrachloroethylene by inhalation in rats and mice 1993. https://www.epa.gov/iris/supporting-documents-tetrachloroethylene-perchloroethylene .

82. Bois FY, Zeise L, Tozer TN. 1990. Precision and sensitivity of pharmacokinetic models for cancer risk assessments: Tetrachloroethylene in mice, rats, and humans. Toxicol Appl Pharmacol 102:300-315.

83. Cichocki JA, Furuya S, Konganti K, et al. 2017a. Impact of nonalcoholic fatty liver disease on toxicokinetics of tetrachloroethylene in mice. J Pharmacol Exp Ther 361(1):17-28. http://doi.org/10.1124/jpet.116.238790.

84. Luo YS, Hsieh NH, Soldatow VY, Chiu WA, Rusyn I. Comparative analysis of metabolism of trichloroethylene and tetrachloroethylene among mouse tissues and strains. Toxicology. 2018 Nov 1;409:33-43. doi: 10.1016/j.tox.2018.07.012. Epub 2018 Jul 24. PMID: 30053492; PMCID: PMC6186498.

Case 7:23-cv-00897-RJ Document 465-3 Filed 08/24/25 Page 50 of 67

85. Glass DC, Gray CN, Jolley DJ, Gibbons C, Sim MR, Fritschi L, Adams GG, Bisby JA, Manuell R. Leukemia risk associated with low-level benzene exposure. Epidemiology. 2003 Sep;14(5):569-77. doi: 10.1097/01.ede.0000082001.05563.e0. PMID: 14501272.

88. Hosgood, H.D., Rahman, M.L., Blansky, D., Hu, W., Davitt, M., Wen, C. et al. (2022) Targeted proteomic scan identifies alteration of serum proteins among workers occupationally exposed to low levels of trichloroethylene. Environmental and Molecular Mutagenesis, 63(8-9), 423–428. Available from: https://doi.org/10.1002/em.22518.

Additional references will be produced within 7 days.

Appendix A

CURRICULUM VITAE

I. PERSONAL DATA

Name: Timothy M Mallon, MD, MPH, FACOEM
Address: 6508 Folded Leaf Square, Columbia, MD 21044
E-Mail/Tel#:mallonti03@gmail.com/ 443-370-9267

II. EDUCATION

Year	Degree	Type of Degree / Institution
1977	BPS	Bachelor Professional Studies Clarkson University Potsdam, NY
1986	MS	Resource Policy and Management School of Natural Resources University of Michigan
1987	MS	Environmental Health Hunter College City University of Ney York

III. POST GRADUATE EDUCATION

Year	Position	Type of Degree / Institution
1991	Medical Student	Doctor of Medicine Upstate Medical University Syracuse, NY
1992	Resident Year 1	Internship in Internal Medicine Tripler Army Medical Center, Honolulu, HI
1995	Resident Year 2	Master of Public Health School of Hygiene & Public Health Johns Hopkins, Baltimore, MD
1996	Resident Year 3	Occ. & Env. Medicine Residency US Army Public Health Center Edgewood Area-APG, Gunpowder, MD

IV. ACADEMIC APPOINTMENTS

Year	Position	Institution
2016	Professor/Adjunct Professor	Uniformed Services University
2012	Associate Professor	Uniformed Services University
2004	Assistant Professor	Uniformed Services University
1996	GPM Residency Faculty	Madigan Army Medical Center
1995	Teaching Fellow	Johns Hopkins University School of Medicine

V. CURRENT POSITIONS

Veterans Evaluation Services | **Occupational Medicine Contract Consultant** | **Oct 2017 to Present**

Duties/Accomplishments Hours per work- 30
-Review Camp Lejeune & Agent Orange cases for service members and Veterans
-Review Gulf War Injury Claims, PACT Act TERA Claims and write medical opinion for VBA
-Address causal connection between exposure and related health outcomes

Montgomery County Retirement | **Occupational Medicine** | **Oct 2017 to Present**

Duties/Accomplishments Hours per work- 5
-Review disability cases for Montgomery County employees
-Apply standards of medical fitness for police, firefighters, other employees who are injured
-Advise management regarding whether medical documentation supports ongoing disability

Federal Occupational Health Bethesda, MD | **Occupational Medicine Contract Consultant** | **Oct 2016 to Present**

Duties/Accomplishments Hours per work- 10
- Review ADA and FMLA cases for medical employability determinations
- Review preventive medicine informational booklets for technical accuracy
- Review respirator questionnaires and make recommendations for respirator wear

Department of Prev. Med. and Biostatistics, USU | **Adjunct Professor** | **July 2016 to Present**

Duties/Accomplishments: Hours per week 10
- Serve as mentor to colleagues in PMB on current research projects
- Serve as Specialty Editor for the Textbook of Military Medicine

VI. PRIOR POSITIONS HELD

Health Research Sys Admin. Comp. Injury Countermeasures | **Occupational Medicine Consultant** | **April 2022 to May 2023**

Duties/Accomplishments Hours per work- 10
-Review claims for injuries related to COVID-19 vaccinations
-Make determination of whether injury exists and causation
-Prepare recommendations for program director & legal review

Brown and Brown Physician Disability Associates | **Occupational Medicine Consultant** | **April 2017 to Oct 2021**

Duties/Accomplishments Hours per work- 5
-Review disability cases for multiple insurance companies
-Apply standards of medical fitness for workability for injured/ill employees
-Advise management regarding whether medical documentation supports ongoing disability

Prior Jobs (Cont)	Duty Title	Dates
Department of Prev. Med. and Biostatistics, USU	**Professor and OEM Residency Director**	**July 2012 to June 2016**

Duties/Accomplishments: Hours per week 80

- Serve as Residency Director of the OEM Residency Program at USU,
- Selected, trained, and mentored OEM physicians for the Department of Defense.
- Revised training and assessment of residents to document ACGME competencies.
- Oversaw the training of 25 military OEM physicians from the US and Canada.
- Led efforts nationally among residency directors to implement ACGME Milestones, developed Milestones Translation Tools and shared best practices.
- Led ACOEM President's Task Force on Recruiting physicians to OEM
- Prepared the residency for an accreditation site visit, received maximal accreditation.
- Preceptor for Occupational medicine residents and medical students. Served as course director for four occupational medicine courses.
- Authored 8 book chapters and 45 peer reviewed journal articles
- Invited to speak at national meetings including the AOHC, APHA, and ACPM conferences and presented multiple poster and oral presentations.
- Chaired Residency Advisory Committees for OEM Residencies at Madigan and Pensacola and served on Committees for Dayton, Johns Hopkins, Walter Reed & USUSU Prev. Medicine

Dept of Preventive Med. and Biostatistics USU	**Vice Chair for Prev Med.**	**July 2010 to June 2012**

Duties/Accomplishments: Hours per week: 40

- Led efforts to support for Medical School Curriculum Reform, enlarged role of Public Health.
- Led the PMB leadership committee, providing policy guidance to the Chair
- Served on the Medical School Student Promotions Committee for the University.
- Served as Chair of the Preventive Medicine Leadership Committee.
- Participated on the Medical School Curriculum Committee representing the Department.

US Army Surgeon General's Office	**Consultant in OEM**	**July 2008 to June 2012**

Duties/Accomplishments: Hours per week 30

- Served as subject matter expert & consultant to Army Surgeon General.
- Provided OEH consults to 130 OH clinics worldwide.
- Recommended to Human Resources Command assignments/deployments of OEM physicians.
- Developed OH Improvements that focused on Staffing, Training, Credentialing & performance.
- Validated workload, staffing requirements successfully obtained $54.5 million for OH Program.
- Developed Army web-based OHP checklist to track OH clinic performance.
- Updated DoD OEM physician credentialing requirements for OH providers.
- Served as Chair of DoD OEM Working Group: Updated OH Surveillance Manual (DoD 6055.05M) that provides guidance on meeting federal law and regulations from OSHA.
- Led efforts to develop a DoD Biomarker Policy; developed DoD process/outcome performance measures for OH Program execution.
- Led VA and DoD efforts to revise the DoD Post Deployment Health Assessment DD FORM 2796 to better capture soldier deployment OEH health exposure concerns.

- Linked deployment exposures in Defense Medical Surveillance System with health outcomes.

Dept of Preventive Med. and Biostatistics | **OEM Residency Director** | **July 2004 to June 2010**

Duties/Accomplishments: Hours per week: 40

- Serve as Residency Director of the OEM Residency Program at USU,
- Selected, trained, and mentored OEM physicians for the Department of Defense.
- Revised training and assessment of residents to document ACGME competencies.
- Obtained additional training starts and successfully recruited best DoD physicians to the field.
- Doubled the size of the residency from eight to sixteen residents a year each year.
- Oversaw the training of sixty military OEM physicians from the US and Canada.
- Led residency programs nationally in implementing the Milestones and was commended by the National Capital Consortium and ACGME for these efforts
- Prepared the residency for two ACGME site visits and received the maximal accreditation.
- Preceptor for Occupational medicine residents and medical students. Served as course director for four Occupational medicine courses.
- Authored a book chapter and 13 peer reviewed journal articles and was invited to speak at national civilian medical meetings including the American OH Conference and Federal Occupational Health Conference and presented multiple poster and oral presentations.

Army Center for Public Health, Aberdeen Proving Grounds, Gunpowder, MD | **Director, OEM** | **August 2000 to July 2004**

Duties/Accomplishments:

- Served as Director of the OEM Directorate at the US Army Public Health Command.
- Provided oversight of Army OEH worldwide technical consultations.
- Supervised staff of 32 and managed a budget of over $3.9 million
- Developed policy and programs to reduce injuries, illnesses; lower FECA costs; obtained $1 million for pilot project demonstrated medical case managers effective and achieved a 4:1 ROI.
- Developed policy and advised commanders on FHP measures related to CRBN threats.
- Primary author of "Occupational Health" for the 2005 revision of DA Pamphlet 40-11.
- Assessed the quality of Army worker's compensation, OH, and NBC surety programs.
- Developed OH templates for the electronic medical record, AHLTA.
- Standardized OH business practices world-wide as proponent for the MEDCOM commander.
- Coordinated OH support for Pentagon and World Trade Center response: developed exposure guidelines for contaminants to support consequence management and building re-entry
- Oversaw health assessments of 8000 soldiers who deployed to the WTC, Pentagon.

Madigan Army Med. Ctr, Fort Lewis WA | **Chief & Region Consultant Occ. & Env. Med. Service** | **July 1996 to August 2000**

Duties/Accomplishments: Hours per week: 50

- Served as Western Region Medical Cmd. OEM Consultant, oversaw delivery of care in eleven OH clinics in six states from Alaska to Southern California, supported 60,000 personnel.
- Significantly improved patient care, customer satisfaction, and OH clinic utilization.
- Standardized region respiratory protection, blood borne pathogens, latex allergy programs.
- Served as Chief of OEM at Madigan Army Medical Center, provided OM services for 10,000 employees and 40,000 active, guard and reserve solders.

- Supervised staff of 39 providers, His, OHNs and support staff.
- Updated Blood Borne Pathogen, Latex & Infection Control Programs, commended by Joint Commission for model infection control and disaster response programs.
- Chaired the Infection Control, member Hospital Executive, QA/QI and Safety Committees.
- Overhauled tuberculosis (TB) surveillance program to meet JC and OSHA requirements.
- Enhanced chemical response capability through training and exercises.
- Developed and implemented a region wide heat injury prevention plan.

Patterson Army Cmty Hospital, Fort Monmouth, NJ | **Chief of Prev. Medicine** | **July 1992 to June 1994**

Duties/Accomplishments: Hours per week: 45

- Oversaw delivery of PM services for five installations in NY and NJ;
- Supervised 4 MDs, 4 Industrial Hygienists, 7 nurses, 7 medics, 6 staff.
- Served on PACH Executive Committee, Chair of Infect Control Cmtte, hospital QA/QI.
- Upgraded OH services in region by organizing, updating SOPs and QI programs for PM that resulted in accessible, high quality care and commended by Joint Commission.
- Provided oversight of disease, injury prevention programs at two OH clinics, acute care clinic.
- Ensured workplace IH monitoring conducted that guided worker medical surveillance programs, obtained $250K for IH regional support.
- Provided Installation Commanders advice on community health, safety, lead poisoning and TB prevention and control plans, Travel Medicine, Post Deployment Surveillance for soldiers.

VII. CERTIFICATION AND LICENSURE

	Date
American Board of Preventive Medicine	
Board Certification in Occupational Medicine	16 Jan 1997

License: Maryland

VIII. MEMBERSHIP IN SCIENTIFIC SOCIETIES\PROFESSIONAL ORGANIZATIONS.

Association of Military Surgeons of the United States
American College of Occupational and Environmental Medicine (ACOEM)
American College of Preventive Medicine (ACPM)

IX. FUNDED GRANTS

Title	Role	Funded (amount)	Grant Period
Exposure biomarkers & health outcomes in Iraq and Afghanistan, funded by DoD/NIEHS	PI	$4,650,000	9/8/2013 to 7/31/2019

X. PRIOR TEACHING ACTIVITIES

PMO 973	OEM Journal Club- Co-course Director
PMO 542	Clinical Occupational / Environmental Medicine- Co-course Director
PMO 655	Safety and Injury Prevention- Course Director
PMO 642	Clinical PM Services and Selected Topics in OEM- Co-course Director
PMO 558	Intro to Preventive / Occ. Medicine Residencies- Co-course Director
PMO 549	Toxicology - Course lecturer

XII. **OTHER PROFESSIONAL ACTIVITIES**

Specialty Editor, Textbook of Military Medicine in Occupational Medicine 2019
Special Editor J. Occupational and Environmental Medicine Supplement December 2019
- Deployment Environmental Exposures, Metabolomics, Inflammatory and microRNA
- Biomarkers and Health Outcomes Related to Burn Pits in Iraq and Afghanistan. 2016
- Federal Workers Compensation Programs, Published March 2015.

Editor, Mil. Med. Supplement July 2011, Hazardous Exposures in Military Populations.
Reviewer, Military Medicine on Preventive and Occupational Medicine topics, 2007 to present.

XIII. **CLINICAL ACTIVITIES**

Staff occupational medicine physician, Federal Occupational Health, Bethesda, MD.
Staff Occupational Medicine Physician Walter Reed Army Medical Center 2004 to 2016

XIV. **COMMITTEES** (national advisory, professional societies, hospitals)

Member, Residency Review Committee for Preventive Medicine, Accreditation Council for Graduate Medical Education- 7/2016 to 7/2019
Member, American Board of Preventive Medicine- 7/2016 to 7/2019

XV. **HONORS AND AWARDS**

ACOEM Award for Leadership in Academic Medicine and Research, April 2016
Delta Omega Public Health Honor Society as USU Faculty 2015
Defense Superior Service Medal 2016
US Army Surgeon General's "A-Designator" Award for Academic Excellence
Recipient, Military Order of Medical Merit
Fellow, American College of Occupational and Environmental Medicine.

XVI. **BIBLIOGRAPHY**

Publications (Peer Reviewed)

Krahl PL., Mallon TM., Gaydos JG. Response to Letter to the Editor Regarding Commentary "Hazardous Non-combat Exposures in the Department of Defense". December 2022 Military Medicine 188(5-6). DOI:10.1093/milmed/usac421

Thomas RJ. Krahl PL., Mallon TM., Gaydos JG. Preparedness of Military Public Health for Epidemic and Pandemic Recognition and Response. October 2022. Military Medicine 188(2) DOI: 10.1093/milmed/usac323.

Krahl PL., Mallon TM., Thomas RJ, Gaydos JG. The Future of Military Occupational and Environmental Medicine in the Department of Defense Journal of occupational and environmental medicine. September 2021 DOI: 10.1097/JOM.0000000000002384.

Krahl PL., Mallon TM., Gaydos JG. Hazardous Non-Combat Exposures in the U.S. Department of Defense. June 2021 Military Medicine 187(10). DOI: 10.1093/milmed/usac166

Forging a Healthy and Productive Navy Civilian Workforce. Krahl PL., Thomas RJ., Mallon TM., Gaydos JC. July 2021 US Naval Institute Proceedings Vol. 147/7/1,421.

Krahl PL., Thomas RJ., Gaydos JC., Mallon T.M. Training Occupational & Environmental Medicine (OEM) Residents at the Uniformed Services University, JOEM, Vol 63: Number

5, May 2021.

Krahl PL., Mallon TM., Thomas RJ, Gaydos JG. Training Occupational and Environmental Medicine (OEM) Residents at the Uniformed Services University. The Medical Journal. US Army Center of Excellence. Oct-Dec 2020: pp 4-58.

Mallon, Timothy M.; Krahl, Pamela K.; Haines, Kevin M. Jr.; Use of Biomarkers to Assess Environmental Exposures and Health Outcomes in Deployed Troops. Journal of Occupational and Environmental Medicine. 61:S1-S4, December 2019.

Krahl, Pamela L.; Benchoff, Edward; Mallon, Timothy. Advances in Comprehensive Exposure Assessment: Opportunities for the US Military. Journal of Occupational and Environmental Medicine. 61:S5-S14, December 2019.

Smith, Matthew Ryan; Uppal, Karan; Walker, Douglas I.; Utell, Mark J.; Hopke, Philip K.; Mallon, Timothy M.; Krahl, Pamela L.; Rohrbeck, Patricia; Go, Young-Mi; Jones, Dean P. Environmental Chemicals Altered in Association With Deployment for High Risk Areas. Journal of Occupational and Environmental Medicine. 61:S15-S24, December 2019.

Go, Young-Mi; Smith, Matthew R.; Walker, Douglas I.; Uppal, Karan; Rohrbeck, Patricia; Krahl, Pamela L.; Hopke, Philip K.; Utell, Mark J.; Mallon, Timothy M.; Jones, Dean P. “Metabolome-Wide Association Study of Deployment to Balad, Iraq or Bagram, Afghanistan”. Journal of Occupational and Environmental Medicine. 61:S25-S34, December 2019.

Smith, Matthew Ryan; Woeller, Collynn F.; Uppal, Karan; Thatcher, Thomas H.; Walker, Douglas I.; Hopke, Philip K.; Rohrbeck, Patricia; Mallon, Timothy M.; Krahl, Pamela L.; Utell, Mark J.; Go, Young-Mi; Jones, Dean P. “Associations of Benzo(ghi)perylene and Heptachlorodibenzo-p-dioxin in Serum of Service Personnel Deployed to Balad, Iraq, and Bagram, Afghanistan Correlates With Perturbed Amino Acid Metabolism in Human Lung Fibroblasts”. Journal of Occupational and Environmental Medicine. 61:S35-S44, December 2019.

Thatcher, Thomas H.; Woeller, Collynn F.; Thakar, Juilee; Khan, Atif; Hopke, Philip K.; Smith, Matthew Ryan; Uppal, Karan; Walker, Douglas I.; Go, Young-Mi; Jones, Dean P.; Krahl, Pamela L.; Mallon, Timothy M.; Sime, Patricia J.; Phipps, Richard P.; Utell, Mark J. “Analysis of Post deployment Serum Samples Identifies Potential Biomarkers of Exposure to Burn Pits and Other Environmental Hazards of Exposure to Burn Pits and Other Environmental Hazards”. Journal of Occupational and Environmental Medicine. 61:S45-S54, December 2019.

Khan, Atif; Thatcher, Thomas H.; Woeller, Collynn F.; Sime, Patricia J.; Phipps, Richard P.; Hopke, Philip K.; Utell, Mark J.; Krahl, Pamela L.; Mallon, Timothy M.; Thakar, Juilee. “Machine Learning Approach for Predicting Past Environmental Exposures From Molecular Profiling of Post-Exposure Human Serum Samples”. Journal of Occupational and Environmental Medicine. 61:S55-S64, December 2019.

Thakar, Juilee; Thatcher, Thomas H.; Smith, Matthew Ryan; Woeller, Collynn F.; Walker, Douglas I.; Utell, Mark J.; Hopke, Philip K.; Mallon, Timothy M.; Krahl, Pamela L.; Rohrbeck, Patricia; Go, Young-Mi; Jones, Dean P.; Uppal, Karan. “Integrative Network Analysis Linking Clinical Outcomes With Environmental Exposures and Molecular Variations in Service Personnel Deployed to Balad and Bagram”. Journal of Occupational and Environmental Medicine. 61:S65-S72, December 2019.

Smith, Matthew Ryan; Walker, Douglas I.; Uppal, Karan; Utell, Mark J.; Hopke, Philip K.; Mallon, Timothy M.; Krahl, Pamela L.; Rohrbeck, Patricia; Go, Young-Mi; Jones, Dean P. "Benzo[a]pyrene Perturbs Mitochondrial and Amino Acid Metabolism in Lung Epithelial Cells and Has Similar Correlations With Metabolic Changes in Human Serum". Journal of Occupational and Environmental Medicine. 61:S73-S81, December 2019.

Woeller, Collynn F.; Thatcher, Thomas H.; Thakar, Juilee; Cornwell, Adam; Smith, Matthew R.; Jones, Dean P.; Hopke, Philip K.; Sime, Patricia J.; Krahl, Pamela; Mallon, Timothy M.; Phipps, Richard P.; Utell, Mark J. "Exposure to Heptachlorodibenzo-p-dioxin (HpCDD) Regulates microRNA Expression in Human Lung Fibroblasts". Journal of Occupational and Environmental Medicine. 61:S82-S89, December 2019.

Bedno SA.,Forst L. Mallon TM Systems Evaluation of Occ. Injuries and Illness in the US Army. JOEM, Volume 61, Number 6, June 2019.

Gaydos JC., Mallon TM., Rice WA. "The U.S. Army OEM Residency at Aberdeen Proving Ground, MD: 1960-1996." Mil Med. 2016 Nov;181(11):e1637-e1643.

Mallon TM., Rohrbeck P. Haines KM., Baird CP., Gaydos JC., "Introduction to Department of Defense Research on Burn Pits, Biomarkers, and Health Outcomes Related to Deployment in Iraq and Afghanistan". JOEM Supplement, Volume 58: Number 8S. August 2016.

Walker DI., Mallon TM, Hopke PK, Uppal K, Go YM, Rohrbeck PI, Pennell KD, Jones DP. "Deployment-Associated Exposure Surveillance with High-Resolution Metabolomics". JOEM Supplement, Volume 58: Number 8S. August 15, 2016.

Woeller CF., Thatcher TH. Twist DV., Pollock SJ., Croadsdell A. Kim N., Hopke PK., Xia X. Thakar J., Mallon TM., Utell MJ. Phipps RP. "Detection of serum microRNAs from Department of Defense Serum Repository: correlation with cotinine, cytokine and polycyclic aromatic hydrocarbon levels." JOEM Supplement, Volume 58: Number 8S. August 15, 2016.

Walker DI., Pennell KD., Uppal K., Xia X., Hopke PK., Utell MJ., Phipps RP., Sime PJ., Rohrbeck PI., Mallon TM., Jones DP. "Pilot Metabolome-Wide Association Study of Benzo(a)pyrene in Serum from Military Personnel". JOEM Supplement, Volume 58: Number 8S. August 15, 2016.

Liu KH, Walker DI., Uppal K., Tran VL., Rohrbeck PI., Mallon TM., Jones DP. "High-resolution metabolomics assessment of military personnel." JOEM Supplement, Volume 58: Number 8S. August 15, 2016.

Go YM. Walker DI., Uppal K., Rohrbeck PI., Mallon TM., Jones DP. "Metabolic Pathways and Networks Associated with Tobacco Use in Military Personnel". JOEM Supplement, Volume 58: Number 8S. August 15, 2016.

Accardi, CJ., Walker DI. Uppal K., Quyyumi AA. Rohrbeck PI., Pennell KD. Mallon TM., Jones DP. "High-Resolution Metabolomics for Nutrition and Health Assessment of Armed Forces Personnel". JOEM Supplement, Volume 58: Number 8S. August 15, 2016.

Xia X., Carroll-Haddad A., Brown N., Utell MJ., Mallon TM., Hopke PK. "Polycyclic Aromatic Hydrocarbons and Polychlorinated Dibenzo-p-Dioxins/Dibenzofurans in Microliter Samples of

Human Serum as Exposure Indicators." JOEM Supplement, Volume 58: Number 8S. August 15, 2016.

Dalgard CL., Polston KF., Sukumar G., Wilkerson MD., Mallon TM., Pollard HB. "MicroRNA Expression Profiling of the Armed Forces Health Surveillance Branch Cohort for Identification of "Enviro-miRNAs". JOEM Supplement, Volume 58: Number 8S. August 15, 2016.

Woeller CF., Thatcher T., Twisk DV., Pollock S., Croadsdell A., Xia X., Hopke PK., Thakar J., Sime P., Mallon TM,. Utell MJ., Phipps RP. "MicroRNAs as Novel Biomarkers of Deployment Status and Exposure to PAHs, Dioxins and Dibenzofurans". JOEM Supplement, Volume 58: Number 8S. August 15, 2016.

Masiol M. Mallon TM., Haines, KM., Utell MJ. Hopke, PK. "Airborne Dioxins, Furans, and Polycyclic Aromatic Hydrocarbon Exposure". JOEM Supplement, Volume 58: Number 8S. August 15, 2016.

Masiol M. Mallon TM., Haines, KM., Utell MJ. Hopke, PK. "Source Apportionment of Airborne Dioxins, Furans and Polycyclic Aromatic Hydrocarbons at A U.S. Forward Operating Air Base During the Iraq War". JOEM Supplement, Volume 58: Number 8S. August 15, 2016.

Rohrbeck PI. Hu Z., Mallon TM. "Assessing Health Outcomes after Environmental Exposures Associated with Open Pit Burning in Deployed U.S. Service Members." JOEM Supplement, Volume 58: Number 8S. August 15, 2016.

Mancuso, J. Mallon, T. Gaydos, J. "Needs Group Capabilities Assessment for the Department of Defense (DoD) Serum Repository", Military Medicine, Vol. 180, pp 13-24. October Supplement 2015, available at http//publications.amsus.org/doi/pdf/10.7205/MILMED-D-14-00732.

"Hauret, K., Bedno, S., Loringer, K., Kao, D., Mallon, T., Jones, B. "Epidemiology of Exercise- and Sports-Related Injuries in a Population of Young, Physically Active Adults: A Survey of Military Service Members". Am J. Sports Med. 2015; 43(11):2645-53.

Mallon, TM., Grizzell, TL. Hodgson, MJ. "Federal Workers' Compensation Programs: Department of Defense and Veterans Health Administration Experiences". Journal of Occupational & Environmental Medicine: March 2015 - Volume 57 - Issue - p S1–S3. doi:10.1097/JOM. 0000000000000367, Federal Workers' Compensation Supplement.

Mallon, TM., Grizzell, TL., Nelson, CL.Hodgson, MJ. "Federal Workers' Compensation Program Basics". Journal of Occupational & Environmental Medicine: March 2015 - Volume 57 - Issue – p S4–S11. doi: 10.1097/JOM. 0000000000000407. Federal Workers' Compensation Supplement.

Mallon, TM., Grizzell, TL., Nelson, CL. "Managing Federal Workers' Compensation Injuries and Costs". Journal of Occupational & Environmental Medicine: March 2015 - Volume 57 - Issue - p S12–S19. doi: 10.1097/JOM. 0000000000000410. Federal Workers' Compensation Supplement.

Nelson, CJ. Bigley, DP. Mallon, TM. "Analysis of New Workers' Compensation Claims in the Department of Defense Civilian Workforce, 2000–2012". Journal of Occupational &

Environmental Medicine: March 2015 - Volume 57 - Issue - p S20–S26 doi: 10.1097/JOM.0000000000000368. Federal Workers' Compensation Supplement.

Mallon, TM. Cherry, SE. “Investigating the Relationship Between Worker Demographics and Nature of Injury on Federal Department of Defense Workers' Compensation Injury Rates and Costs From 2000 to 2008”. Journal of Occupational & Environmental Medicine: p S27–S30 .doi: 10.1097/JOM.0000000000000416. Federal Workers' Compensation Supplement.

Mallon, TM. Ortiz, JM. Candler, WH. Rogers, G. Hilburn, R. J. “Investigation of an Outbreak of Anemia Cases at an Army Trinitrotoluene Munitions Production Plant From 2004 to 2005 and Subsequent Surveillance 2005–2013”. Mil. Med. Nov 2014, Vol. 179, No. 11, pp. 1374-1383.

Freeman RJ, Jankosky C, Olsen CH, Mallon T. “Occupational effect on the occurrence of idiopathic venous thromboembolism”. Mil Med. 2012 Oct;177(10):1217-22. PMID 23113451

Bedno, S. Soltis, M. Mancuso, J, Burnett, D. Mallon, T. “The In-Service Examination Score as a predictor of Success on the American Board of Preventive Medicine Certification Examination”, Am J. Prev. Med 2011; 41 (6): 641-644.

“Progress in Implementing recommendations of the National Academy of Sciences Reports: protecting those who serve: strategies to protect the health of deployed US Forces”, Mallon, T. J Mil Med, 7 Suppl. July 6, 2011.

Bedno SA. Hauret, K. Loringer, K. Kao TC. Mallon, TM. Jones, B. “Effects of Personal and Occupational Stress on Injuries in a Young, Physically Active Population: A Survey of Military Personnel”. Military Medicine Nov 2014, Vol. 179, No. 11, pp. 1311-1318.

Cloeren M, Mallon TM, Firestone LM, Burch HC. “Contract Case Managers Prove Cost Effective In Federal Workers”, Mil Med. 2008 Mar;173(3):253-8.

Mallon TM., Parker D. Balmer J. et. al. Chapter 5 US Army Occ. Health Programs and Services in Textbook of Military Medicine, Occupational Health and the Service Member Mallon TM (Editor). Office of the Surgeon General, US Army Borden institute, San Antonio, Texas, 2019. Pages 55-69.

Heller JM, Mallon TM, Baird CP, et. al. Chapter 6, History of Army Occ Health, 1991 2015 in Textbook of Military Medicine, Occupational Health and the Service Member Mallon TM (Editor). Office of the Surgeon General, US Army Borden institute, San Antonio, Texas, 2019. Pages 71-111.

Mallon TM. Chapter 7, Army Occupational Health Program Management in Textbook of Military Medicine, Occupational Health and the Service Member Mallon TM (Editor). Office of the Surgeon General, US Army Borden institute, San Antonio, Texas, 2019. . pp 113-126.

Cameron J. L. Nelson, Sheryl A. Bedno, and Timothy M. Mallon. Chapter 9 Federal Workers' Compensation Programs in Textbook of Military Medicine, Occupational Health and the Service Member Mallon TM (Editor). Office of the Surgeon General, US Army Borden institute, San Antonio, Texas, 2019. pp 139-151.

Timothy M. Mallon, Cameron J.L. Nelson, David P. Deeter, and Janet M. Ruff. Chapter 10 Medical Surveillance in Textbook of Military Medicine, Occupational Health and the Service

Member Mallon TM (Editor). Office of the Surgeon General, US Army Borden institute, San Antonio, Texas, 2019. pp.153-170.

Bedno, S., Loringer, K., Mallon, T. Injury Occurrence from Participation in Sports, April 2008 Status of Forces Survey. US Army Public Health Center Technical Report. August 2011.

Health Hazards to Healthcare Workers, Melissa A. McDiarmid, Kevin P. Michaels, Marlene Sanchez, Gary E. Herr, Michael J. Testa, Daniel J. Caldwell, and Timothy M. Mallon, Chapter 11 in Textbook of Military Medicine, Occupational Health and the Service Member Mallon TM (Editor). Office of the Surgeon General, US Army Borden institute, San Antonio, Texas, 2019. pp 171-198.

Respiratory Protection. Timothy M. Mallon, Cameron J. L. Nelson, Tifani Gleason, Brandon Gardner, Gregory J. Martin, and John P. Barrett. Chapter 13, in Textbook of Military Medicine, Occupational Health and the Service Member Mallon TM (Editor). Office of the Surgeon General, US Army Borden institute, San Antonio, Texas, 2019. pp.219-234.

Beryllium, Dale Harman, Nicole S. Chavis, and Timothy M. Mallon, Chapter 23 in Textbook of Military Medicine, Occupational Health and the Service Member Mallon TM (Editor). Office of the Surgeon General, US Army Borden institute, San Antonio, Texas, 2019. , pp 505--519

Explosives and Propellants. Timothy M. Mallon, Peter G. Matos, W. Scott Monks, Raul A. Mirza, and Donald T. Bodeau, Chapter 28, in Textbook of Military Medicine, Occupational Health and the Service Member Mallon TM (Editor). Office of the Surgeon General, US Army Borden institute, San Antonio, Texas, 2019. pp 561-592.

Mallon TM. Phipps RP. Thakar J. Woeller C. et. al. Chapter 29 Biological Monitoring in Textbook of Military Medicine, Occupational Health and the Service Member Mallon TM (Editor). Office of the Surgeon General, US Army Borden institute, San Antonio, Texas, 2019. pp 593-616.

Bedno, S., Loringer, K., Tzu-Cheg,K., Hauret,K., Mallon, T. Jones B. "Injury Occurrence from Participation in Sports, Exercise, and Recreational Activities Among Active Duty Service Members, Descriptive Analysis of Data from the April 2008 Status of Forces Survey of Active Duty Members. US Army Public Health Command Technical Report. August 2011.

Cloeren M, Mallon T. "Managing Workers Compensation Costs in the Military Setting: The Army's Story". Clin Occup Environ Med. 2004. May; 4(2):vii, 323-39. Review.

Textbook Chapters

Mallon TM., Parker D. Balmer J. et. al. Chapter 5 US Army Occ. Health Programs and Services Pages 55-69, in in Occ. Health & the Service Member, TM Mallon, editor, 632 pages, 2019.

Heller JM, Mallon TM, Baird CP, et. al. Chapter 6, History of Army Occ Health, 1991-2015, pp 71-111 in Occupational Health & the Service Member, TM Mallon, editor, 632 pages, 2019.

Mallon TM. Chapter 7, Army Occupational Health Program Management. pp 113-126. in Occupational Health and the Service Member, TM Mallon, editor, 632 pages, 2019.

Nelson CJL., Bedno SA., Mallon TM. Chapter 9 Federal Workers' Compensation Programs. Pages 139-151, in Occ. Health & the Service Member, TM Mallon, editor, 632 pages, 2019.

Mallon TM. Nelson CJL. Deeter DP. Ruff JM. Chapter 10 Medical Surveillance. pp 153-170, in Occupational Health and the Service Member, TM Mallon, editor, 632 pages, 2019.

Mcdiarmid MA. Michaels KP. Sanchez M. Herr GE. Testa MJ. Caldwell DJ. Mallon TM. Chapter 11 Health Hazards to Healthcare Workers. pp. 171-198, in Occupational Health and the Service Member, TM Mallon, editor, 632 pages, 2019.

Mallon TM. Nelson CJL., Gardner B. Martin GJ. Barrett JP. Chapter 13 Respiratory Protection. pp. 219-234, in Occupational Health & the Service Member, TM Mallon, editor, 632 pages 2019.

Dale Harman D. Chavis NS. Mallon TM. Chapter 25 Beryllium. pp. 505-519. in Occupational Health and the Service Member, TM Mallon, editor, 632 pages, 2019.

Mallon TM. Matos PG. Monks WS. Mirza RA. Bodeau DT. Chapter 28 Explosives and Propellants. pp 561-592, in Occupational Health and the Service Member, TM Mallon, editor, 632 pages, 2019.

Mallon TM. Phipps RP. Thakar J. Woeller C. et. al. Chapter 29 Biological Monitoring, pp 593-616, in Occupational Health and the Service Member, TM Mallon, editor, 632 pages, 2019.

Appendix B

Dr. Timothy Mallon, MD, MPH
Legal Expert Fee Schedule

Date: August 30, 2024. This fee schedule supersedes any prior fee schedule agreement for my services.

Retainer

- Retainer fee of $3000, prepaid in full before services are scheduled and confirmed, credited towards services below. Any residual balance will be returned after I have acknowledged receipt of notification of closure of the case and after final bill payment.

Case Review (billed in increments of 1 hour)

- Initial Review of Case, Telephone consultation, Face to Face Consultation: $600/hour
- Report writing: $600/hour

Depositions:

- Two thousand eight hundred ($2600) flat fee for depositions up to 4 hours (irrespective of the final amount of time). If more time is needed, the fee for additional deposition time is six hundred ($650) per hour with no fractionation.
- Deposition fees are non-refundable and due thirty (30) calendar days in advance.
- Preparation time billed at Telephone Consultation rate in the Case Review section.

Trial Testimony:

- Local/Out of Town: $2600 per day flat fee for trial testimony up to 4 hours (irrespective of the final amount of time) plus expenses. Additional hours beyond the minimum will be billed at $650/hour.
- Trial testimony fees (both live and electronic) are non-refundable and are due 30 calendar days in advance.
- For any work that requires travel outside my office, the billing time starts when I leave the office and ends when I return to the office, plus expenses.
- Preparation time billed at Telephone Consultation rate in the Case Review section.

Other Terms:

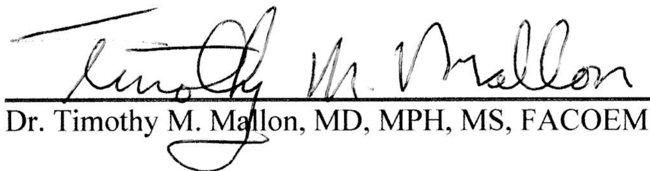
- Please send all records in electronic format.
- All lodging, transportation, and reasonable out of pocket expenses related to these services (including copying charts, printing, certifying, etc) are reimbursed at actual cost.
- An Invoice for the balance of charges not covered in the advance payments will be submitted monthly. Payments for the balance of charges are to be made within thirty (30) days from the date of the bill. Late payments will result in additional fees of 10% of the amount owed per month, unless I have agreed in writing to waive such fees. Failure to pay within this time period-by which I mean failure to receive any form of payment or failure of the check to clear, etc. will be construed as a complete termination of my consultative responsibilities. Receipt of payment will be interpreted as a request for continuation of services under these agreed terms.
- All payments should be made to Timothy Mallon as listed on the W-9.
- I reserve the right to withdraw if I feel participation will compromise my professional reputation or for any personal reasons.
- Secure document storage fee on encrypted password protected hard drive of $200 per case.

- If you agree with all these terms, please submit a payment. Receipt of payment will be interpreted as agreement with the terms listed here.

Contact Information:

Premier Occupational Health Services
Timothy M. Mallon, MD, MPH, MS, FACOEM
6508 Folded Leaf Square, Columbia, MD 21044
Phone: Mobile 443-370-9267 Office: 410-531-7914
Email: mallonti03@gmail.com

I reserve the right to change, modify, add, or remove portions of this fee schedule at any time.
I will provide this document anytime upon request.



Dr. Timothy M. Mallon, MD, MPH, MS, FACOEM 8/30/2024