Exhibit 95

GENERAL CAUSATION REPORT
CAMP LEJEUNE WATER VOLATILE ORGANIC CHEMICALS AND KIDNEY CANCER

Prepared for:

Environmental Torts Litigation

U.S. Department of Justice

Washington, DC

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1.0 INTRODUCTION

My report was prepared by request for the United States in the *Camp Lejeune Water Litigation*, Case No: 7-23-cv-897. The over-arching position of the plaintiffs is that their exposures to volatile organic compounds (VOCs) found in water several decades ago at Camp Lejeune caused them to suffer diseases, illnesses, injuries, and conditions, thereby affecting their quality of life or longevity. The VOCs at issue in this litigation are trichloroethylene (TCE), tetrachloroethylene (PCE), benzene, and vinyl chloride (VC). The claimed pathways of exposure to the human body for these VOCs include ingestion, inhalation, and dermal contact. The current bellwether cases focus on five diseases: bladder cancer, kidney cancer, non-Hodgkin's lymphoma (NHL), leukemia, and Parkinson's disease. This report focuses on kidney cancer. I have produced two other reports, one on bladder cancer and one on both NHL and leukemia.[1]

2.0 PURPOSE STATEMENT

Plaintiffs' expert, Dr. Kathleen Gilbert, expresses an opinion, amongst others, that TCE, alone, or in combination with PCE, benzene, and vinyl chloride, can cause kidney cancer through mechanisms that involve perturbations of the immune system or inflammatory processes. Other plaintiffs' experts have commented on the intersections between the Camp Lejeune VOCs, immunotoxicity, and kidney cancer in their reports. As is discussed in Dr. Julie Goodman's general causation report for kidney cancer, epidemiology evidence does not support a causal association between TCE and kidney cancer except at very high occupational exposures (i.e., > 335 ppm-yr) and does not support a causal association between the remaining VOCs and kidney cancer. Thus, the purpose of my investigation was to perform a complete, independent, and unbiased analysis to evaluate the VOCs' effects on the immune system to determine whether modulation of the immune system is a relevant mechanism by which the VOCs can cause kidney cancer. My analysis includes review, careful consideration, and, where warranted, critique of the opinions of plaintiffs' experts as expressed in their reports.

[1] Plaintiffs' experts, throughout their general causation reports, have expressed many duplicative opinions. I have attempted to address their opinions on kidney cancer as they relate to the scope of my analysis in this report. I incorporate the opinions expressed in my other two reports (Expert Report on Bladder Cancer of Michael J. McCabe, Jr., Ph.D. (dated February 7, 2025) and Expert Report on Non-Hodgkin's Lymphoma and Leukemia of Michael J. McCabe, Jr, Ph.D. (dated February 7, 2025)) as if they were set out fully herein.

3.0 SUMMARY OF OPINIONS

I conclude the following:

Opinion 1: My detailed independent analysis demonstrates that relevant animal and human studies do not show that modulation of the immune system is a plausible mechanistic pathway by which TCE, PCE, benzene, and vinyl chloride cause kidney cancer.

Opinion 2: Plaintiffs' expert, Dr. Kathleen Gilbert, has opined that TCE causes immunotoxicity that has been linked to kidney cancer.[2] It is my opinion that Dr. Gilbert's novel opinion is without support and is merely a hypothesis that heretofore has not been adequately tested. The existing data and available scientific studies do not show that perturbations of the immune system or inflammatory processes by TCE, PCE, benzene, or vinyl chloride, alone, or in combination with one another, are operant mechanistically as causes of kidney cancer. Hypothesis testing is a fundamental component of the scientific method. Leapfrogging over the necessity to test a hypothesis by adopting the mere hypothesis itself as conclusive, as Dr. Gilbert does, belies the purpose of engaging in the scientific method.

Opinion 3: Other Plaintiffs' experts (e.g., Dr. Timothy M. Mallon, Dr. Benjamin Hatten, Dr. Michael D. Freeman and Dr. Steven B. Bird),[3] none of whom are immunologists, opined superficially that there is an intersection between Camp Lejeune VOCs, immunotoxicity, and kidney cancer etiology in their respective reports. Their analyses were not sufficiently detailed to reliably support the opinions asserted. They fail to critically analyze the data and experimental studies concerning TCE, PCE, benzene, and vinyl chloride with respect to their positive effects on the immune system and inflammatory responses. Again, relevant studies show no effects on the immune system and inflammatory responses to support plaintiffs' experts' opinions that TCE, PCE, benzene, and vinyl chloride can cause kidney cancer.

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[2] See General Causation expert report of Kathleen M. Gilbert, PHD on TCE and kidney cancer – dated December 8, 2024 ("Gilbert Kidney Cancer Report"), p. 22. Dr. Gilbert indicated that her report focused on TCE, since work in the area of TCE immunotoxicity has been the emphasis of her research (Gilbert Kidney Cancer Report, p. 5). Dr. Gilbert does not express an opinion that the other VOCs (PCE, benzene, and vinyl chloride) individually play a role in immunotoxicity and kidney cancer etiology. In opinion 5 of her report, without evidence or analysis, Dr. Gilbert opines that TCE-induced kidney cancer could be augmented by cumulative co-exposure to other VOCs. See Gilbert Kidney Cancer Report, p. 31.

[3] See General Causation Expert Report of Dr. Timothy M. Mallon (undated) ("Mallon Kidney Cancer Report"); Camp Lejeune: Kidney Cancer Expert Report of Dr. Benjamin Hatten (dated December 8, 2024)("Hatten Kidney Cancer Report"); Kidney Cancer Report of Dr. Michael D. Freeman (dated December 8, 2024) ("Freeman Kidney Cancer Report"); and General Causation Expert Report of Dr. Steven B. Bird, Kidney Cancer (dated December 9, 2024)("Bird Kidney Cancer Report").

4.0 QUALIFICATIONS

I, Michael J. McCabe, Jr., Ph.D., was retained by the Department of Justice to perform a thorough, independent and unbiased analysis concerning the toxicological issues in this case. I am an expert in the fields of toxicology, immunology, and related disciplines having earned a Ph.D. degree in Biomedical Studies in 1991 from Albany Medical College (New York) and having completed post-doctorate training from 1990 to 1992 in mechanistic toxicology at the Karolinska Institute (Stockholm, Sweden). My graduate education at Albany Medical College was through the Department of Microbiology and Immunology, which entailed didactic course work and qualifying examinations in immunology, microbiology, virology, cell and molecular biology, biochemistry, pharmacology, and toxicology. I trained in the laboratory of David A. Lawrence, Ph.D., who, in addition to running a first-rate research program focused on cellular immunology, operated the Albany Medical Center's clinical immunology laboratory. Also, in addition to my course work and thesis work, I moonlighted in various hospital laboratories (e.g., serology, bacteriology, blood bank) while at Albany Medical College.

After graduating and being awarded my Ph.D. degree, I was offered a post-doctoral position in the Institute of Environmental Medicine at the Karolinska Institutet under the mentorship of Sten Orrenius, M.D., Ph.D., who in addition to engaging in ground-breaking research concerning physiologic cell death (i.e., apoptosis), was a member of the Swedish Royal Academy of Sciences and Nobel Committee. Following my postdoctoral training period, I embarked on a career in academia. I have held academic appointments in the toxicology departments and environmental health science centers at Wayne State University (Detroit, Michigan) from 1992 to 2000 and the University of Rochester (Rochester, New York) from 2000 to 2017. At Wayne State, my academic responsibilities included serving as the Director of the Imaging and Cytometry Facility Core within the University's Environmental Health Science Center *Molecular and Cellular Toxicology with Human Applications*. Also, while on the faculty in the School of Medicine at the University of Rochester, I served as the Director of the Immunomodulators and Immunopathogenesis Research Core within the University's Environmental Health Science Center *Environmental Agents as Modulators of Human Disease and Dysfunction*. Currently, and since 2017, I have served as adjunct teaching faculty at Temple University (Philadelphia, Pennsylvania), where I teach a graduate level course in forensic toxicology.

I am an active 36-year member of the Society of Toxicology, which nationally and internationally is recognized as the premier scientific body dedicated to the purpose of advancing and promoting the field of toxicology. I am active in various sub-groups within the Society of Toxicology including the Immunotoxicology Specialty Section and the Ethical, Legal, Forensics, and Societal Issues (ELFSI) Specialty Section. I have served on numerous

national and international advisory committees including for the National Institutes of Health (NIH), the National Academy of Sciences, the US Environmental Protection Agency (EPA), the Department of Defense and the World Health Organization (WHO). Also, I have sat on the editorial boards of four toxicology journals, including *Toxicology Letters* (2009-2013), *Journal of Immunotoxicology* (2004-2013), *Toxicology and Applied Pharmacology* (1999-2013), and *Toxicological Sciences* (2008-2015). As detailed on my CV, I have been widely published in peer-reviewed scientific journals and have received numerous research grants from the NIH both as Principal Investigator and as Co-Investigator.

In 2009, I left full-time employment in academia and embarked on a career in medico-legal consulting. Since 2009, I have been engaged hundreds of times to apply my expertise to assess the potential effects of chemical or biological exposures on human health. As a human disease causation expert, I often am called upon to apply fundamental principles of toxicology, immunology, and immunotoxicology in performing investigations and rendering opinions concerning potential adverse health effects associated with exposures to toxic substances. I have testified in forty-two matters at deposition, hearing or trial in the past four years. My current and complete *Curriculum Vitae* is appended to this report and includes a listing of my testimonies over the previous four years.

5.0 METHODOLOGY

My opinions in this case were arrived at using the same methodology and scientific rigor that I have applied throughout my academic and consulting career performing research, authoring peer-reviewed manuscripts for publication, competing for and obtaining extramural funding for my research program, and assessing the scientific merit of ideas and works of other scientists through the peer review process. By and large, my approach involved testing a hypothesis via the scientific method and consideration of attribution elements (e.g., Bradford Hill criteria) by relying on and searching the peer-reviewed scientific literature and other resources as well as my education, training, and experience.

My opinions and findings expressed in this report were derived from methodology that is generally accepted and relied upon by life scientists and toxicology experts. These opinions and findings are held to a reasonable degree of scientific certainty and are based on my extensive knowledge, education, training and experience in the fields of toxicology, immunology, cell biology, biochemistry and related disciplines over the span of nearly 40 years. As additional information becomes available, I may supplement or modify my opinions.

5.1 The Scientific Method and Bradford Hill Criteria

Plaintiffs' expert Dr. Kathleen Gilbert asserts that epidemiological studies support an association between kidney cancer and TCE.[4] Plaintiffs' other experts, Drs. Mallon, Hatten, Dr. Freeman and Bird, assert that epidemiological studies support an association between kidney cancer TCE, PCE, benzene, and vinyl chloride alone, or in combination with one another.[5] Other experts (e.g., Dr. Julie E. Goodman and Dr. Peter E. Shields) are rebutting this assertion. The "jumping in" place for me starts with, "how can TCE, PCE, benzene, and vinyl chloride, alone or in combination with one another, causes kidney cancer"?

My work on this case is guided by the scientific method. The scientific method is a systematic approach used to conduct investigations in order to solve problems. The use of this method helps to ensure that scientific inquiry is objective, repeatable, and based on evidence.[6] My approach also considers what are known as Bradford Hill criteria (Hill, 1965), or modified Bradford Hill criteria (Adami et al., 2011; Fedak et al., 2015; Miller et al., 2000), which are a set of attribution elements that epidemiologists, toxicologists and other scientists employ in performing a causation analysis. The nine attribution elements are strength of association, consistency, specificity, temporality, biological gradient, biological plausibility (i.e., mechanism of action), coherence, experiment, and analogy. It is generally accepted that not all attribution elements must be met in order to establish causation. As indicated above, my work on this case focuses on the analysis and consideration of biological plausibility, addressing the question of whether there are mechanistic pathways (or modes of action) whereby TCE, PCE, benzene, and vinyl chloride, alone, or in combination with one another, may be linked to the etiology of kidney cancer.

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[4] Gilbert Kidney Cancer Report, p. 11.

[5] Again, Dr. Gilbert's report addresses primarily TCE. Plaintiffs' other experts summarily discuss all four VOCs. Gilbert Kidney Cancer Report.

[6] The scientific method involves several key steps as follows: (1) Observation: Gathering background information or noticing something about a subject that prompts a question; (2) Hypothesis: Formulating a testable explanation or prediction based on the background information that has been collected; (3) Experimentation: Conducting experiments, gathering data or retrieving information to test the hypothesis; (4) Analysis: Examining the results of the experiments or retrieved information to determine whether the data support or contradict the hypothesis; (5) Conclusion. Drawing conclusions based on the analysis and deciding whether the hypothesis is supported or needs revision; (6) Replication: Repeating the experiment or study to verify results and ensure reliability; (7) Theory: If repeated testing confirms the hypothesis, it may become part of a broader scientific theory.

6.0 Analysis and Basis of Opinions

My analysis and consideration of biological plausibility in this case (i.e., the mechanism(s) or mode(s) of action that demonstrate how TCE, PCE, benzene, and vinyl chloride, alone or in combination with one another, could lead to the development of kidney cancer, if at all) involves the intersection of scientific principles related to toxicokinetics (the study of how the VOCs at issue are absorbed, distributed, metabolized, and excreted by the body), carcinogenesis (the study of cancer development), and immunology (the study of the human immune system, how it functions and responds to pathogens and other threats, and how it can become disordered).

In the sections that follow, I assess the toxicokinetics of PCE, TCE, benzene and vinyl chloride, explain the importance of mechanisms of toxicity, and offer criticisms of the mechanistic opinions offered by plaintiffs' experts. I then discuss basic principles of carcinogenesis, provide an overview of the immune system, including immune responses such as immunosuppression, inflammation and oxidative stress, and discuss the intricacies of the role that the immune system plays in both the prevention and promotion of kidney cancer. This information provides the conceptual framework necessary to address the opinions of Dr. Gilbert and other plaintiffs' experts concerning the alleged interconnections between TCE, PCE, benzene, and vinyl chloride, alone or in combination with one another, and their etiologic roles, if any, in the role of kidney cancer through immune/inflammatory mechanisms. My analysis continues with comprehensive discussions of peer-reviewed studies on TCE immunotoxicity in humans and animals, followed in turn by peer-reviewed studies concerning the immunotoxicity of PCE, benzene, and vinyl chloride in humans and animals. My analysis as presented in these sections reveals that the current state of knowledge concerning TCE, PCE, benzene, and vinyl chloride immunotoxicity does not support the conclusion that immunomodulation (i.e., the process of changing the body's immune response) by these chemicals is operant in causing kidney cancer.

Having set out the conclusion of my analysis, I then outline criticisms of the opinions of plaintiffs' experts by pointing out deficiencies in the underpinnings of their opinions concerning mechanisms (i.e., modes of action, biological plausibility) of TCE-, PCE-, benzene-, or vinyl chloride-induced kidney cancer.

6.1 Volatile Organic Chemicals (VOCs) Identified at Camp Lejeune

Volatile organic compounds (VOCs) are a group of carbon-containing chemicals that often are used as industrial solvents. VOCs have a high vapor pressure at room temperature—therefore, they can evaporate (i.e., volatilize) into air easily. Pathways of human exposure to VOCs include inhalation, as may occur with occupational exposures, or through ingestion or dermal contact. The VOCs at issue in the Camp Lejeune litigation are

trichloroethylene (TCE), tetrachloroethylene (PCE), benzene, and vinyl chloride (VC). The toxicokinetics of each of these chemicals in turn are discussed in the subsections that follow.

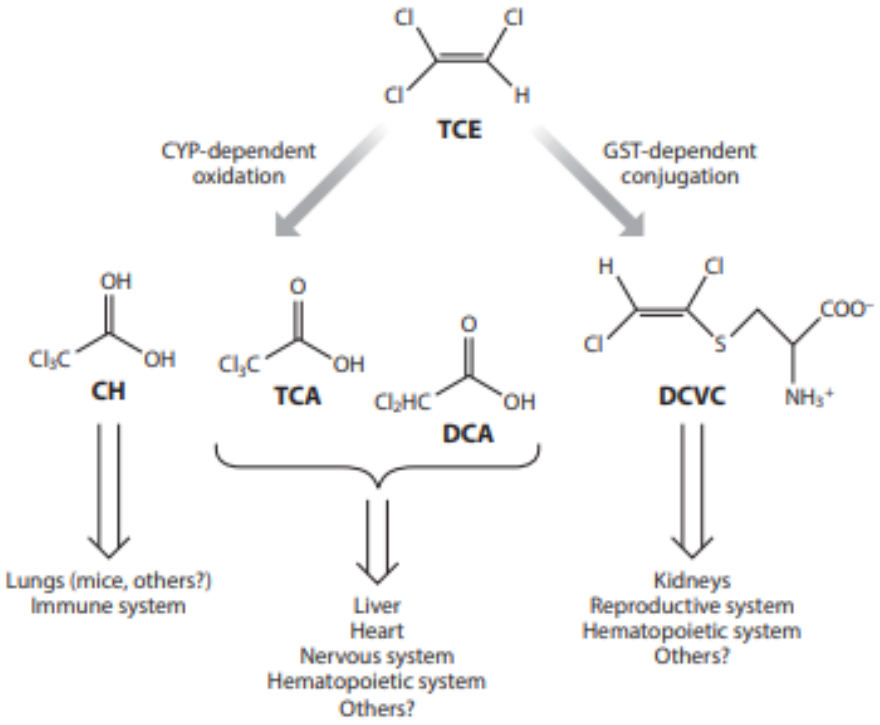
6.1.1 TCE Toxicokinetics

TCE is a small, volatile, colorless, volatile liquid chemical that readily crosses cell membranes and is metabolized[7] in the liver. Humans are exposed to TCE from a variety of sources and by different routes, including inhalation, ingestion, and dermal (ATSDR 2019; USEPA 2011). Regardless of the route of exposure, TCE readily crosses biological membranes, rapidly equilibrating from the circulation into richly perfused tissues including liver, kidney, and lung (Lash et al., 2000).

Although the metabolism of TCE is highly variable across sexes, species, tissues, and individuals, metabolism of TCE occurs through two separate pathways: (1) the oxidative metabolic pathway through cytochrome P450 (primarily CYP2E1), and (2) the glutathione (GSH) conjugation pathway (USEPA, 2011). In the oxidative pathway, metabolism yields chloral hydrate, trichloroacetate (TCA), and dichloroacetate (DCA). Although GSH conjugation of xenobiotics (i.e., foreign chemical substances) is often associated with detoxification, in the case of TCE, conjugation results in bioactivation through the formation of reactive and chemically unstable metabolite species (USEPA, 2011; ATSDR, 2019). Glutathione conjugation of TCE occurs primarily via glutathione-S-transferases (GSTs) in the liver, ultimately yielding S-dichlorovinyl-L-cysteine (DCVC). Both metabolic pathways are summarized in Figure 1. After metabolism, TCE is excreted either unchanged in exhaled air or as metabolites in the urine (ATSDR, 2019). Excretion of TCE in the bile apparently represents a minor pathway of elimination.

[7] Metabolization, in this context, means the body's process of breaking down and transforming a substance, thereby facilitating its detoxification and excretion from the body.

Figure 1. Metabolism of TCE (Lash, 2025).



6.1.2 PCE Toxicokinetics

Perchloroethylene (also known as tetrachlorethylene, PERC, or PCE) is a colorless liquid at room temperature and highly lipophilic PCE is known for its use in the dry-cleaning industry, as a degreasing solvent and as a chemical synthesis intermediate. (ATSDR, 2019b). PCE is readily absorbed following inhalation (primary route), oral, and minimally by direct dermal exposure (ATSDR, 2019b). In both animal studies and human cases of accidental death, absorbed PCE is distributed throughout the body regardless of the route of exposure, with highest concentrations measured in the adipose tissue, liver, and kidney (Dallas et al. 1994a, 1994b; Levine et al. 1981; Lukaszewski 1979; Pegg et al. 1979; Savolainen et al. 1977).

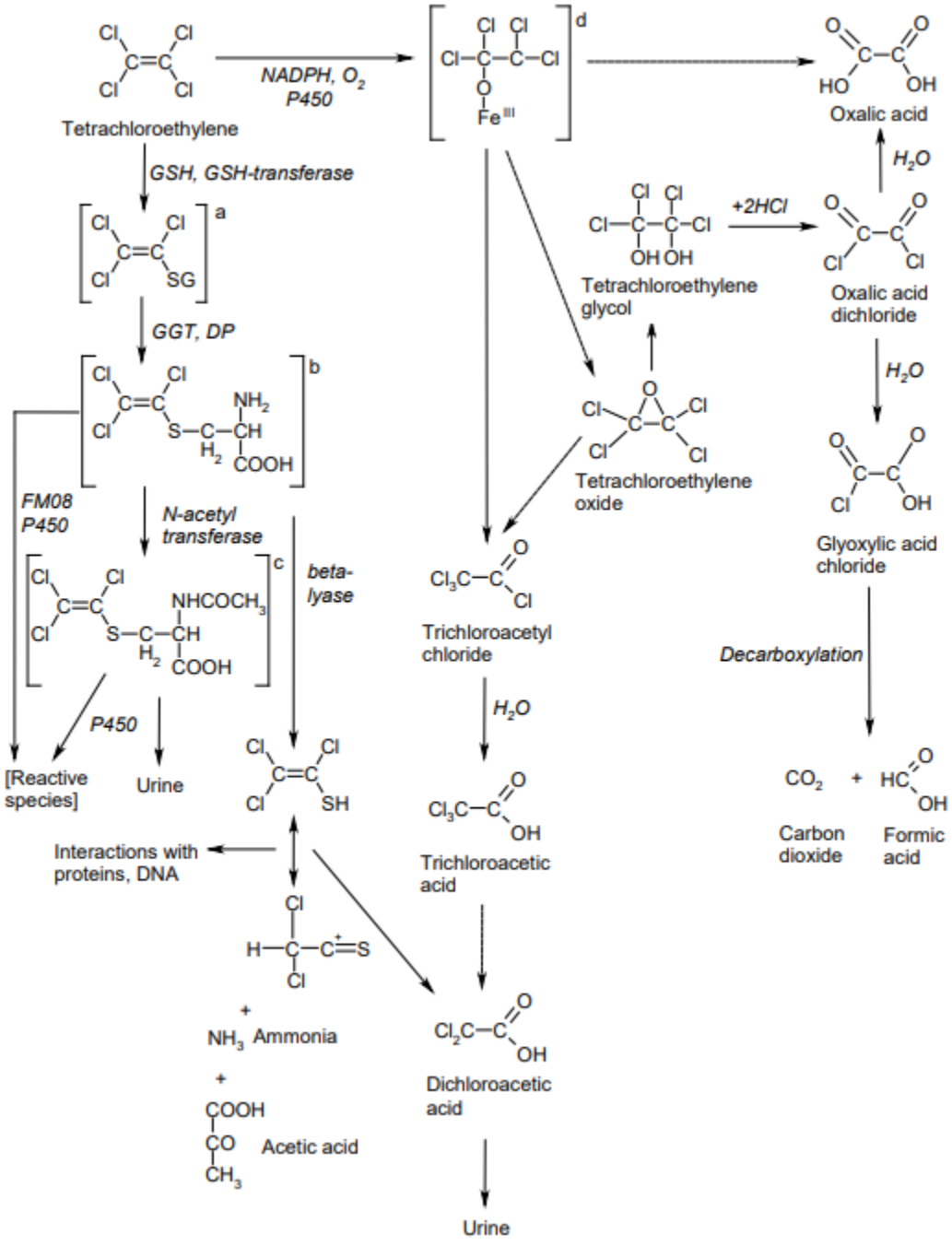
PCE is metabolized through the same metabolic pathways as TCE – (1) through oxidation by cytochrome P-450 isozymes and (2) glutathione conjugation via glutathione-S-transferase in humans, rats, and mice. While pathways are similar in humans and rodents, the predominant pathway varies by species and exposure route, with evidence for dose-dependency as well (ATSDR, 2019b). In humans, regardless of the route of exposure, only 1–3% of the absorbed PCE is metabolized to trichloroacetic acid by humans. Of note, mice and rats metabolize more PCE to trichloroacetic acid (144 and 710 nmol/minute/kg) compared to humans (13 nmol/minute/kg).

Oxidative metabolism occurs in the liver, lung, and kidney mediated by CYP2E1, based on data for similar compounds, but other isozymes may also be involved (Chiu and Ginsberg 2011; Lash and Parker 2001). Oxidation is believed to yield a Fe-O intermediate, which is converted to trichloroacetyl chloride and then hydrolyzed to trichloroacetic acid (Chiu and Ginsberg 2011). An epoxide intermediate, initially believed to be the progenitor to trichloroacetic acid, was shown to decompose to ethanedioyl dichloride and then to CO and CO_2; this pathway is believed to be minor (Chiu and Ginsberg 2011). Oxalic acid is also a metabolite of PCE oxidation and may occur via either the epoxide or Fe-O intermediate (ATSDR, 2019b). The urinary metabolites of tetrachloroethylene are trichloroacetic acid and dichloroacetic acid and are the proximate toxicants responsible for the liver toxicity and carcinogenicity seen in PCE-exposed mice (Buben and O'Flaherty 1985; Chiu and Ginsberg 2011; Lash and Parker 2001).

Glutathione conjugation occurs primarily in the liver and kidney, producing trichlorovinyl glutathione (a in Figure 2) and then S-trichlorovinyl-L-cysteine (b in Figure 2, also TCVC) (Chiu and Ginsberg, 2011; Lash and Parker, 2001). TCVC can then be metabolized to reactive species via beta-lyase or flavin-containing monooxygenases (FMOs) (Anders et al., 1988; Krause et al., 2003). Dichloroacetic acid (DCA) is also formed from dechlorination of trichloroacetic acid and believed to be an end product of beta-lyase activation after glutathione conjugation (Volkel et al. 1998). TCVC may also be N-acetylated to N-acetyl trichlorovinyl cysteine (NAcTCVC), which may be converted to reactive species through CYP3A sulfoxidation or excreted in the urine (Werner et al., 1996).

Regardless of the route of exposure, most (>80%) of the absorbed dose of PCE is exhaled unchanged in humans (ATSDR, 2019b). The major urinary metabolite in humans is trichloroacetic acid, which is at a 100-fold higher concentration than the second major urinary metabolite, NacTCVC (Volkel et al., 1998). No dichloroacetic acid was detected in human urine. The elimination half-life in humans was 45.6 hours for trichloroacetic acid and 14.1 hours for NAcTCVC (Birner et al., 1996).

Figure 2. Metabolism of PCE. (ATSDR 2019b)



6.1.3 Benzene Toxicokinetics

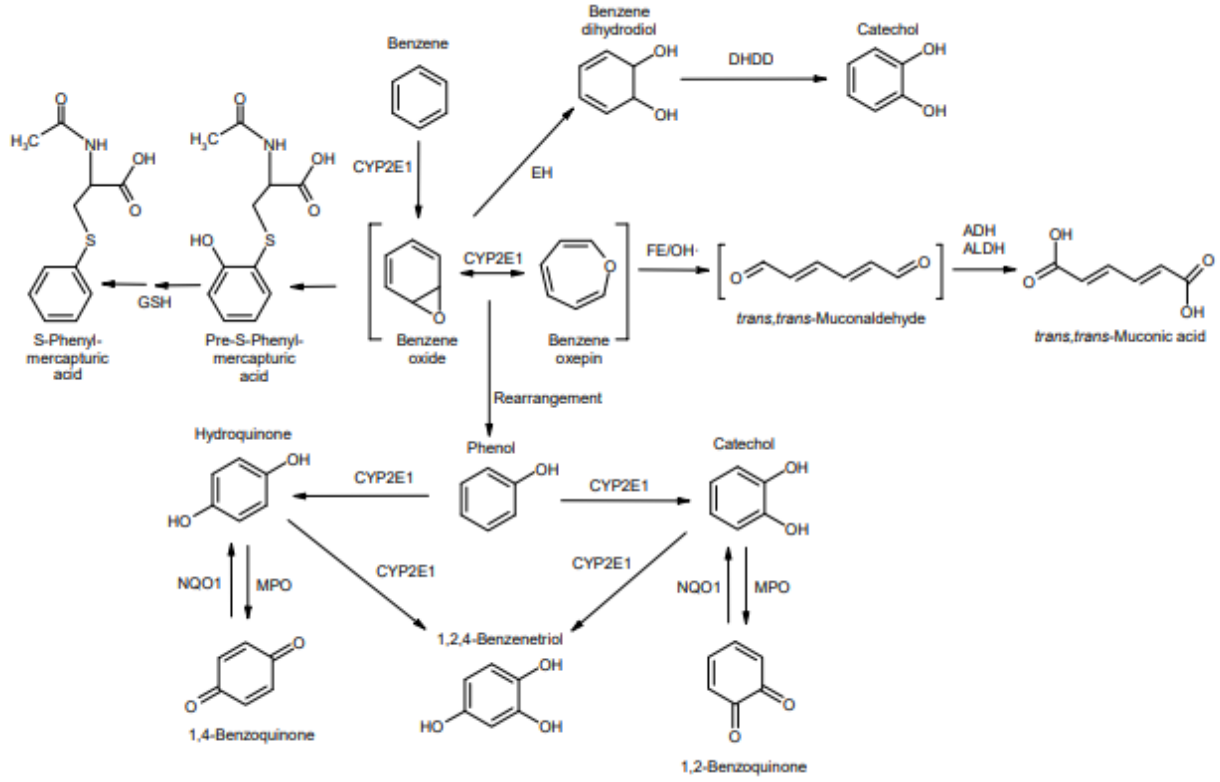
Benzene is an aromatic hydrocarbon and comes mostly from anthropogenic sources, including combustion (ATSDR, 2024b). It is ubiquitous in the environment as part of gasoline, vehicle exhaust, industrial emissions, and tobacco smoke, and has been used as a solvent in industry and consumer products.

Benzene is readily absorbed via inhalation, oral, and dermal routes in both animals and humans (ATSDR, 2024b). Inhalation exposure is the major route of human exposure to benzene; at concentrations between 47 and 110 ppm, absorption is highest in the first few minutes of exposure (70–80%) but decreases by about 1 hour to approximately 50% (range, 20–60%) with considerable individual variability (Srbova et al. 1950). Since benzene is lipophilic (tending to combine with or dissolve in lipids or fats), it is distributed throughout the body following absorption into blood and distribution to fatty tissue as expected.

Benzene is metabolized by cytochrome P450 2E1 (CYP2E1), forming an epoxide, benzene oxide. Benzene oxide may then proceed through several alternative metabolic pathways (Jerina et al., 1968; Lovern et al., 1997). In one pathway, benzene oxide rearranges nonenzymatically to form phenol, the major product of initial benzene metabolism. Phenol is further oxidized by CYP2E1 to hydroquinone. Further oxidation of hydroquinone to p-benzoquinone is catalyzed by myeloperoxidase (MPO). In a second pathway, benzene oxide can also react with glutathione (GSH) to form phenylmercapturic acid and thereafter be converted by epoxide hydrolase to benzene dihydrodiol with subsequent formation of catechol. In a third pathway, an iron-catalyzed ring-opening reaction results in the formation of trans,trans-muconaldehyde (MUC) with further metabolism to trans,trans-muconic acid (MA). All of the phenolic products may be conjugated with sulfate or glucuronic acid, with the conjugates of phenol and hydroquinone the major benzene metabolites excreted in urine (Sabourin et al., 1989; Wells and Nerland, 1991). Benzene metabolism also occurs in the bone marrow and other tissues.

Benzene is excreted both unchanged via the lungs and as metabolites (but also as parent compound in small amounts) in the urine. The rate and percentage of excretion via the lungs are dependent on exposure dose and route. Qualitatively, the metabolism and elimination of benzene appear to be similar in humans and laboratory animals (Henderson et al., 1989; 1996; Sabourin et al., 1989).

Figure 3. Metabolism of Benzene[8]



6.1.4 Vinyl Chloride Toxicokinetics

Vinyl chloride (VC) is a volatile compound used almost exclusively by the plastics industry to produce polyvinyl chloride (PVC) (ATSDR, 2024). VC is rapidly and efficiently absorbed via the inhalation and oral routes and is rapidly converted to water-soluble metabolites in both animals and humans (ATSDR, 2024).

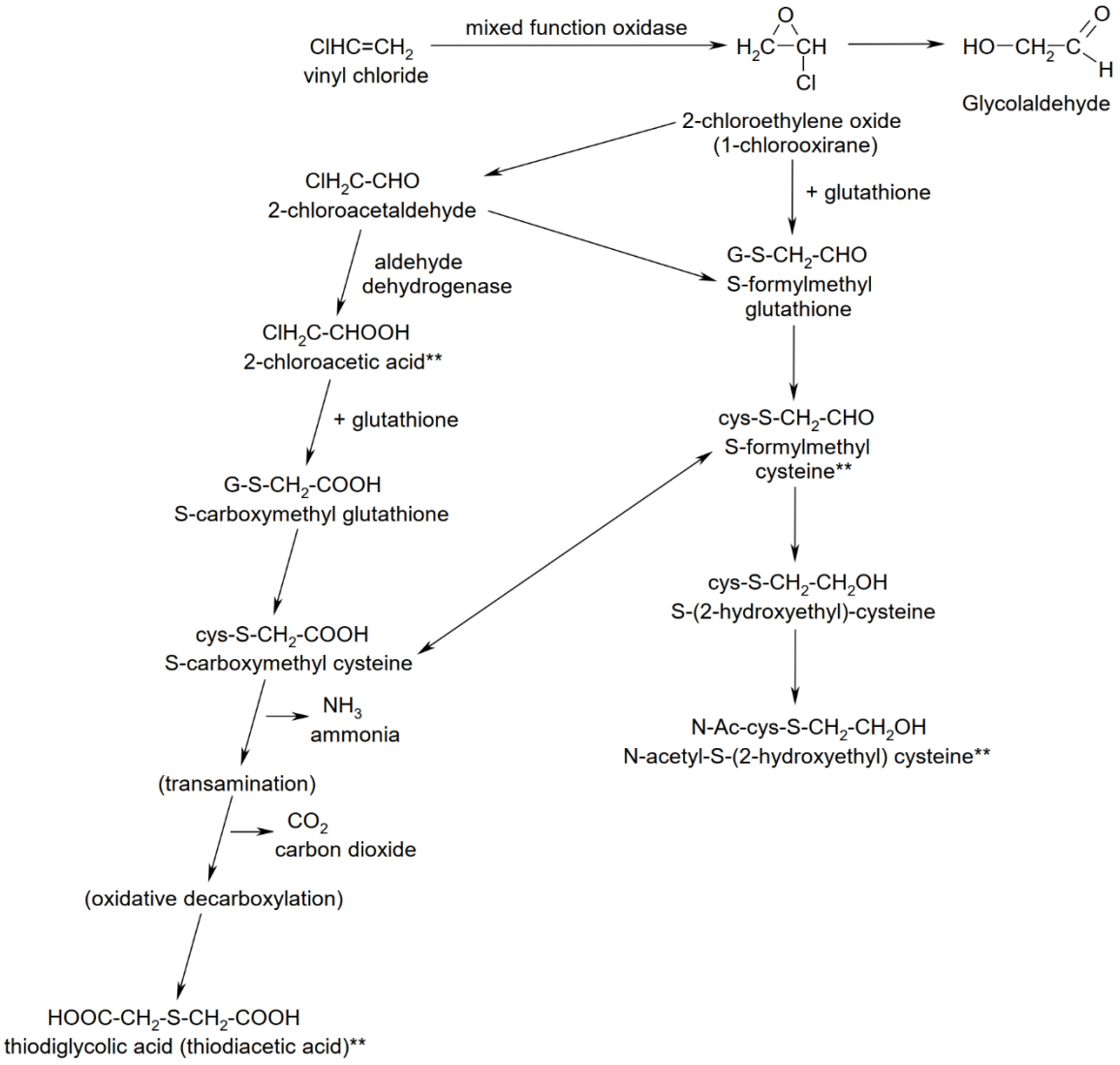
In rats, metabolic pathways for VC are consistent for both inhalation and oral exposure, with the primary route of metabolism though cytochrome P450 2E1 to form chloroethylene oxide (ATSDR, 2024). CYP2B1 plays a role in VC metabolism rodents (Ivanetich et al., 1977). Chloroethylene oxide (CEO) is a highly reactive, short-lived epoxide that rapidly rearranges to form chloroacetaldehyde (CAA), a reactive halocarbonyl compound; CEO is also a substrate for epoxide hydrolase (Pessayre et al., 1979). Both of these metabolites are detoxified primarily via glutathione (GSH) conjugation catalyzed by

[8] Key: ADH = alcohol dehydrogenase; ALDH = aldehyde dehydrogenase; CYP2E1 = cytochrome P450 2E1; DHDD = dihydrodiol dehydrogenase; EH = epoxide hydrolase; GSH = glutathione; MPO = myeloperoxidase; NQO1 = NAD(P)H:quinone oxidoreductase (from ATSDR, 2024b).

glutathione S-transferase (Jedrychowski et al., 1985; Leibman, 1977; Tarkowski et al., 1980). CEO can also be detoxified by epoxide hydrolase to yield glycolaldehyde (IARC 2012). Mitochondrial aldehyde dehydrogenase 2 (ALDH2) may also play a role in detoxifying CEO (Chen et al. 2019). A simplified diagram of the metabolism of VC is shown in Figure 4.

At low concentrations, VC metabolites are rapidly excreted primarily in urine, while at high exposure concentrations, unchanged VC is also eliminated in exhaled air (ATSDR, 2024). Urinary metabolites in rats exposed by inhalation include polar compounds at low exposure concentrations (Hefner et al. 1975b; Watanabe et al. 1976b) and 2-chloroacetic acid at high exposure concentrations (Hefner et al. 1975b). CAA and CEO GSH conjugated products are excreted in urine as substituted cysteine derivatives and include thiodiglycolic acid, S-formylmethylcysteine, and N-acetyl-S-(2-hydroxyethyl) cysteine (Bolt et al. 1980; Hefner et al. 1975b).

Figure 4. Metabolism of Vinyl Chloride



**Excreted in urine.

6.1.5 Genotoxic and Non-genotoxic Agents

Chemicals are often divided into two categories based on whether their general mode of action is genotoxic or non-genotoxic. Genotoxic agents interact with DNA, resulting in damage or structural change and are typically mutagenic in a dose-responsive manner (Klaassen, 2019). These DNA-reactive agents can be further subdivided according to whether they can directly bind to DNA without being metabolized (direct-acting) and those that require biotransformation to bind DNA (indirect-acting). Most chemical agents that function

at the initiation stage of the cancer process are indirect-acting genotoxic compounds that require metabolic activation in the target cell to result in DNA damage. The plaintiffs' experts' proposed genotoxic mechanisms are addressed below in Section 6.2, Mechanisms of VOC Toxicity.

Non-genotoxic agents do not directly interact with nuclear DNA but may change gene expression, modify normal cell function, bind to or modify cellular receptors, and increase cell growth (Klaassen, 2019). Non-genotoxic agents function through epigenetic mechanisms, changing DNA expression without modifying or directly damaging its structure. Non-genotoxic chemicals can make a cell or tissue more susceptible to DNA damage from other natural or xenobiotic (i.e., foreign chemical) sources. The plaintiffs' experts' proposed non-genotoxic mechanisms for immune system modulation are address in the in Section 6.5, Immunotoxicity.

6.2 Mechanisms of VOC Toxicity

The toxicity of a chemical is determined by its toxicokinetics, the factors discussed above (i.e., a chemical's structure and how it is absorbed, distributed, metabolized and excreted or detoxified by the body). Much is known about the metabolism of TCE, PCE, benzene, and vinyl chloride and the importance of different metabolic pathways and formation of different reactive metabolites in the potential mechanisms of their toxicities. Metabolism of TCE, PCE, benzene and vinyl chloride can result in both intoxication and detoxification, meaning that the chemicals are metabolized in the body in ways that can sometimes have harmful effects or in ways that transform them into compounds that can be easily excreted from the body.

The metabolites produced when these chemicals are broken down in the body are often target-organ specific. For example, as shown in Figure 1, different modes of action and target-organs specific effects of TCE have been found with various TCE metabolites (Lash, 2025). As described earlier, metabolism of TCE occurs through two separate pathways: (1) the oxidative metabolic pathway, and (2) the GSH conjugative pathway. The oxidative pathway that begins with the cytochrome P450 (CYP)-dependent oxidation of TCE to chloral hydrate (CH) is associated with immune system effects, while the oxidative metabolites TCA (trichloroacetate) and DCA (dichloroacetate) mediate effects on the liver, heart, nervous system, hematopoietic system and possibly other tissues. The GHS conjugative pathway starts with a conjugation reaction between TCE and glutathione (GSH) catalyzed by the enzyme glutathione-S-transferase (GST) to form cysteine-S-conjugate S-(1,2-dichlorovinyl)-L-cysteine (DCVC). The DCVC metabolite is associated with toxicity for the kidney, reproductive system, hematopoietic system and possibly others. Thus, different metabolites are produced depending on the metabolic pathway, and those various metabolites are target-organ

specific, meaning that a metabolite that is formed in the liver may have no effect on a different organ or tissue such as the kidney or the immune system.

Although metabolism of certain VOCs is similar, there are also important differences, including the quantify of potentially reactive metabolites produced. For example, PCE and TCE metabolism are qualitatively similar, but quantitative differences in the flux and yield of metabolites exist. For example, like TCE, the oxidative metabolism of PCE is believed to be carried out by CYP2E1, but the formation of the CH and DCA metabolites is more prominent with TCE. In PCE-exposed rodents, DCA is formed in the kidney, not through oxidative metabolism, but through the GSH conjugation pathway; however, this source of DCA attributable to PCE exposure has not been demonstrated in humans. Also, like TCE, GSH conjugation of PCE catalyzed by GST occurs in the liver and kidney with DCVC and TCVC being the precursors for reactive metabolites produced for TCE and PCE, respectively. Of note, in humans and experimental animals, the total metabolic flux through oxidation has been shown to greatly exceed GSH conjugation, which means that the quantity of the respective metabolites that are produced through both pathways are not equivalent. Therefore, there are significant differences between the quantity of various metabolites produced for both TCE and PCE that impact their toxicities – they are not the same. These differences are significant when analyzing the VOC's effects on the immune system.

Humans are exposed to potentially harmful substances on a daily basis, but those exposures do not necessarily lead to disease. There are complex interactions between intrinsic factors (e.g., genes) and extrinsic factors (e.g., environmental) that ultimately determine whether an adverse biological response occurs. As an example, the reactive metabolites derived from the glutathione conjugation pathway of TCE and PCE have been shown to elicit downstream biochemical reactions as well as cellular disruptions such as mitochondrial dysfunction and oxidative stress, and a myriad of other effects that have been shown in animal (*in vivo*) and *in vitro* studies to be capable of causing genotoxic and non-genotoxic outcomes. These findings provide a conceptual framework supporting the plausibility that such adverse toxic effects could be operant mechanistically in the carcinogenic process, generally. However, the manifestation of these toxic effects depends on numerous variables including exposure dose and duration, the triggering of detoxifying mechanisms (e.g., antioxidant enzymes, DNA repair mechanisms), and a person's physiological characteristics such as age, gender, and genetic polymorphisms (i.e., the different genetic makeup of each person).[9]

[9] Interestingly, GST polymorphisms in humans may play a role in interindividual variability in susceptibility to the toxicity of TCE and PCE (Cichocki et al., 2019; Lash et al., 2014; Moore et

6.2.1 *Criticisms of Proposed Mechanisms of VOC Toxicity*

The importance of these details above are, by and large, dismissed, ignored, or glossed over by plaintiffs' experts. Individually and collectively, plaintiffs' experts take the position that all exposures to TCE, PCE, benzene, and vinyl chloride, in all combinations, produce harmful toxic effects that can contribute to kidney cancer (as well as a host of other cancer and non-cancer diseases) through the same vaguely described mechanisms. Each expert seemingly takes an approach that amounts to "checking the box" with respect to Biological Plausibility as a Bradford Hill attribution element.

6.2.1.1 *Dr. Gilbert's Proposed Mechanisms*

Dr. Gilbert's report, by and large, focuses on TCE and kidney cancer. She expounds on TCE metabolism via the glutathione conjugation pathway producing reactive metabolites that under certain conditions can be shown to be genotoxic and nephrotoxic (Gilbert Kidney Cancer Report pp. 17-18). Dr. Gilbert infers that levels of TCE exposure encountered at Camp Lejeune produced kidney cancer via genotoxic mechanisms. Although epidemiology and water quality experts are addressing Dr. Gilbert's premise that epidemiological studies *"…do provide evidence that TCE, at levels of exposure comparable to those encountered at Camp Lejeune, can cause cancers, including but not limited to kidney cancer,"* (Gilbert Kidney Cancer Report p. 17) in my opinion, Dr. Gilbert must recognize that there is weak support for this argument.[10] Consequently, that likely is the reason why Dr. Gilbert, plaintiffs' only immunologist, is charged with addressing potential non-genotoxic mechanisms of action. Of all of the plaintiffs' experts, Dr. Gilbert could have provided a more balanced analysis concerning plausible genotoxic versus non-genotoxic mechanisms of TCE action. However, she failed to do so. Instead, to support the disjointed conclusions that she reaches in her report, she implicates TCE broadly in multiple mechanisms of action (i.e., genotoxicity,

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al., 2010). That this is a specific example of the complex interactions that occur between intrinsic and extrinsic factors that are the focus of contemporary environmental medicine research. Understanding these specific gene-to-environment interactions are key to our improved understanding of the etiologies of many idiopathic chronic diseases.

[10] There is some evidence supporting that TCE, at high exposure levels, can cause kidney cancer in rodents through a genotoxic mechanism mediated by reactive metabolites of TCE resulting in mutations (i.e., initiation). Also, reactive metabolites of TCE through oxidative stress and cytotoxicity leading to regenerative cell proliferation (i.e., promotion) may also be a mechanism contributing to kidney cancer in rodents (USEPA, 2011; ATSDR, 2019: IARC, 2014; Lash, 2025). However, there is uncertainty as to whether these mechanisms of action apply to TCE causing kidney cancer in humans.

oxidative stress, immunomodulation, and inflammation), all of which amount to hypotheses that have not been sufficiently tested experimentally.

6.2.1.2 *Dr. Bird's Proposed Mechanisms*

Dr. Steven Bird indicates that the mechanism of action for each of the Camp Lejeune VOCs causing kidney cancer stepwise involves metabolic activation, which leads to the generation of reactive metabolites, which can either directly or indirectly, through oxidative stress, damage biomolecules and cause genotoxicity or cytotoxicity. All of those events could conceivably occur. However, the body's normal protective response would entail that the damaged cells would likely die by apoptotic or necrotic mechanisms depending on the dose of chemical, or reactive metabolite, present in the tissue—higher doses would cause necrosis. Dead cells do not become cancerous. Dr. Bird suggests that compensatory cell proliferation, to replace the dead cells, "…can enhance the likelihood of mutations and cancer development."[11] Indeed, Dr. Bird states a hypothesis but then fails to critically test the hypothesis by demonstrating the experimental studies and data that support that these tumor promotion and progression events actually occur and result in kidney cancer following exposure to Camp Lejeune VOCs.

Dr. Bird mentions that specific somatic mutations in the VHL gene occur with TCE exposure, and that this is critical in the pathogenesis of clear-cell renal carcinoma. However, gene variants in VHL that increase the risk of developing kidney cancer account for only a small portion (less than 5%) of kidney cancers overall.

6.2.1.3 *Dr. Hatten Proposed Mechanisms*

Dr. Hatten opines that there are biologically plausible mechanistic pathways for TCE, PCE, benzene and vinyl chloride to cause kidney cancer. However, in this regard, Dr. Hatten does not appear to appreciate the difference between a plausible hypothesis concerning mechanism of action for chemical carcinogenesis and experimental evidence demonstrating that it is so. Dr. Hatten's opinion regarding the mechanism by which TCE causes kidney cancer by and large centers on the glutathione conjugation pathway of TCE metabolism that has been implicated in kidney toxicity.[12] Per Dr. Hatten, the mechanism by which PCE causes kidney cancer follows that of TCE (i.e., glutathione conjugation), because as Dr. Hatten points out the metabolism of PCE and TCE are similar[13], which is true qualitatively but not quantitatively. Dr. Hatten provides no critical assessment concerning differences between TCE and PCE metabolism, formation of reactive metabolites, and differences in outcomes

[11] Bird Kidney Cancer Report, p. 17.

[12] Hatten Kidney Cancer Report, p. 23.

[13] Hatten Kidney Cancer Report, p. 28

concerning toxicity between the two compounds. These known differences undermine Dr. Hatten's conclusion that the biologically plausible mechanism for TCE and PCE are the same.

Dr. Hatten acknowledges that *"…the literature base is too limited to define a precise pathway or mechanism of injury for vinyl chloride exposure leading to the development of kidney cancer"*[14], but he infers that the mechanism of vinyl chloride causing kidney cancer could involve activation of the RAS and p53 oncogenes.[15] However, Dr. Hatten fails to point out that vinyl chloride-induced RAS mutations are species and cell type dependent (i.e., they have been found in *rat liver* tumors induced by vinyl chloride) (Boivin-Angele et al., 2000). Moreover, mutations of RAS do not appear to play a major role in the initiation and progression of kidney cancers (Richter et al., 2020; Nanus et al., 1990). Mutations in p53 also have been associated with *liver* tumors in humans and rodents exposed to vinyl chloride (ATSDR, 2019). However, the role of the p53 oncogene in kidney cancer is questionable (Swiatkowska, 2022, Gurova et al., 2004). I am not aware of any studies demonstrating vinyl chloride-induced mutations in p53 or RAS that have been implicated mechanistically in kidney cancer—and Dr. Hatten did not cite any studies to that effect.

With respect to benzene, Dr. Hatten acknowledges that *"research is lacking to elucidate the full pathway for exposure to benzene and development of kidney cancer."* [16]Nevertheless, despite the lack of information, Dr. Hatten opines that it is reasonable to conclude that a biologically plausible mechanism of action exists that links benzene exposure to kidney cancer. Finally, Dr. Hatten states that *"…the absence of well-developed mechanistic and animal models does not imply lack of causation."*[17] Although I don't agree with that statement, it certainly is true that failing to critically evaluate the existing mechanistic data does not aid in establishing causation.

6.2.1.4 *Dr. Freeman's Proposed Mechanisms*

Dr. Michael Freeman reported that the **hypothesized** modes of action linking TCE to kidney cancer included genotoxicity, cytotoxicity and regenerative proliferation, peroxisome proliferation activated receptor α (PPARα) activation, α2u-globulin nephropathy, and formic acid-related nephropathy. The latter three mechanisms were unique to Dr. Freeman's opinion and were not discussed as mechanisms of TCE toxicity by the other plaintiffs' experts.[18]

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[14] Hatten Kidney Cancer Report, p. 44

[15] Hatten Kidney Cancer Report, p. 35

[16] Hatten Kidney Cancer Report, p. 32.

[17] Hatten Kidney Caner Report, p. 5.

[18] Freeman Kidney Cancer Report, p. 41-42.

Regarding PCE and kidney cancer, Dr. Freeman indicates that genotoxicity and cytotoxicity **may** contribute to the renal carcinogenicity of PCE.[19] As with other experts, Dr. Freeman discusses the role of the glutathione conjugation pathway in PCE toxicity. Dr. Freeman acknowledges that the proposed mechanisms of action for TCE and PCE causing kidney cancer are hypotheses (emphasis added in bold above).

Dr. Freeman mentions that there is data to suggest that the primary mechanism for vinyl chloride carcinogenicity involves direct interaction with DNA (i.e., implicating cancer initiation via genotoxicity) rather than secondary responses due to cytotoxicity (i.e., not implicating the promotion and progression stages of carcinogenesis).[20] But Dr. Freeman provides no evidence that this limited action of vinyl chloride at levels of exposure relevant to Camp Lejeune is operant in actually causing kidney cancer. Finally, Dr. Freeman provides a general discussion concerning benzene toxicity and carcinogenesis and the association between benzene under certain circumstances and leukemia.[21] However, Dr. Freeman fails to explain how these observations inform that benzene causes kidney cancer. The gap in this information, which Dr. Freeman's analysis does not close, is too great to support his conclusion that there is a mechanistic causal association between benzene and kidney cancer.

6.2.1.5 *Dr. Mallon's Proposed Mechanisms*

Dr. Timothy Mallon opines that the mechanism of TCE causing kidney cancer involves mutagenic (i.e., genotoxic) and cytotoxic events tied to the metabolism of TCE via the glutathione conjugation pathway.[22] However, Dr. Mallon did not discuss in sufficient detail how these genotoxic/cytotoxic events actually lead to kidney cancer. Although TCE-induced genotoxicity and cytotoxicity can occur under certain circumstances, the body's normal protective response entails damaged cells likely dying by apoptotic or necrotic mechanisms. Dead cells do not become cancerous. Dr. Mallon's analysis fails to establish how TCE contamination of the water at Camp Lejeune caused genotoxic events that could have initiated the carcinogenic process rather than activating cell death pathways. Dr. Mallon provides a discussion of PCE metabolism via the oxidative and glutathione conjugation pathways in his report.[23] This discussion provides certain anecdotes about PCE metabolism, but nowhere does it provide a cohesive analysis that supports a biologically plausible

[19] Freeman Kidney Cancer Report, p. 50.

[20] Freeman Kidney Cancer Report, p. 54.

[21] Freeman Kidney Cancer Report, p. 60-61.

[22] Mallon Kidney Cancer Report, p. 22.

[23] Mallon Kidney Cancer Report, p. 38.

mechanism whereby PCE causes kidney cancer.

With respect to benzene, Dr. Mallon mentions that studies show that benzene has been shown to be metabolically active, causes oxidative stress and is genotoxic, and immunosuppressive.[24] However, he did not elaborate further on how these effects of benzene evidence a mechanistic pathway leading to kidney cancer. In particular, Dr. Mallon did not provide a critical analysis concerning the evidence of benzene immunosuppression and how it might be mechanistically linked to causing kidney tumor progression versus regression. Dr. Mallon provides a discussion on the well-known association between benzene, at high doses, and hematotoxicity (i.e., toxic effects of benzene on blood cell formation), which may be linked to leukemogenesis—particularly acute myeloid leukemia (AML). However, Dr. Mallon failed to explain why these effects of benzene have anything to do with kidney cancer. In my opinion they do not. Also, Dr. Mallon indicates that benzene alters aryl hydrocarbon receptor (AhR) binding, which is not entirely correct.[25] Benzene is a ligand for the AhR (i.e., it binds and activates the AhR). The relevance of benzene-AhR interaction is that benzene is the only Camp Lejeune VOC that binds to the AhR. Thus, through AhR activation, benzene can have unique downstream effects on cells that are not shared by TCE, PCE and vinyl chloride. Plaintiffs' experts recurrently infer that formation of reactive metabolites is the common biologically plausible mechanistic pathway whereby Camp Lejeune VOCs cause kidney cancer. However, while, generally, there are similarities, there also are many differences that impact fundamental principles of toxicology including dose responsiveness, additivity-synergy-antagonism, and target organ toxicity to name a few. Finally, with respect to vinyl chloride, Dr. Mallon provides a discussion of metabolic activation and the formation of reactive metabolites that may damage biomolecules. However, he fails to close the loop on how these mechansims are relevant in linking vinyl chloride to kidney cancer causation.

As mentioned above, plaintiffs' experts, particularly Dr. Gilbert, implicate immunotoxicity associated with Camp Lejeune VOCs as a plausible mechanism involved in the etiology of kidney cancer. Except for Dr. Gilbert, none of the other plaintiffs' experts are immunologists. My opinion is that experimental studies and data do not support that modulation of the immune system is a plausible mechanism by which TCE, PCE, benzene, and vinyl chloride can cause kidney cancer. In the sections that follow, I present basic principles of carcinogenesis, provide an overview of the immune system, including immune responses such as immunosuppression, inflammation, and oxidative stress, and discuss the intricacies of the role that the immune system plays in both the prevention and promotion of kidney

[24] Mallon Kidney Cancer Report, p. 29.

[25] Mallon Kidney Cancer Report, p. 30.

cancer. This information provides the conceptual framework necessary to follow my ensuing analysis and understand my opinion as well as the flaws in the opinions of Dr. Gilbert and other plaintiffs' experts concerning the alleged interconnections between TCE, PCE, benzene, vinyl chloride, alone or in combination with one another, and their etiologic roles, if any, in the role of kidney cancer through immune/inflammatory mechanisms.

6.3 Overview of the Immune System

Overall, the immune system is a complex network of cells (collectively called immunocytes) and soluble mediators (e.g., antibodies, cytokines, complement proteins, etc.) within the body that function to protect against infections such as viral or bacterial pathogens or other threats to the integrity of the self, while simultaneously preserving the functioning of the body's own cells, tissues and organs. (Parham, 2015). In this way, the immune system essentially functions as the body's Department of Defense. The immune system achieves this through a combination of so-called innate immune and adaptive immune responses.

6.3.1 Innate and Adaptive Immunity

6.3.1.1 *Innate Immunity*

Innate immunity is the body's first line of defense against invading pathogens and responds more quickly upon the body's first encounter with a pathogen.[26] Innate immunity also referred to as natural immunity because the mechanisms affording protection are conserved evolutionarily and present at birth. Generally, innate immunity is more primitive than adaptive immunity, and antigenic recognition by cells of the innate immune system is non-specific and involves less diversity. Innate immunity is comprised of physical barriers such as the skin and mucous membranes, as well as various cell types including phagocytes (i.e., white blood cells) such as macrophages and dendritic cells. Innate immunity also is comprised of other white blood cells (i.e., leukocytes) that have specialized functions including mast cells, basophils, eosinophils, neutrophils and natural killer cells. Natural killer cells (NK cells) play a particularly important role in the body's defense against viruses and cancer.

6.3.1.2 *Adaptive Immunity*

Adaptive immune responses, or **adaptive immunity**, involve the development of immunological memory, that is, the ability of the immune system to recognize and respond more effectively to pathogens or antigens that have been encountered previously. Features

[26] The components of a pathogen or other perceived foreign entity to which the immune system responds are called antigens.

of immunological memory include quicker onset and amplification of the immune response upon re-encounter with pathogens. These features of immunological memory are fundamental to the success and efficacy of vaccine immunization programs.

Vaccines, which typically are biological preparations containing antigenic components of pathogens or killed or attenuated pathogen variants, activate the adaptive immune response, thereby creating immunological memory that confers long-lasting protective immunity specific to the vaccine target pathogen. The benefit of vaccination is that, upon subsequent encounter with the vaccine target pathogen, the attack by the immune system is more robust, thereby protecting the host from the harmful effects of infection. [27]

Memory immunity is not just important for vaccines; it is a feature of many secondary immune responses (i.e., immune responses that occur subsequent to a host's first-time encounter with an antigen). Therefore, adaptive immunity entails the response of antigen-specific B lymphocytes and T lymphocytes to antigen. Antigen-specific B lymphocytes differentiate into plasma cells, which secrete antibodies that bind to pathogens or antigens (i.e., immune recognition)[28] and facilitate their destruction and/or removal through immune effector processes that include neutralization, opsonization or death of antigen-expressing cells (i.e., cytotoxicity).

6.3.1.2.1 T Cell Subpopulations

In adaptive immunity, there are many subpopulations of antigen-specific T lymphocytes (Fig. 7). Functionally distinct T lymphocytes express different arrays of receptors (e.g., different combinations of CD4, CD8, CD25 and CD45RA—all of which are designations for cell surface markers on T cells) on their cell surfaces, which impart specialized roles for the T cell subtype during an immune response.

CD4+ cells, also called T helper cells, function by regulating the activities of other immunocytes and "helping" them to perform their roles such as, for example, B cells differentiating into antibody-secreting plasma cells.[29] There are various subpopulations of

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[27] For example, although polio and measles are both extrinsic pathogenic viruses, when a host is infected solely with measles virus, the immune response is targeted specifically to activate against measles, and not polio (or any of the other incalculable number of pathogens or antigenic threats that could be encountered by the host in other circumstances).

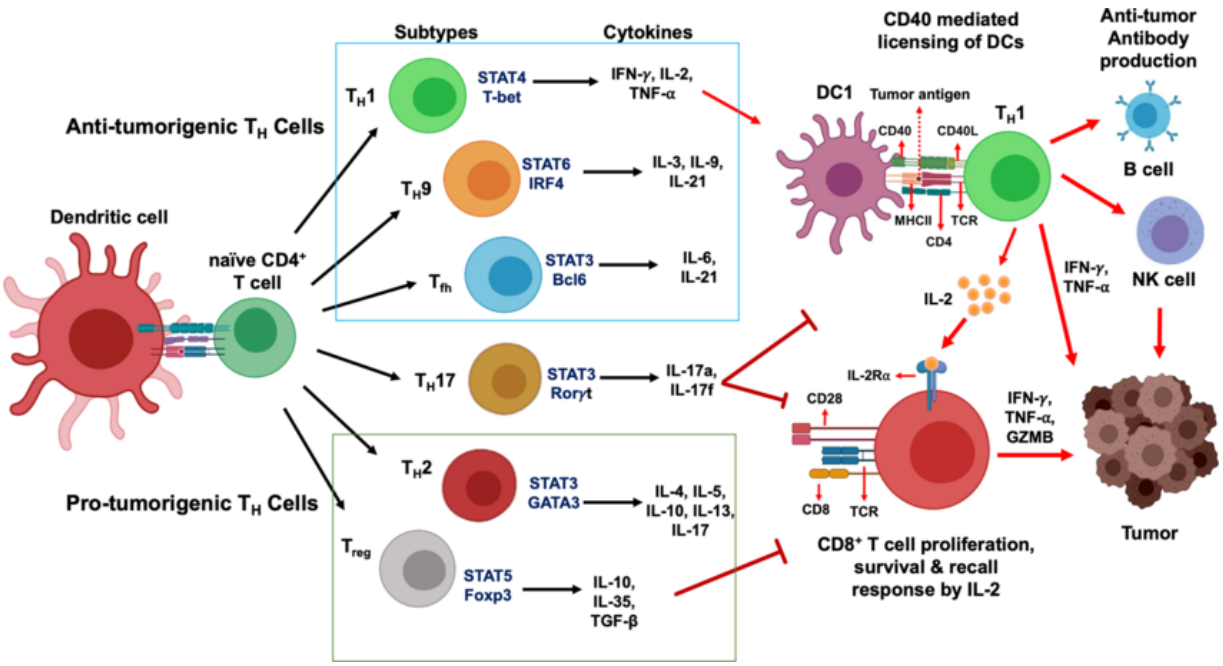
[28] Immune recognition is the process by which certain specialized cells of the immune system identify specific antigens thereby distinguishing between self and non-self. Immunology: The Science of Self-Nonself Discrimination. John Wiley & Sons. The concepts of specificity and self-nonself discrimination are fundamental tenets of immunology.

[29] The critical importance of CD4+ cells in immunity is exemplified by Acquired Immunodeficiency

CD4+ helper T cells, which are functionally distinct and control different aspects of the immune response based on the cytokines that they produce (Basu et al., 2021; Geginat et al., 2014; Kunzli & Masopust., 2023). For example, CD4+ Th1 cells produce interleukin-2 (IL-2), tumor necrosis factor (TNF-α), and interferon gamma (IFN-У); whereas, CD4+ Th2 cells produce interleukin-4 (IL-4), interleukin-5 (IL-5), interleukin-10 (IL-10), and interleukin-13 (IL-13). The effector functions of Th1 and Th2 cells differ, in that, Th1 cells tend to aid cell-mediated immune responses (e.g., CD8+ CTL responses); whereas Th2 cells tend to aid humoral immune responses (e.g., antibody production by B cells).

Another subpopulation of CD4+ cells is called Tregs (i.e., Regulatory T cells) that function normally to suppress (i.e., turn-off) immune responses through a variety of mechanisms including secretion of IL-10 and transforming growth factor-β (TGF-β). Changes in the activities of Tregs is associated with many chronic diseases including allergies, autoimmune diseases and cancer. The following figure illustrates the complex central role that CD4+ T cell differentiation and different CD4+ T cell subsets play in immunity.

Figure 5. CD4+ T cells development and their functional subsets in immunity (Basu et al., 2021).



Syndrome (AIDS), where infection with the Human Immunodeficiency Virus (HIV) is characterized by massive reduction of CD4+ T cells. Consequently, left untreated, HIV infection leads to severe immunodeficiency followed by death and morbidity due to opportunistic infections and certain malignancies that develop secondary to impaired immune responses to infectious agents.

CD8+ cytotoxic T lymphocytes (CTLs) also play a major role in the body's adaptive immune defenses and ability to fight viral infections. When certain viruses infect cells, they express proteins or otherwise cause cell surface changes that can be recognized by CTLs as being "foreign." Recognition of the virus-infected cells by CTLs then triggers a targeted effector function whereby the CTL delivers a "hit" in the form of a cytotoxic granule containing the protein perforin to the virus infected cell.

6.4 Role of the Immune System in Cancer Development

By and large, the mechanisms the immune system employs to fight infections with pathogens are the same, or similar, as those directed toward controlling the growth of a cancerous tumor. The importance of a properly functioning immune system in controlling cancer is exemplified through subjects who have primary immunodeficiencies (e.g., rare congenital defects that appear as inborn errors of immunity due to genetic defects in one or more key immune system components) or secondary immunodeficiencies (e.g., organ transplant patients receiving immunosuppressive drugs). Subjects who have primary or secondary immunodeficiencies are at increased risk of various cancers, including kidney cancer (Mortaz et al., 2016). However, the immunosuppression claimed by some to be associated with TCE exposure is nowhere near as obvious that which occurs in circumstances of primary or secondary immunodeficiency. There are no studies that show that TCE exposure, alone, or in combination with other VOCs, directly affects any of the mechanisms within the tumor microenvironments of any cancers—including the complex tumor microenvironment of kidney cancer.

The immune system can combat cancer cells by recognizing novel tumor antigens and stimulating adaptive and innate immune effector responses intended to eliminate cancer cells before they can cause disease. Cancer essentially arises as a consequence of abnormal and invasive cell proliferation and cell survival (i.e., tumor growth). The process by which normal cells are transformed into cancer cells is called **carcinogenesis**. A normal cell becoming a disease-causing cancer cell involves a multistage process that entails the accumulation of numerous independent mutations, which individually have escaped the cell's intrinsic safety mechanisms for repairing mutated DNA and/or causing abnormally behaving cells to die by apoptosis (aka, programmed cell death or cell suicide). Characteristics of the transformation process include alterations in cellular morphology, growth characteristics and biochemical properties, including changes in protein expression in ways that make the cancer cell appear foreign to the immune system (i.e., by expressing tumor antigens). In order to understand carcinogenesis (i.e., how a normal cell becomes a disease-causing cancer), one must understand **immunosurveillance**, the ability of the immune system to recognize and destroy cancer cells, and **immunoediting**, and the process by which immunosurveillance, is bypassed.

6.4.1 Immunosurveillance

The ability of the immune system to recognize and destroy cancer cells is known as **immunosurveillance** or cancer immunosurveillance (Finn, 2018). Through the mechanisms of immunosurveillance, most potentially cancerous cells are identified and eliminated before they can cause harm—only a small minority of such cells are able to proliferate, survive, and give rise to clinical disease. Those that do develop into clinical cancer do so by avoiding destruction by the immune system.

For example, CTLs (CD8+ cytotoxic T lymphocytes) can recognize cancer cells and infiltrate the tumor microenvironment thereby recognizing and killing cancer cells expressing tumor antigens on their cell surfaces. Experimental studies have shown that an early infiltration into the tumor microenvironment of CD4+ helper T cells producing Th1-like cytokines (e.g., IL-2, TNF-α and IFN-У) as well as activated CD8+ CTLs and NK cells producing soluble cytotoxins (e.g., granzymes, perforin) associates with a favorable prognosis (Joseph & Enting, 2019; Clemente et al., 1996; Oldford et al., 2006; Dieu-Nosjean et al., 2008; Kusuda et al., 2005; Tosolini et al. 2011; Vesalainen et al., 1994; Ubukata et al., 2010; Fridman et al., 2012; Kitamura et al.; 2015)—including kidney cancer (Kondo et al., 2006).

Some mutated cells are able to avoid destruction by the immune system. Indeed, the avoidance of immune detection and elimination is a hallmark of cancer progression. Answering the question of how cancer cells avoid destruction by the immune system requires understanding the complexity of how cancer cells and the immune system both evolve within the changing tumor microenvironment. Paradoxically, through pro-inflammatory processes, the immune response can both destroy cancer cells (i.e., good inflammation) and, conversely, promote tumor progression by shaping tumor immunogenicity and suppressing anti-tumor immunity. (i.e., bad inflammation).

6.4.2 Inflammation

Normal physiologic inflammation is a tightly regulated process involving, among other things, the recruitment of phagocytic cells and the production of soluble inflammatory mediators (e.g., cytokines) that facilitate the destruction and removal of harmful agents from the body. Characteristics of inflammation include redness (caused by increased blood flow to the affected area), swelling (caused by accumulation of fluid in the affected area), pain (caused by release of inflammatory mediators that activate pain receptors), and heat (caused by increased blood flow to and metabolic activity in the affected area). A benefit of discomforts characteristic of inflammation is that they enable the cells and soluble mediators of the immune system to be brought rapidly and in large numbers to the infected or affected tissue. Inflammation is a normal protective process that, when controlled properly, resolves once the potential for harm has been eliminated.

Unresolved inflammation (also called dysregulated inflammation or chronic inflammation) is a characteristic linked to the development or progression of numerous

chronic disorders and diseases—including cancer. In essence, "good" inflammation (i.e., acute inflammation) occurs when it acts as part of a defense mechanism to heal injuries or fight infections by causing the physiological changes (e.g., redness, swelling, heat, pain, etc.) that facilitate recruitment of phagocytes and other white blood cells to the affected area. "Bad" inflammation (chronic inflammation) may occur when it persists even after the initial threat has been resolved, when the response is not proportional to the magnitude of the threat, or when inflammation occurs in the absence of a clear trigger (Oronsky et al. 2022).

Phagocytosis is the process by which certain white blood cells (i.e., phagocytes) surround, engulf, and destroy foreign substances, such as bacteria, dead cells, and other particles, thereby protecting the body against foreign invaders. The destruction of the foreign substance by the phagocyte involves a transient increase in oxygen consumption known as the 'respiratory burst,' which involves the production of various toxic reactive oxygen species (ROS). This respiratory burst is an example of normal ROS formation playing a beneficial and protective role within the body. However, when the ROS products from the respiratory burst leak out of the phagocytes or become imbalanced by overcoming normal anti-oxidant measures, this can cause damage, mediated by oxidative stress and pro-inflammatory processes, to the surrounding tissues.

6.4.3 Oxidative Stress

Oxidative stress occurs when there is an imbalance of free radicals (i.e., unstable molecules) and antioxidants in the body that can cause damage to cells). When there is an over production of ROS, an organism is thought to be in oxidative stress, resulting in damage to cellular macromolecules including nucleic acids (e.g., DNA), proteins and lipids (Reddy, 2023; Ghezzi et al., 2017).

One theory of disease posits that free radical reactive molecules build up in the body over time and lead to cellular damage, which plays a key role in the development and progression of various diseases including cancers. Many studies in cell systems have found antioxidants to be effective at preventing damage. Early work in this area led to the belief that antioxidants prevent disease and promote human health resulting in increased consumption of antioxidant supplements. However, early *in vivo* findings in animals have called this into question. For example, in laboratory experiments performed using a nematode *C. elegans* (i.e., roundworms) genetically engineered to overproduce free radicals, lifespans did not differ from controls (Doonan et al., 2008). Additionally, mice engineered to overproduce antioxidants didn't live any longer than their control counterparts (Perez et al, 2009). In humans, one study found antioxidant supplements counteracted the health-promoting effects of exercise (Ristow et al., 2009), and evaluation of 56 randomized clinical trials with a low risk of bias found that antioxidant supplements were actually associated with higher mortality (Bjelakovic et al., 2013a; 2013b). The point here is that the *sin qua non* viewpoint that all chemical exposures increase oxidative stress thereby being a plausible

mechanism of disease is unfounded.

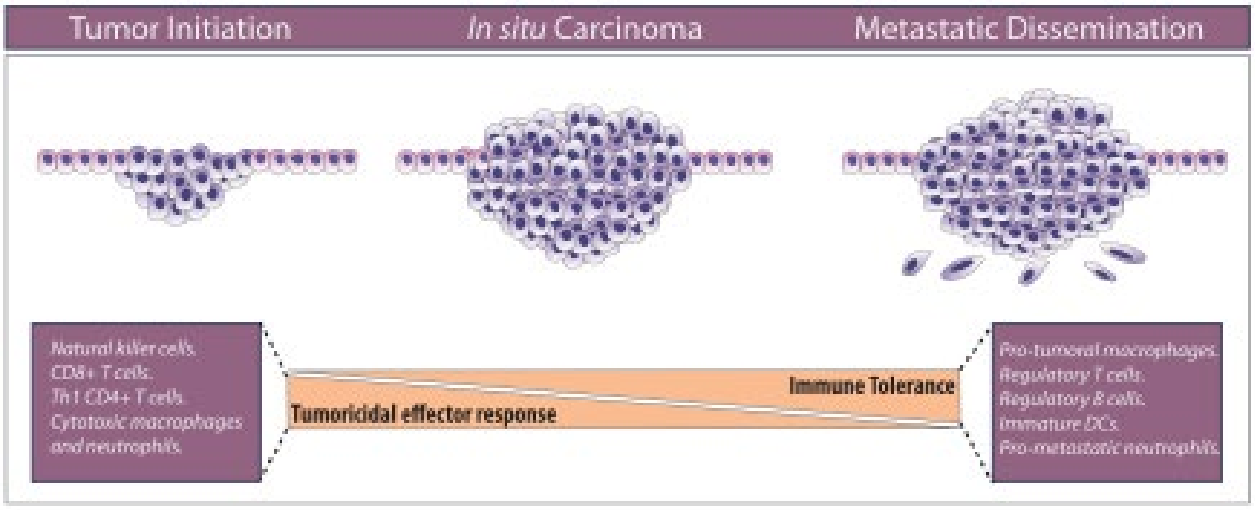
6.4.4 Immunoediting

The duality of the immune system in combating and promoting tumor growth is called cancer **immunoediting**. Cancer immunoediting consists of three phases, known as the "three E's," which are i) **elimination**, ii) **equilibrium**, and iii) **escape** (Teng et al., 2015; Fridman et al., 2011; 2012; 2013).

In the first **elimination** phase, innate and adaptive immunity work in concert to recognize and destroy developing tumors before they become clinically apparent. During the second **equilibrium** phase the outgrowth of rare tumor cell variants that survived elimination is held in check by the immune system, thereby establishing a balance between immune system and tumor cells. In the third and final phase, **escape**, the abnormal growth of tumor cells eventually escapes control of the immune system, thereby leading to malignancy. The mechanisms by which tumor cells escape control by the immune system include 1) downregulation of tumor antigens or loss of mechanisms that facilitate antigen presentation to T cells (i.e., loss of immune recognition); 2) upregulation of resistance mechanisms against the cytotoxic effectors of immunity (i.e., loss of immune system functions that destroy pathogens and remove them from the body) or upregulation of pro-survival or growth factor genes (i.e., outrunning the immune system's ability to destroy and eliminate pathogens), and 3) establishment of an immunosuppressive tumor microenvironment (i.e., chronic inflammation) through increased or changed production of inhibitory cytokines and growth factors (e.g., VEGF, TGF-β), induction or recruitment of functional immunosuppressive cells (e.g., Tregs, MDSCs, M2 macrophages), or induction of adaptive immune resistance by stimulating inhibitory receptors (i.e., immune checkpoints) on immune effector cells.

The following figure depicts that tumor progression is accompanied by changes in the tumor microenvironment whereby over time immune effector functions change from being tumoricidal to being tolerogenic.

Figure 6. Roles of the immune system in cancer: from tumor initiation to metastatic progression (Gonzalez et al., 2018).



Immunoediting demonstrates that the immune system has both pro-tumorigenic and anti-tumor effects, the balance between the two influencing the progression of an individual tumor. This balance is illustrated in Figure 6, which shows that potential upregulation vs. downregulation of various immune effector functions can have a negative effect, a positive effect, or no effect depending on when during the carcinogenic progression they act.

6.4.5 Role of the Immune System in Kidney Cancer

Much of the discussion above concerning the role of the immune system in cancer generally is relevant to the role of the immune system in kidney cancer specifically. Generalizations about immunotoxic effects of TCE in other contexts may not necessarily be relevant to the immunobiology of kidney cancer. The tumor microenvironment in kidney cancer has been described as being dauntingly complex and different from that of other tumors (Drake & Stein, 2018). Interestingly, unlike the case in the majority of cancers, as renal cell carcinoma progresses, increased density of tumor infiltrating CD8+ T cells (i.e., CTLs) is associated with poor prognosis. The precise mechanisms involved are unclear but probably involve some unique silencing of CTL functioning within the evolving renal cell carcinoma tumor microenvironment.

Renal cell carcinoma (RCC) is the most common type of kidney cancer; it accounts for ~95% of kidney related malignancies, which are a heterogeneous group of diseases classified according to their histological characteristics (Kruk et al., 2023). Clear-cell RCC is the most common form of RCC; about 7 out of 10 people with RCC have this kind of cancer (www.cancer.org/cancer/types/kidney-cancer/about/what-is-kidney-cancer .html) and it, reportedly, is the renal carcinoma preferentially claimed to be associated with TCE exposure (Wartenberg and Gilbert, 2014).

According to the American Cancer Society Cancer Facts & Figures Data[30], it is estimated that more than 81,000 new cases of kidney cancer were projected to be diagnosed and that more than 14,000 people were projected to die from the disease in the United States in 2024. Risks[31] for developing kidney cancer include genetic/hereditary factors as well as environmental/lifestyle factors. For example, heritable genes associated with kidney cancer have been identified (e.g., von Hippel-Lindau mutation or VHL gene), where individuals with certain gene variants are at increased risk of developing kidney cancer. However, these genotypes account for only a small portion (less than 5%) of kidney cancers overall. Normally, the product of VHL gene expression functions as a tumor suppressor by regulating the degradation of hypoxia-inducible factor-alpha (HIF-α), which is a redox sensitive protein. When VHL is mutated or inactivated it leads to the accumulation of HIF-α, which promotes tumor growth through increased angiogenesis and tumor cell proliferation due to the dysregulated response to low oxygen conditions that occur in the tumor microenvironment. Possessing an inherited genetic variant that increases susceptibility to developing a particular disease is an example of an intrinsic risk factor. Other examples of intrinsic risk factors are age and gender. Generally, cancer is a disease of aging, and males are approximately twice as likely as women to be diagnosed with kidney cancer.

Differences in environmental exposures and lifestyle are extrinsic factors. To that end, accounting for nearly half the cases in the United States, cigarette smoking and excess body weight are major risk factors for kidney cancer, probably due to pro-inflammatory mechanisms (Kruk et al., 2023). Chronic high blood pressure (i.e., chronic hypertension) and chronic renal disease also are risk factors for kidney cancer. The ACS and the National Cancer Institute[32] both list occupational exposure to trichloroethylene as a risk factor for kidney cancer particularly in TCE-exposed subjects who expressed somatic variants of the VHL gene

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[30] https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2024/2024-cancer-facts-and-figures-acs.pdf

[31] According to the ACS, a risk factor is anything that increases a person's chance of getting a disease such as cancer. Having a risk factor, or even several risk factors, does not mean that a person will get the disease, and some people who get the disease may have few or no known risk factors. Having several risk factors could make a person more likely to develop kidney cancer, but even if a person with kidney cancer has a risk factor, it is often very difficult to know how much that risk factor contributed to the cause of the person's disease.

[32] https://www.cancer.gov/types/kidney/hp/renal-cell-carcinoma-genetics

(Brüning et al., 1997; Brauch et al. 1999; 2004), which is the vast minority of kidney cancer patients. The significance of VHL mutations in TCE-induced kidney cancer is not clear.

6.4.6 Posited Mechanistic Interconnections between TCE and Kidney Cancer

The importance of a properly functioning immune system in controlling cancer is exemplified through subjects who have primary immunodeficiencies (e.g., rare congenital defects that appear as inborn errors of immunity due to genetic defects in one or more key immune system components) or secondary immunodeficiencies (e.g., organ transplant patients receiving immunosuppressive drugs). Subjects who have primary or secondary immunodeficiencies are at increased risk of various cancers, including kidney cancer (Mortaz et al., 2016). However, the immunosuppression claimed by some to be associated with TCE exposure is nowhere near as obvious that which occurs in circumstances of primary or secondary immunodeficiency. There are no studies that show that TCE exposure, alone, or in combination with other VOCs, directly affects any of the mechanisms within the tumor microenvironments of any cancers—including the complex tumor microenvironment of kidney cancer.

The vast majority of patients with kidney cancer are not known to have experienced appreciable exposure to TCE, alone, or in combination with PCE, benzene, or vinyl chloride. The vast majority of people who have been exposed to TCE, even at high levels, are not known to have developed kidney cancer. Moreover, the vast majority of people who have been exposed to TCE, even at high levels that may occur in occupational settings, have not been shown to display clinically apparent immune dysfunction. Hence, the characteristic polarization of the immune response that is characteristic of kidney cancer progression occurs independent of TCE exposure or exposure to other VOCs found at Camp Lejeune.

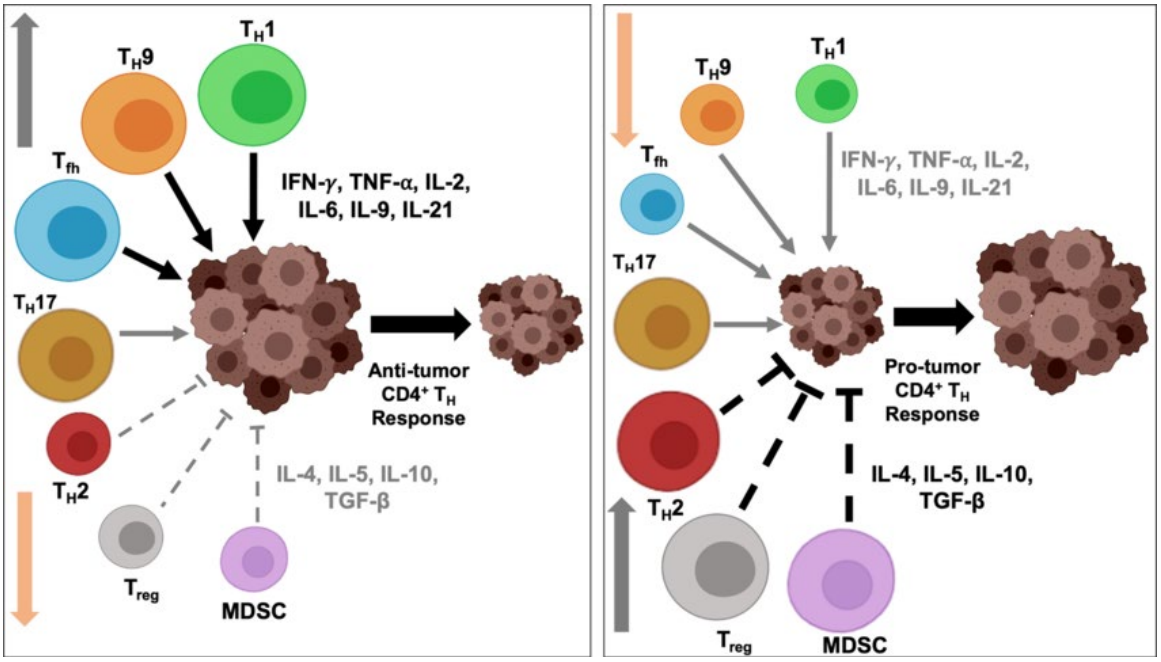
As one basis to her opinion that TCE causes kidney cancer through immunotoxic mechanisms, Dr. Gilbert claims that most (emphasis added) treatments for kidney cancer target the immune system (Gilbert Kidney Cancer Report, p. 11). This is factually incorrect,[33] as immunotherapy is not the treatment of choice for most kidney cancer patients. To the contrary, the application of therapies that, for example, target immune checkpoint inhibitors (i.e., soluble mediators that suppress anti-tumor T cell effector functions) are typically used for advanced (i.e., Stage IV) kidney cancer patients (Rose et al., 2024; Adikari et al., 2024), which is characterized by increased tumor invasiveness (i.e., metastasis). I did not see that it was Dr. Gilbert's position that the posited effects of TCE on kidney cancer progression

[33] https://www.cancer.gov/types/kidney/patient/kidney-treatment-pdq#_50

through immunomodulatory mechanisms were exclusively restricted to metastasis, nor is there any experimental evidence supporting that it would be.

In addition, anti- versus pro-tumorigenic CD4+ helper T cell activities determine kidney cancer regression versus regression (Fig. 7). In the section that follows, which details what is known about TCE immunotoxicity from human and animal studies, I will show that the collective data provide a conceptual framework where TCE perturbation of various immune system components align more with anti-tumor effects than with pro-tumor effects.

Figure 7. CD4+ T cell Subtypes and Tumor Regression/Progression (Basu et al., 2021).



6.5 Immunotoxicity

Immunotoxicology is broadly defined as the study of the adverse effects of exposures to environmental, occupational, or therapeutic agents on the immune system. Conceptually, these adverse effects could either be due to immunosuppression or immune stimulation.

6.5.1 TCE Immunotoxicity

There is an extensive scientific literature concerning TCE and its posited effects on the immune system (Ordaz et al., 2017), but its potential effects on the immunobiology of kidney cancer has not been studies directly in humans. Much of the literature concerning the immunotoxicity of TCE comes from observations made with human subjects who were exposed to TCE in the workplace, usually at high levels, or from experimental studies with animals, usually mice, oftentimes dosed with high levels of TCE following which various immune endpoints have been measured.

6.5.1.1 *Human Studies*

Federal and international agencies have concluded that the immune system is a *potential* target of TCE toxicity, but there is no evidence for a mode of action, immune or otherwise, by which TCE causes kidney cancer by its effects on immune or inflammatory processes. The following sections provide a comprehensive discussion of studies that have explored the effects of TCE on the immune systems of humans and animals (mostly rodents). The findings from these studies are not generalizable, as plaintiffs' experts opine, to informing that TCE causes kidney cancer by affecting the immune system. The scientific literature does not support that TCE immunotoxicity has been linked to kidney cancer, and that claim has not been made in any peer-reviewed scientific studies.

The amassed scientific literature concerning TCE and the human immune system, including the studies listed by Dr. Gilbert in Table II of her report (all of which are addressed below), does not support the hypothesis that TCE causes kidney cancer through immune/inflammatory mechanisms. Dr. Gilbert simply listed 8 studies concerning effects of TCE exposure on immune parameters in human subjects (Gilbert Kidney Cancer Report, p. 21). She provided no analysis, discussion or critique of the individual papers or collective literature. Summarized in Table 1 below are my conclusions as to these human studies

Table 1: Human Studies Concerning TCE Immunotoxicity

Study	*My Conclusions*
1) Iavicoli et al., 2005	Given the observation that Th1 cytokines were increased in the TCE-exposed workers, these findings do not align with the premise that TCE causes kidney cancer through perturbations of the immune system. To the contrary, these results suggest that, rather than promoting tumor progression, exposure to TCE could foster a protective immune response by promoting the early infiltration into the tumor microenvironment of CD4+ helper T cells producing Th1-like cytokines.
2) Zhang et al., 2013	Based solely on their levels of serum immunoglobulins, which were the only immune data measured, the vast majority of the subjects in this study, irrespective of their TCE exposure, were immunocompetent—not immunodeficient or immunosuppressed. Moreover, studies have shown that changes in serum IgG levels in kidney cancer patients during treatment can be a potential indicator of treatment response and prognosis, with a decrease in IgG often correlating with better treatment outcomes in metastatic kidney cancer patients (Cui et al., 2024; 2025). Thus, the Zhang study falls far short of supporting the conclusion that TCE causes human kidney cancer by affecting immunological mechanisms.
3) Lee et al., 2019	Given these complexities, the findings of the Lee study concerning the modest decrease in the CD4+ effector memory cell compartment in TCE-exposed subjects compared to controls, which also was not found to be dose-dependent, is not generalizable to immune control of kidney cancer, and does not stand as evidence

	supporting that posited, but unverified, effects of TCE on TEM cells are mechanistically tied to kidney cancer causation. More pointedly, there were no known reports of kidney cancer arising in any of the low TCE-exposed subjects in this study.
4) Lan et al., 2010	These findings do not support a conceptual framework that alterations of the immune system due to TCE exposure cause kidney cancer by affecting immunological mechanisms.
5) Hosgood et al., 2012	No comments were made by the authors that the findings support an association between TCE and kidney cancer. The authors stated that caution should be used when interpreting the study findings until confirmed in additional studies given the small sample size and the potential confounding from additional factors that could influence lymphocyte cell counts.
6) Bassig et al., 2016	The data in this study show that the vast majority of the subjects in this study across the exposure groups, ranging from control to low-TCE to high-TCE, fall within *normal* counts for circulating B cells as well as other lymphocyte subpopulations that were assessed. Thus, this study does not provide evidence that TCE is mechanistically tied to kidney cancer through immunosuppression.
7) Bassig et al., 2013	The finding that TCE-exposed workers have reduced serum IL-10 runs *counter* to the proposition that TCE causes kidney cancer through perturbation of the immune response.
8-10) Zhang et al., 2017; Jia et al., 2012; Xuequin et al., 2018	These three OMDLT studies show differing and, in the case of the Jia and Xuequin studies, opposite results. Therefore, they are not generalizable to support the leap in logic that inflammation in other contexts—such as kidney cancer—is caused by TCE exposure.
11) Kamijima et al., 2013	These findings detail how the immune system reacts specifically to latent herpes virus reactivation, which is not relevant to the immunobiology of kidney cancer.
12) Li et al., 2019	The findings from this study are not generalizable to the immunobiology of kidney cancer, and if they were to be taken so, they more aptly support the hypothesis that TCE exposure promotes kidney cancer regression through activation of Th1-mediated immunity.

1) Iavicoli et al., 2005.[34]

In this study of Guangdong, China factory workers, Iavicoli reported statistically significant differences in serum levels of certain cytokines between TCE-exposed factory workers and controls. The TCE-exposed subjects worked in the printing sector and had been exposed to TCE from degreasing processes at a mean workplace air concentration of 35 ± 14 mg/m3(6.3 ppm) for at least 3 years. Thus, inhalation of TCE (i.e., presence of TCE in the breathing zone) was the primary route of exposure to TCE for these subjects, although other routes (e.g., dermal) also could have occurred. The workers' exposures to TCE were

[34] Dr. Gilbert did not include Iavicoli et al., 2005 in her list of epidemiological studies of TCE and immunotoxicity.

confirmed by monitoring their urinary levels of trichloroacetic acid (TCA)—a metabolite of TCE. Comparisons were made between the serum levels of cytokines for the TCE-exposed workers and an "internal control group" (i.e., workers from the same factory who performed the same job functions but did not engage in degreasing processes and were not near sources of TCE within the factory) as well as an "external control group" (i.e., office workers from the same factory who were not exposed to any known occupational sources of TCE). Although immune function was not assessed in this study, the results showed that the levels of interleukin-2 (IL-2) and interferon-У (IFN-У), which are Th1-like cytokines, were significantly increased in the TCE-exposed workers compared to controls, while the levels of interleukin-4 (IL-4), which is a Th2-like cytokine, were significantly decreased in the TCE-exposed workers compared to controls. **Thus, given the observation that Th1 cytokines were increased in the TCE-exposed workers, these findings do not align with the premise that TCE causes kidney cancer through perturbations of the immune system. To the contrary, these results suggest that, rather than promoting tumor progression, exposure to TCE could foster a protective immune response by promoting the early infiltration into the tumor microenvironment of CD4+ helper T cells producing Th1-like cytokines.**

2) Zhang et al., 2013.

In another study of Guangdong, China factory workers exposed to TCE, Zhang (2013) observed statistically significant decreased levels of serum immunoglobulins (IgM and IgG, but not IgE) for TCE-exposed subjects relative to controls, who had not been exposed to any known source(s) of TCE. The study design consisted of high and low TCE exposure groups based on air monitoring results during the month prior to serum immunoglobulin assessment. The high exposure group was characterized as having TCE exposure exceeding 12 ppm (mean TCE 38.4 ± 44.6 ppm) in air, and the low exposure group was characterized as having TCE exposure below 12 ppm (mean TCE 5.2 ± 3.2 ppm) in air. A control population (i.e., "TCE-unexposed") comprised of subjects who did not have any known TCE exposure history was included in the study design. Workers exposed to TCE had a 17.5% decrease and a 38% decrease in the reported levels of IgG and IgM, respectively, relative to the levels measured in control, TCE-unexposed subjects. The magnitudes of the decreased values were similar in workers exposed to low and high levels of TCE, and the reduced levels of serum immunoglobulins did not correlate with decreased B cell counts that the study authors had previously reported for the same TCE-exposed workers (Lan et al., 2010). Like most of the descriptive cross-sectional studies that have compared immune endpoints between TCE-exposed and control subjects, this study lacked any functional assessment of immunocompetence. The study authors speculated that the lower levels of serum immunoglobulins found in the TCE-exposed subjects may be indicative of reduced immune capacity or greater susceptibility to infection, but they had no data to support this premise. Susceptibility to cancer was not mentioned, which, perhaps, is notable in view of the fact that

the study was published in the journal *Carcinogenesis*. In short, although this study appears to show statistically significant reduced levels of serum immunoglobulins in TCE-exposed subjects relative to controls, the demonstrable biological relevance of the finding is difficult to grasp. The normal levels of serum immunoglobulins in humans are quite variable with IgG ranging between 700 to 1600 mg/dL and IgM ranging between 40 to 230 mg/dL (Dati et al., 1996). Although the data in the Zhang study are presented as box and whisker plots and in different units (i.e., µg/mL instead of mg/dL—the norm for clinical lab reporting), the vast majority of the subjects in this study across the exposure groups, ranging from control to low-TCE to high-TCE, fall within normal serum IgG and IgM ranges. **As such, based solely on their levels of serum immunoglobulins, which were the only immune data measured, the vast majority of the subjects in this study, irrespective of their TCE exposure, were immunocompetent—not immunodeficient or immunosuppressed. Moreover, studies have shown that changes in serum IgG levels in kidney cancer patients during treatment can be a potential indicator of treatment response and prognosis, with a decrease in IgG often correlating with better treatment outcomes in metastatic kidney cancer patients (Cui et al., 2024; 2025). Thus, the Zhang study falls far short of supporting the conclusion that TCE causes human kidney cancer by affecting immunological mechanisms.**

3) Lee et al., 2019.

The Lee study also reported on effects of occupational TCE exposure on serum immunoglobulin levels based on the same worker populations assessed in Zhang (2013), but the study design changed slightly by defining the low TCE-exposed and high TCE-exposed populations as below 10 ppm and above 10 ppm, respectively, to align with international occupational TCE exposure standards—with 10 ppm purported to be a common regulatory standard. The data showed statistically significant decreased levels of serum IgG and IgM in the TCE-exposed workers relative to controls. For the control group the IgG level was 1,099 ± 297 mg/dL and the IgM level was 118 ± 82 mg/dL. For the low (i.e., < 10 ppm) TCE group the IgG level was 924 ± 166 mg/dL and the IgM level was 76 ± 34 mg/dL. Finally, for the high (i.e., > 10 ppm) TCE group the IgG level was 894 ± 215 mg/dL and the IgM level was 71 ± 37 mg/dL. Again, given accepted reference ranges for serum immunoglobulins (IgG = 700 to 1600 mg/dL, and IgM = 40 to 230 mg/dL), based on their reported serum IgG and IgM levels, irrespective of TCE exposure, the subjects in this study were immunocompetent (i.e., they had normally functioning immune systems)—not immunodeficient or immunosuppressed. There is no evidence that the TCE exposed subjects in this worker population demonstrated any indications of immune dysfunction ranging between functional immunosuppression (i.e., hypo-immunity) and chronic inflammation (i.e., hyper-immunity).

This study also showed a modest, but statistically significant, decreased number of what are known as CD4+ effector memory T cells (i.e., T_{EM} cells) between controls and

subjects in the low TCE exposure group. The effect was not dose dependent, in that, significantly lower T_{EM} cells were found only in the low TCE exposure group and not the high TCE exposure group. For the control group, the CD4+ T_{EM} count was 224.9 ± 92.9. For the low (i.e., < 10 ppm) TCE group the CD4+ T_{EM} count was 181.8 ± 56.7. Finally, for the high (i.e., > 10 ppm) TCE group the CD4+ T_{EM} count was 184 ± 86.1. The study authors speculated that a decrease in the number of CD4+ effector memory cells could lead to a decreased capacity of the body to respond to antigenic-related inflammation, but they had no data to support their premise. For example, TCE-exposed subjects were not demonstrated to have any immune-mediated disorders that tie to insufficient immune memory.[35]

It is improbable that the workers, both TCE-exposed and unexposed, in the Lee study had T_{EM} cells specific to kidney tumor antigens circulating in their blood. The collection of effector memory T cells that were quantified in each of these subjects represented various unknown antigenic specificities in various unknown states of clonal expansion. **Given these complexities, the findings of the Lee study concerning the modest decrease in the CD4+ effector memory cell compartment in TCE-exposed subjects compared to controls, which also was not found to be dose-dependent, is not generalizable to immune control of kidney cancer, and does not stand as evidence supporting that posited, but unverified, effects of TCE on T_{EM} cells are mechanistically tied to kidney cancer causation. More pointedly, there were no known reports of kidney cancer arising in any of the low TCE-exposed subjects in this study.**

4) Lan et al., 2010.

Using the same cross-sectional study design as described in the preceding papers, Lan conducted a study with the Guangdong, China factory workers aimed at assessing the effects of TCE exposure on peripheral blood cells including total T cells, CD4+ cells, CD8+ cells and NK cells. Modest, but statistically significant, decreases in the numbers of these cell populations were found in the high TCE-exposed (i.e., > 12 ppm) group relative to controls but not the low TCE-exposed (i.e., < 12 ppm) group. Although the data appear to show statistically significant lower cell counts for all lymphocyte subsets in the high TCE-exposed group relative to the control unexposed group, there was no functional immunosuppression assessed in this study. Irrespective of the statistical differences, no functional immunosuppression would be expected based on the findings because the data establish

[35] Circulating CD4+ effector memory cells are a subset of CD4+ helper T cells that have developed memory characteristics after encountering an antigen. Having developed memory characteristics, they are poised to rapidly respond to future challenges with the same antigen—given that specificity is a characteristic feature of adaptive immunity and immunological memory. Essentially, upon encounter with antigen in the bloodstream, circulating effector memory T cells activate and migrate to where they are needed and quickly take charge of the fight to ward off the specific antigenic threat imposed on the body.

that the vast majority of the subjects in this study across the exposure groups, ranging from control to low-TCE to high-TCE, fall within *normal* counts for each of the lymphocyte subpopulations tabulated.[36] The normal range (i.e., reference values) for total T cells in blood is 700 to 2508 per mm^3 (a mm^3 is a microliter or µl of blood, not a milliliter or ml as indicated by Dr. Gilbert in Table II of her report—the difference is three orders of magnitude or 1000-fold).[37] Thus, the Lan study data showed that the immune systems of TCE-exposed subjects are normal with respect to peripheral blood lymphocyte subset counts. The data support that the vast majority of the subjects in this study, irrespective of their TCE exposure, are immunocompetent (i.e., have lymphocyte subset counts within normal ranges)—not immunodeficient or immunosuppressed. **As such, these findings do not support a conceptual framework that alterations of the immune system due to TCE exposure cause kidney cancer by affecting immunological mechanisms.**

5) Hosgood et al., 2012.

In yet another study based on the Guangdong, China factory workers, Hosgood expanded the analysis to include assessment of the effects of TCE exposure on various T cell subsets such as CD4+ naïve and CD4+ memory T cells, CD8+ naïve and memory T cells, and regulatory T cells. Again, statistically significant modest decreases in cell counts for some of the T cell subsets were found for TCE-exposed workers in comparison to control unexposed subjects. However, no functional assessment of immunocompetence were performed to establish that the observed modest decreases in T cell subset numbers, all of which were within normal reference ranges, were immunomodulatory. The authors concluded that the results of this study provide support for the biologic plausibility that TCE is associated with the risk of NHL, which in my opinion is an overstatement. **No comments were made by the authors that the findings support an association between TCE and kidney cancer.**

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[36] Various sources provide information concerning reference values for normal lymphocyte counts in blood. The normal range for CD4+ T cells is 464 to 1721 per mm^3 of blood. The normal range for CD8+ T cells is 135 to 852 per mm^3 of blood. The normal range for B cells is 92 to 515 per mm^3 of blood. Finally, the normal range for NK cells is 82 to 594 per mm^3 of blood. (See for example Apoil et al., 2017 and Table 1 of Supplemental data from Lan et al., 2010). As shown, the normal range for cell counts for each subset are quite broad. Thus, the modest, albeit statistically significant, differences in the lymphocyte subset counts between unexposed controls and high TCE-exposed subjects reported in the Lan study are most likely functionally irrelevant and clinically meaningless.

[37] Although this may have been a simple mistake, the error suggests to me that Dr. Gilbert is not aware of normal reference ranges for lymphocyte subpopulations in peripheral blood, and, therefore, did not recognize that the subjects in this study, irrespective of their TCE exposure, had normal lymphocyte subset counts.

Finally, the authors stated that caution should be used when interpreting the study findings until confirmed in additional studies given the small sample size and the potential confounding from additional factors that could influence lymphocyte cell counts.

6) Bassig et al., 2016.[38]

These investigators expanded the analysis of the Guangdong, China factory workers to include analysis of TCE effects, and other solvents, on the B lymphocyte compartment. The occupational exposure assessments in these workers included TCE as well as benzene and formaldehyde, which was an interesting addition to the study design because the worker cohort appears to be the same as in other studies (i.e., Lan et al., 2010; Hosgood et al., 2012; Lee et al., 2019; Zhang et al., 2013) where only TCE exposure was mentioned. The results showed that workers exposed to TCE and benzene had modest statistically significant decreases in circulating B lymphocytes and decreased B cell activation marker expression; however, the study design did not evaluate if these changes in B cell numbers correlated with any deficits in humoral immune effector functions. **The data in this study show that the vast majority of the subjects in this study across the exposure groups, ranging from control to low-TCE to high-TCE, fall within *normal* counts for circulating B cells as well as other lymphocyte subpopulations that were assessed. Thus, this study does not provide evidence that TCE is mechanistically tied to kidney cancer through immunosuppression.**

7) Bassig et al., 2013.[39]

In another paper based on factory workers who used TCE for metal, optical lens, and circuit board cleaning, Bassig (2013) reported that, compared to unexposed controls, the serum levels of interleukin-10 (IL-10) was decreased by 70% in workers exposed to TCE. No significant differences in levels of IL-6 or TNF-α were observed for TCE-exposed workers compared to unexposed controls. The authors concluded that since IL-10 plays an important role in immunologic processes, particularly in mediating the Th1/Th2 balance (i.e., it counters the activities of pro-inflammatory cytokines), the finding of reduced serum IL-10 in workers exposed to TCE was evidence of its immunotoxicity. Whether this is the case, or not, in consideration of the contexture of the immunobiology of kidney cancer, it has been shown that high serum IL-10 correlates with poor prognosis for renal cell carcinoma (Kim et al., 2023). Thus, the finding that TCE-exposed workers have significantly lower levels of serum IL-

[38] Dr. Gilbert did not include Bassig et al., 2016 in her list of epidemiological studies of TCE and immunotoxicity.

[39] Dr. Gilbert did not include Bassig et al., 2013 in her list of epidemiological studies of TCE and immunotoxicity.

10 does not support the hypothesis that TCE causes kidney cancer by affecting immune responses or inflammatory processes. On the other hand, in advanced renal cell carcinoma characterized by extensive infiltration of tumor-associated macrophages (TAMS) of the M2 phenotype, the accumulation of M2 macrophages producing IL-10 could contribute to the immunosuppressive state of the RCC microenvironment (Mier, 2019). Thus, with respect to the etiologic role of IL-10 in kidney cancer, its location (i.e., systemic, as in serum, versus local, as in the tumor microenvironment), as well as the stage of disease progression (i.e., early versus advanced) are important considerations. Increased production of IL-10 within the tumor microenvironment induces M2 polarization of macrophages—an immunosuppressive macrophage phenotype that also promotes angiogenesis thereby fostering tumor progression (Yang et al., 2024; Joseph & Enting, 2019). **Thus, the finding that TCE-exposed workers have reduced serum IL-10 runs *counter* to the proposition that TCE causes kidney cancer through perturbation of the immune response.**

8-10) Zhang et al., 2017; Jia et al., 2012; Xuequin et al., 2018.[40]

The Zhang (2017) study involved a subset of workers exposed to TCE who developed a particular hypersensitivity dermatitis syndrome called occupational medicamentosa-like dermatitis (OMLDT). The disorder occurs in a small fraction of workers extensively exposed to TCE, mainly by inhalation, who develop generalized skin lesions (i.e., rashes), fever, hepatitis, leukocytosis and lymphadenopathy. It is a rare syndrome that occurs in subjects exposed occupationally to high levels of TCE by inhalation. Not surprisingly, given the etiological involvement of systemic inflammation, alterations in various pro-inflammatory cytokines have been described in OMLDT subjects. For example, Jia et al. (2012) showed that the systemic levels of interleukin-1β (IL-1β), interleukin-6 (IL-6), and TNF-α were significantly elevated in OMLDT subjects in comparison to control subjects who had not been exposed to TCE. But the Jia study also showed that workers who had been exposed to TCE, but did not have OMLDT, did not have elevated levels of pro-inflammatory cytokines. In another study by Xuequin, OMLDT patients were found to have elevated serum levels of IL-10 and increased T-Reg cell type specific transcription factor expression (i.e., *Fox*P3) relative to TCE-exposed workers who were not OMDLT patients or unexposed controls. Relative to unexposed controls, both TCE exposure groups (i.e., OMDLT patients and non-OMDLT subjects) had significantly decreased serum levels of IL-6 and TNF-α the opposite of what was described in Jia. **These three OMDLT studies show differing and, in the case of the Jia and Xuequin studies, opposite results. Therefore, they are not generalizable to**

[40] Dr. Gilbert did not include Zhang et al., 2017 or Xuequin et al., 2018 in her list of epidemiological studies of TCE and immunotoxicity.

support the leap in logic that inflammation in other contexts—such as kidney cancer—is caused by TCE exposure.

11) Kamijima et al., 2013.

The Kamijima study examined serum cytokine profiles in OMLDT subjects who had been hospitalized for clinical evaluation of exfoliative dermatitis (i.e., skin rash) caused by reactivation of latent herpes virus. The data were presented as frequencies of hospitalized TCE-exposed patients who had serum cytokine levels more than three standard deviations (3 SDs) above the mean values for healthy workers.[41] A major conclusion of this study was that the elevated levels of IL-10 and TNF-α correlated with higher viral DNA load and higher anti-herpes virus antibody titers, all of which were associated with exfoliative dermatitis type rash.[42] **These findings detail how the immune system reacts specifically to latent herpes virus reactivation, which is not relevant to the immunobiology of kidney cancer.**

12) Li et al., 2019.

In another study that examined immune endpoints in OMDLT patients in comparison to TCE exposure controls and unexposed worker controls, Li et al., 2019 reported increased numbers of activated CD4+ T cells coupled with increased expression of IL-2, IFN-У and TNF-α, and decreased IL-4 expression in the OMDLT patients. **The findings from this study are not generalizable to the immunobiology of kidney cancer, and if they were to be taken so, they more aptly support the hypothesis that TCE exposure promotes kidney cancer regression through activation of Th1-mediated immunity.**

6.5.1.2 Summary of Human Studies on TCE Immunotoxicity

As detailed in the preceding section, many studies involving human subjects have observed statistically significant but modest differences in components of immunity between TCE-exposed and control subjects. In most instances, the experimental designs of these studies were not particularly sophisticated, did not establish that TCE exposure caused functional immunosuppression or frank immunodeficiency, and were conducted with subjects who had experienced high occupational exposures to TCE. Studies that compared serum immunoglobulins (e.g., Zhang et al., 2013; Lee et al., 2019) and lymphocyte subset counts (e.g., Lee et al., 2019; Lan et al., 2010; Hosgood et al., 2012; Bassig et al., 2016) between TCE-exposed and control unexposed subjects showed that the majority of subjects, irrespective of

[41] The frequencies of patients with serum cytokines more than 3 SDs above the mean of healthy workers were reported as follows: 79% (TNF-α and IL-10), 57% (IL-6), 43% (IFN-У), and 25% (IL-5). The frequencies of healthy workers with serum cytokines more than 3 SDs above the mean were as follows: 0% (IL-5 and IFN-У), 2% (IL-6 and IL-10), and 4% (TNF-α).

[42] Dr. Gilbert only included the TNF-α data from Kamijima et al., 2013 in Table II of her report.

TCE exposure, had *normal* biomarkers of immunity. Studies that explored apparent changes in cytokine expression profiles, while not generalizable to the immunobiology of kidney cancer, show that TCE exposure is immuno-protective against kidney cancer through the activities of anti-tumor CD4+ T cells. **As such, the amassed scientific literature concerning TCE and the human immune system supports neither the hypothesis nor the conclusion that TCE can cause kidney cancer through perturbations of the immune response or inflammatory processes.**

6.5.1.3 Animal Studies

The utility of animal studies is that they allow for the testing of hypotheses through experiments that are not possible, or ethical, with humans. Oftentimes, there is more control over experimental variables with animal studies. Most importantly, mice can be genetically modified in order to isolate and study the role that individual genes or gene clusters play in regulating the immune response. There are many similarities in the immune system components in mice and humans, although there also are some important differences.

Animal studies support that TCE may cause or exacerbate certain systemic autoimmune diseases (Cooper et al., 2009; Gilbert 2014).[43] However, the value of studying TCE in autoimmune prone mice lies less with environmental relevance, but more with having an inducible animal model of systemic autoimmunity where the mechanistic features attributable to autoimmune disease etiology can be studied (i.e., to study the causes of autoimmune disease). Plaintiffs' expert, Dr. Gilbert, has made many important contributions to the literature in this area. Notably, none of Dr. Gilbert's publications state that the immunotoxicity of TCE, in the contexture of systemic autoimmune disease, is applicable to any cancer—including kidney cancer. This holds true even for a chapter that she co-authored on TCE and kidney cancer where nary a word was mentioned concerning immune or inflammatory mechanisms of action being involved (Wartenberg & Gilbert, 2014). Like most chronic diseases, the etiology of autoimmune diseases is complex and multifactorial. Cancers, including kidney cancer, also are complex multifactorial chronic diseases. Although there may be some overlap between the intrinsic and extrinsic factors etiologically involved in autoimmune diseases and cancers, there are as many differences—likely more—as there are similarities.[44] The mice used in these experimental studies had genetic backgrounds that

[43] Autoimmune diseases are diseases where the immune recognition event is directed toward self-antigens or the immune effector responses involve unregulated and unchecked chronic inflammation (i.e., diseases in which the body's immune system attacks itself).

[44] There are hundreds of different autoimmune diseases, which are similar enough that they can be classified as such, but they have distinct pathologies and different intrinsic and extrinsic factors involved in their etiologies. The immunotoxicology literature does not implicate TCE causatively in all autoimmune diseases—interpreting it as being so would require a leap in logic that ignores the complexity and multifactorial basis of each disease and their differences.

made them autoimmune disease prone and, often were exposed to doses of TCE aimed to provoke alterations of immunity consistent with autoimmune disease pathogenesis. The genetic backgrounds that make these mice autoimmune disease prone are not known to also make them prone to kidney cancer. Therefore, generalizations cannot be made about the effects of TCE on these mice that are relevant to kidney cancer.

Several studies have shown that exposure to TCE in the drinking water of autoimmune disease-prone mice caused the expansion of effector/memory CD4+ T cells with an interferon-γ secreting pro-inflammatory Th1-like phenotype coupled with decreased IL-10 secreting T-Reg cells (Choudhury et al., 2024; Banerjee et al., 2020; Griffin et al., 2000; Liu et al., 2022; Li et al., 2018). Applying these findings to the contexture of the immunobiology of kidney cancer, the expectation is that, by virtue of stimulating Th1-mediated immunity at the early stage of carcinogenesis or inhibiting T-Reg activities later during carcinogenesis, TCE could have a *protective effect* rather than an effect that promotes disease progression. The effects of TCE on the Th1/Th2/Th17/T-Reg paradigm align causatively with autoimmune disease more so than they do with cancer. **The results of experiments showing effects of TCE on CD4+ T cell subsets in autoimmune prone mice do not support a conceptual framework that similar effects lead to kidney cancer in humans. No experiments have been done to address the effects of TCE on the myriad CD4+ helper T cell subsets that influence kidney cancer regression versus progression.**

It has been shown in a particular autoimmune prone strain of mice called MRL +/+, that exposure to TCE via the drinking water alters the production of the cytokine IFN-γ through epigenetic mechanisms (Gilbert et al., 2012; 2016a; 2016b). The posited relevance of this TCE effect found in autoimmune prone mice to the contexture of human kidney cancer is questionable, particularly because IFN-γ plays a complex role in the tumor microenvironment by having pro- and anti-tumor effects that can influence tumor progression or regression, respectively (Jorgovanovic et al., 2020). Dr. Gilbert acknowledges that IFN-γ is pleiotropic (i.e., a single gene mutation influences multiple traits),[45] but then seemingly ignores the significance of this by concluding that TCE effects on IFN-γ found in autoimmune prone mice are generalizable in informing a mechanism of TCE-induced kidney cancer.[46] **In the absence of direct experimentation showing that TCE modulation of IFN-γ is operant mechanistically in kidney tumor progression, this generalization cannot possibly be made given the complex pro- and anti-tumor effects of IFN-γ. There are no studies that show that TCE causes epigenetic changes in the contexture of kidney cancer.**

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[45] Gilbert Kidney Cancer Report, p. 22.

[46] Gilbert Kidney Cancer Report at p. 27, Figure 2.

The older animal literature, which entailed classic immunotoxicity testing, showed effects of high dose administration of TCE on various immune endpoints. For example, Wright et al. (1991) examined the effects of intraperitoneal injection of Sprague-Dawley rats and B6C3F1 mice, at 0, 0.05, 0.5, 5.0 and 10.0 mmol/kg per day for 5 days, on splenocyte counts, B cell and T cell mitogenic responses, and hepatic and splenic NK cell activities. The data showed that NK cell cytotoxicity was significantly decreased in rats and mice injected with TCE, and the response was dose dependent. The authors concluded that the data suggested the possibility that the decreased natural (i.e., innate immunity) cytotoxicity response could explain how TCE caused liver tumors in rodents. **These effects of TCE on NK cell activity have not been repeated in humans exposed to environmentally or occupationally relevant concentrations of TCE.**

Two other peer-reviewed studies reported on TCE exposure and NK activity in mice. Peden-Adams et al. (2006) exposed B6C3F1 mice to 0, 1400 or 14000 ppb TCE in drinking water for 3 or 8 weeks from gestation day zero. No effects of TCE on NK activity were observed. Keil et al. (2009) used a similar exposure design (i.e., 0, 1400 or 14000 ppb TCE in drinking water for 27 or 30 weeks), but compared the effects of TCE exposure on immune endpoints between normal (B6C3F1) and autoimmune prone (NZBWF1) mice. No effects of TCE on NK activity were observed in either mouse strain. The strain specificity of TCE on immunity was also reported by Blossom et al. (2006), who showed that the ability of trichloroacetaldehyde hydrate (TCAH), a major oxidative metabolite of TCE, to increase the number of IFNγ-producing CD4+ lymphocytes required an autoimmune-prone genetic background. **These findings support that particular gene-environment interactions may drive TCE-induced *autoimmune disease* in mice but are not readily applicable to predicting how TCE might affect the immunobiology of human kidney cancer.**

The immunotoxicity of TCE was further assessed by Boverhof et al. (2013) in Sprague-Dawley rats after inhalation exposure through evaluation of the antibody response to sheep red blood cells, which is a common assay employed in immunotoxicity testing. In this study, rats were exposed to TCE at 0, 100, 300 or 1000 ppm for 6 hours per day for 20 days The highest dose (i.e., 1000 ppm) was selected to produce moderate liver and kidney toxicity. Relative to unexposed control animals, a significant (i.e., 70%) decrease in the antibody forming cell response was observed only in the high TCE-exposed group. **These results indicate that TCE was immunosuppressive in rats but only at very high levels of exposure.**

Sanders et al. (1982) examined the effects of TCE exposure on immunity in an outbred strain of mice. CD-1 male and female mice were exposed to TCE via the drinking water at 0.1,

1.0, 2.5, and 5 mg/mL for 4 to 6 months[47]. The immune parameters assessed were humoral immunity, cell-mediated immunity, lymphocyte responsiveness, bone marrow function and macrophage function. The results showed that the immune responses of female mice were more affected than the immune responses of males. Cell-mediated immunity and bone marrow stem cell colonization were inhibited at all doses of TCE; whereas, humoral immunity was only suppressed at the highest doses.

Thus, the immune suppression caused by TCE in this study was gender specific in mice and only occurred at high levels of exposure, the relevance of which to human exposures is highly questionable.

6.5.1.4 Summary of Animal Studies on TCE Immunotoxicity

Potential effects of TCE, or any of the other Camp Lejeune VOCs, on the progression of kidney cancer via immune or inflammatory mechanisms has not been studied in any animal models of kidney cancer. The immunotoxicity of TCE, has been explored in rodents under experimental paradigms that support TCE exposure producing both immunosuppressive and immunopotentiating (i.e., immune enhancing) effects. Experimental findings concerning TCE effects on certain immune endpoints in autoimmune disease prone mice are not generalizable for informing how TCE may, or may not, affect immune mechanisms within the tumor microenvironment of humans who have kidney cancer. Autoimmune disease is not kidney cancer. The accompanying genetic predispositions in autoimmune prone mice exacerbated by TCE are not the same, or sufficiently similar, to the genetic factors linked to human kidney cancer. Moreover, much of the literature concerning effects of TCE on immune responses or inflammatory processes were based on high TCE exposures the environmental relevance of which to humans, in general, and human kidney cancer, specifically, is questionable. Several murine models of kidney cancer have been developed to help elucidate the pathogenic mechanisms involved in disease progression as well as to develop new therapeutic agents (John & Said, 2017; Park et al., 2021; Zhang et al., 2015; Fantini et al., 2018; Desponds et al., 2024). No experiments have been performed with any mouse models of kidney cancer to determine the effects of TCE, PCE or benzene exposure, alone, or in combination, on disease progression or regression.[48]

6.5.2 PCE Immunotoxicity

There are very few studies concerning the immunotoxic effects of PCE in humans, and those that have been conducted do not provide a coherent understanding of potential

[47] 5 mg/ml = 5 million parts per billion (ppb); 0.1 mg/mL = 100,000 ppb

[48] Dr. Gilbert acknowledged that mouse models, since they recapitulate human systems very well, are often used to estimate the effects of toxicants on human health. Gilbert Kidney Cancer Report, p. 9.

immunotoxic effects of the role, if any, that PCE perturbation of the immune system may play in any human disease—including kidney cancer.

In a study of Egyptian dry-cleaning workers exposed to ≤140 ppm PCE for 8 hours/day for 6.45 ± 3.62 years, Emara et al. (2010) reported statistically significant increased cell counts for total white blood cell, total lymphocytes, NK cells, CD4+ T cells, and CD8+ T cells in the PCE-exposed workers in comparison to control unexposed workers. There was no reported significant difference between the two groups in cell counts for neutrophils, eosinophils, total T cells, and B cells. Serum levels of IgG, IgM, IgA were unaffected by PCE exposure, but IgE was significantly increased in the PCE-exposed group. The PCE-exposed workers also had modest increased levels of serum and cellular interleukin-4. The authors speculated that the increased IgE and IL-4 in PCE-exposed workers could potentially contribute to allergic reactions of unknown etiology.

In another group of dry cleaning workers exposed to PCE on average for 1.5 years (blood PCE concentration = 561 ± 75 ng/mL) compared to unexposed workers (blood PCE concentration = 1.3 ±0.5 ng/mL), Li et al. (2024) reported significant increases in plasma concentrations of IL-1β and TNF-α, significant decreases in IL-2 and IL-8, and no effect on IFN-У, IL-4 or IL-6 in the PCE-exposed workers. The changes in plasma cytokine levels were accompanied by increased levels of anti-oxidant enzymes (i.e., superoxide dismutase-SOD, catalase-CAT, and malondialdehyde-MDA). The authors of this study concluded that plasma cytokines may be sensitive to PCE exposure.

Another investigation of immunological parameters was performed in a group of dry-cleaning workers exposed to PCE (Andrys et al., 1997). External exposure to PCE was reported as (8h)TWA[49] values in the range 11 – 752 mg/m^3. End of shift biological monitoring showed PCE in exhaled breath in the range 9 – 344 mg/m^3. In comparison to an unexposed control group, the PCE-exposed dry-cleaning workers had statistically significant increases in metabolic activity of phagocytes, serum α2-macroglobulin, C3 and C4 components of complement, secretory IgA (sIgA), and blast transformation responsiveness to T/B cell mitogen. Despite these statistically significant changes in various markers of innate and adaptive immunity, the authors acknowledged that the results, irrespective of PCE exposure, were within long-term laboratory reference values indicating that the data could be explained by normal individual variation in immune reactivity.

[49] An 8-hour time-weighted average (TWA) – the average exposure to a potentially harmful substance over an 8-hour work shift.

In a study examining maternal exposure to 28 different indoor VOCs including TCE and PCE, Lehmann et al. (2002) reported statistically significant decreased percentages of T cells producing several cytokines (i.e., IL-2, IL-4,TNF-α, and IFN-У) in the umbilical cord blood of newborns from homes with higher levels of PCE (> 7.3 µg/m^3, the 75th percentile concentration) compared with subjects from homes with lower levels of PCE, but not necessarily indeterminant levels of other VOCs. For homes with higher levels of TCE (> 1.0 µg/m^3, the 75th percentile concentration), but not necessarily indeterminant levels of other VOCs, only the percentages of cord blood-derived T cells producing IL-2 were decreased in comparison to results from subjects from homes with lower levels of TCE, but not necessarily indeterminant levels of other VOCs. The authors correlated their findings on VOC exposures producing decreased T cell IFN-У production with family history of atopy—the predisposition to produce IgE and develop allergic reactions or asthma. The findings from this study have numerous limitations including potential confounding by co-exposure to multiple VOCs and failure to account for changes in indoor VOC concentrations over time.

As mentioned above, the available data on the immunotoxicity of PCE in humans do not provide a coherent picture concerning potential effects of PCE exposure on health outcomes being attributable to immunomodulatory mechanisms. Moreover, the studies discussed above that examined associations between PCE exposure and various cytokines show, for the most part, inconsistent outcomes (Table 2). Consistency and coherence are both Bradford Hill Criteria, neither of which are met in considering PCE immunotoxicity as being operant in any human disease—including kidney cancer.

Table 2. Summary of human studies reporting effects of PCE on cytokines.

	IL-1β	**IL-2**	**IL-4**	**IL-6**	**IL-8**	**IFN-У**	**TNF-α**
Emara et al., 2010	ND	ND	↑	ND	ND	ND	ND
Li et al., 2024	↑	↓	none	none	↓	none	↑
Lehmann et al., 2002	ND	↓	none	ND	ND	↓	↓
ND = not determined; none = no effect of PCE relative to control; ↑ = increase for PCE relative to control; ↓ = decrease for PCE relative to control							

Few studies on PCE immunotoxicity have been conducted in animals. Most of the rodent studies show minimal effects of PCE on immunological parameters even at high exposures. For example, no effects on the antibody forming cell response or phagocytic activity of alveolar macrophages were observed in Sprague Dawley rats exposed to PCE via inhalation at concentrations up to 1,000 ppm for 6 hours per day for 20 days (Boverhof et al., 2013).

In another study with Sprague Dawley rats and B6C3F1 mice exposed to PCE by intraperitoneal injection, despite the high dose exposure, no effects on splenic or hepatic NK

cell cytotoxicity or lymphocyte responses to B cell and T cell mitogens were observed (Schlichting et al., 1992).

Significant increases in susceptibility to respiratory streptococcus infection were observed in mice exposed to 50 ppm PCE for 3 hours (Aranyi et al., 1986). Of note, interpretation of this study is complicated by the fact that the controls for one of the treated groups of mice had a higher mortality rate than any other group in the study (ATSDR, 2019b).

Finally, two reports by Seo et al. (2008a; 2008b) showed that exposure of Wistar rats to PCE via drinking water (0.01 – 1.0 mg/L for 2 to 4 weeks) enhanced immune effector functions (e.g., mast cell histamine release, passive cutaneous anaphylaxis reaction, IL-4 expression) and increased activities of Th2-type CD4+ helper T cells. Similar experiments showed the same outcomes in mice exposed to PCE (Seo et al, 2012). These were studies that examined effects of PCE exposure on allergic responses. As such, the experimental designs and findings of these studies are not generalizable to informing anything of relevance concerning the immunobiology of kidney cancer. It cannot be concluded that any of the apparent immunomodulatory effects of PCE exposure in rodents are operant etiologically in human kidney cancer.

Therefore, both the animal and human studies discussed above do not support a plausible mechanistic pathway by which PCE could cause kidney cancer.

6.5.3 Benzene Immunotoxicity

Benzene is a known human hematotoxin (Goldstein, 1977). The highly reactive metabolites of benzene have long been known to affect hematopoiesis (i.e., the process by which blood cells are formed in the body. (Wang et al., 2012). The health effects of benzene have been studied extensively in humans and laboratory animals (ATSDR, 2024b). These studies establish that the primary target for benzene toxicity is the hematopoietic tissues. By disrupting hematopoiesis, benzene exposure can lead to decreased numbers of all lymphoid (e.g., B cells, T cells, etc.) and myeloid (e.g., neutrophils, monocytes, mast cells, etc.) cell lineages. By decreasing the numbers of these cells through the disruption of hematopoiesis, benzene can cause immunosuppression of both adaptive and innate immunity.[50] But the relevance of these studies to kidney cancer can only be speculated.

[50] Early experiments in mice showed that short-term (i.e., 6 days for 6 hours per day) inhalation exposures to benzene concentrations ranging between 10 to 300 ppm suppressed mitogenic responses of B and T lymphocytes (Rozen et al., 1984). Another study following a similar exposure paradigm showed that benzene inhalation reduced protective cell-mediated immune responses to sublethal challenge with the bacterium *Listeria monocytogenes* (Rosenthal & Snyder, 1985). Decreased splenic lymphocyte antibody

Effects of benzene on immune parameters have been studied in occupational cohorts. For example, in a study comprised of 250 benzene-exposed shoe workers, Lan et al., 2004 aimed at assessing benzene hematotoxicity at lower occupational exposure levels. The experimental design entailed stratifying the benzene workers into groups based on their exposure levels (i.e., <0.04 ppm, < 1 ppm, 1 to 10 ppm, and > 10 ppm), and then assessing cell counts in peripheral blood for CD4+ cells, CD8+ cells, B cells, and NK cells. Modest, but statistically significant, decreases in the numbers of these cell populations were found in some of the benzene-exposed workers relative to the control population (i.e., < 0.04 ppm benzene).

Although the data appear to show statistically significant lower cell counts for all lymphocyte subsets in benzene-exposed groups relative to the control group, there was no functional immunosuppression assessed in this study. Irrespective of the statistical differences, no functional immunosuppression would be expected based on the findings because the data establish that the vast majority of the subjects in this study across the exposure groups, ranging from control to the various benzene exposures, fall within *normal* counts for each of the lymphocyte subpopulations tabulated. Thus, contrary to the interpretation of the authors, the Lan (2004) study data show that the immune systems of these benzene-exposed subjects were normal with respect to peripheral blood lymphocyte subset counts. The data support that the vast majority of the subjects in this study, irrespective of their benzene exposure, are immunocompetent (i.e., have lymphocyte subset counts within normal ranges)—not immunodeficient or immunosuppressed. **As such, these findings do not support a conceptual framework that benzene causes immunosuppression as a mechanism contributing to the etiology of kidney cancer.**

Generally speaking, plaintiffs' experts take the position that exposures to benzene produce harmful toxic effects that can contribute to kidney cancer through vaguely described mechanisms. As discussed in Section 6.1, different metabolites are produced depending on the metabolic pathway, and those various metabolites are target-organ specific. This means that a chemical, such as benzene, that primarily affects the hematopoietic tissues, may have little or no effect on the kidney.

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production was observed in mice exposed by inhalation to benzene (50, 200 ppm - 6 hours/day for 7 days) (Aoyama, 1986). Inhalation exposure also was shown to inhibit cell mediated tumor surveillance (i.e., cytotoxic T cell function) in mice (Rosenthal & Snyder, 1987),

6.5.4 Vinyl Chloride Immunotoxicity[51]

The peer-reviewed scientific literature concerning potential effects of vinyl chloride on the immune system or inflammatory processes is not extensive. Therefore, the limited number of studies and adequacy of the data are not generalizable to the immunobiology of kidney cancer and cannot inform that vinyl chloride contributes causatively to kidney cancer through immunotoxic mechanisms.

Some workers exposed to high levels of vinyl chloride by inhalation develop a rare syndrome called "vinyl chloride disease," characterized by Raynaud's phenomenon (feelings of numbness and cold in fingers and toes), acro-osteolysis (dissolution of the bones of the terminal phalanges and sacroiliac joints) and scleroderma-like skin changes (tightness, thickening, hardening of the skin). Features of vinyl chloride disease include the presence of high levels of circulating immune complexes, elevated pro-inflammatory cytokines (i.e., TNF-α, IL-1β, IL-6 and IL-8), increased serum immunoglobulins (i.e., IgG, IgM, IgA), and increased activities of complement and acute phase reactive components (ATSDR, 2024). Vinyl chloride disease exhibits characteristics of an autoimmune disease, whereby reactive intermediates of VC metabolism may produce changes in self-proteins (i.e., neoantigens) that are recognized by the immune system thereby stimulating effector functions (e.g., pro-inflammatory cytokine release, complement activation) that mediate the pathological changes observed. The probable triggering events that lead to autoimmune vinyl chloride disease are not readily generalizable to kidney cancer initiation. No studies have reported the formation of unique tumor antigens in the kidneys of subjects exposed to vinyl chloride—or for any other VOCs.

The immunological effects of vinyl chloride exposure also were examined through animal studies in mice and rabbits (Sharma & Gehring, 1979; Sharma et al., 1980). These studies showed that lymphocyte responses to mitogens were increased for mice and rabbits exposed to VC via inhalation at 10, 1000, 1000 ppm for 6 hours per day, 5 days per week, for 2 to 4 weeks. Although vinyl chloride appeared to be immunostimulatory in these studies, it was shown not to affect antigen-specific responses (i.e., it was not generally immunotoxic). The authors speculated that the immunostimulatory effects of vinyl chloride seen in mice and rabbits were somehow consistent with the reported involvement of vinyl chloride in human immune complex disorders. This is an interpretive leap that is unfounded.

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[51] Dr. Gilbert's opinion concerning cumulative co-exposures to VOCs at or from Camp Lejeune did not include consideration that vinyl chloride immunotoxicity contributed to kidney cancer. Accordingly, her report did not include any analysis concerning vinyl chloride immunotoxicity. VC is mentioned briefly in the kidney cancer report. Gilbert Kidney Cancer Report, p. 33. Nevertheless, it is not analyzed in the report itself, nor are PCE and benzene.

Therefore, the animal and human studies do not show a plausible mechanistic pathway by which vinyl chloride could cause kidney cancer.

7.0 CRITIQUE OF PLAINTIFFS' EXPERT'S GENERAL CAUSATION OPINIONS

In order to render an opinion on whether immunological effects of TCE, PCE, benzene, and vinyl chloride can cause kidney cancer, a scientist must perform a critical assessment of all of the available and relevant human and scientific studies that may provide information relevant to the question. Plaintiff experts who have referenced immunological effects of these chemicals and linked them to kidney cancer have failed to do this. In some instances, they have not reviewed certain literature at all. In other instances, they have not critically assessed the literature cited in support of opinions, when a critical evaluation shows that it does not support their conclusions.

In her General Causation Report on TCE and Kidney Cancer, Dr. Gilbert proffered 5 opinions. I will address the opinions that immunotoxicity is implicated in kidney cancer.

In her Opinion 2, Dr. Gilbert opines that TCE causes immunotoxicity that can promote kidney cancer development. Dr. Gilbert suggests that TCE is immunotoxic thereby causing kidney cancer, since the immune system and inflammatory processes are important in kidney cancer. However, Dr. Gilbert failed to acknowledge that no national or international regulatory agencies have concluded that immunomodulation is operant as a mode of action for TCE-induced kidney cancer.[52] Moreover, Dr. Gilbert failed to acknowledge or consider that there are no on-point experimental studies in mouse or man published in the peer-reviewed scientific literature showing that TCE plays any role in kidney tumor progression or regression through immune mechanisms.

The basis of Dr. Gilbert's unique opinion that TCE induces immune dysfunction and chronic inflammation leading to kidney cancer is summarized in Figure 2 of her report.[53] The figure is entitled "Model of how TCE promotes kidney cancer." The content of this figure does not establish that TCE causes kidney cancer through mechanisms that involve immune dysfunction or chronic inflammation. In my view, the figure sets forth nothing more than a conceptual framework for hypotheses that could be tested. For example, there is no direct

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[52] Dr. Gilbert cites to the USEPA Risk Evaluation of Trichloroethylene (2020), wherein it states that "overall, immunotoxicity in the form of both autoimmunity and immunosuppression following TCE exposure are supported by the weight of evidence." Gilbert Kidney Cancer Report, p. 25. However, this document did not conclude that the weight of the evidence linked these mechanisms causatively to kidney cancer. USEPA. Risk Evaluation for Trichloroethylene (2020). National Center for Environmental Assessment, US Environmental Protection Agency, Washington, D.C., USA.

[53] Gilbert Kidney Cancer Report, p. 27.

evidence that TCE disrupts cancer immunoediting leading to kidney cancer by any of the posited immune dysfunctions depicted. The notion that immunosuppression disrupts cancer immunosurveillance, which again is only a hypothesis, is undermined by my analysis (Section 6.5) detailing that statistical associations (e.g., decreased lymphocyte counts and immunoglobulin levels) do not evidence functional immunosuppression in humans. If the hypothesis is undermined, then the conclusion is not valid.

Figure 2 of Dr. Gilbert's report also proposes the hypothesis that chronic inflammation, triggered by TCE causes kidney cancer. Inflammation is ubiquitous—it is caused by many extrinsic factors and intrinsic processes (Singh et al., 2019). As mentioned earlier in this report there is the notion of "good" inflammation, which is a component of immune protection, and there is "bad" inflammation, which has been implicated in the pathogenesis of nearly every chronic disease ranging from A to Z (e.g., from atherosclerosis to Zellweger syndrome). Given the ubiquity of inflammatory processes in many multifactorial complex diseases, including kidney cancer, assigning a causal inference to any particular intrinsic or extrinsic factor, including TCE as a pathogenic mechanism in any disease is highly speculative. Chronic inflammation is a characteristic of kidney cancer, especially advanced RCC, and it occurs *without* TCE exposure. This begs the question - how does Dr. Gilbert propose that chronic inflammation in kidney cancer differs between those who are TCE-exposed versus those who are not? In other words, how do inflammatory mechanisms hypothetically triggered by TCE benzene differ from "background" inflammation that is inherent to the disease? There are no experimental studies in the scientific literature that test these issues separately to answer these questions. There is no scientific basis (i.e., data) supporting that TCE tips the balance toward harmful inflammation. As such, the connection made by Dr. Gilbert between TCE-induced chronic inflammation and kidney cancer is superficially hypothetical. It is untested and unproven.

In her Opinion 3, Dr. Gilbert opines that TCE incudes oxidative stress which has been linked to kidney cancer. Dr. Gilbert notes that TCE can produce oxidative stress. Since oxidative stress appears to be important in kidney cancer etiology, Dr. Gilbert claims that oxidative stress induced by TCE is a mechanism whereby it causes kidney cancer. As explained in Section 6.4.3, the generation of reactive oxygen species (ROS) occurs extensively in normal cells, and the potential for damage is held in check by antioxidants that are important for maintaining homeostasis within the body. When the generation of ROS species exceeds antioxidant defenses, the resulting imbalance is called oxidative stress. Oxidative stress is a catch-all description for a multitude of redox reactions that can become imbalanced resulting in oxidative damage to various cellular constituents. Oxidative stress can be triggered by endogenous factors (e.g., free radicals generated as byproducts of oxygen metabolism) or by numerous exogenous factors (e.g., viruses). Oxidative stress is linked mechanistically to various outcomes including changes in gene expression, genotoxicity, cell cytotoxicity, and inflammation. Dr. Gilbert acknowledges that oxidative

stress can either be causal or secondary to inflammation, which is true. However, she failed to define if the oxidative stress purportedly caused by TCE was causal or secondary to inflammation, and she failed to explain how causal versus secondary oxidative stress attributable to TCE could be determined.

Dr. Gilbert fails to acknowledge the ubiquity of reactive oxygen species in normal cellular processes as well as in disease. As was the case with the basis of her opinion concerning inflammatory processes, Dr. Gilbert would be hard-pressed to separate out TCE-induced oxidative stress from "background" oxidative stress that is inherent to a chronic disease process like kidney cancer. Oxidative stress is ubiquitous as a pathogenic mechanism in many chronic diseases. As such, Dr. Gilbert's opinion that TCE-induced oxidative stress can cause kidney cancer is built on generalities. Her analysis does not inform that TCE exposure at levels found at Camp Lejeune causes more oxidative stress in TCE-exposed subjects or triggers more antioxidant defenses than occur in the absence of TCE exposure. Observations of a role for TCE-induced oxidative stress as a mechanism of disease in particular autoimmune prone mice (Khan & Wang, 2018; Wang et al., 2007) are not generalizable for informing that TCE-induced oxidative stress is operant as a mechanism in causing kidney cancer in humans.

In her Opinion 4, Dr. Gilbert opines that TCE levels at Camp Lejeune were hazardous to human health and are known to cause kidney cancer. Other experts have been tasked with addressing of Dr. Gilbert's fourth opinion (i.e., Drs. Goodman, Shields, etc.). However, I note the striking absence of any attempt by Dr. Gilbert to link her fourth opinion to her second and third opinions. That is to say, Dr. Gilbert failed to demonstrate that the mechanisms that she proposes cause kidney cancer occur at environmentally relevant exposures to TCE, PCE, benzene, and vinyl chloride specific to Camp Lejeune. As detailed in my analysis in section 6.5 of this report, some statistically significant, but functionally irrelevant, effects of TCE have been found in cross-sectional study designs in subjects exposed occupationally to high concentrations of TCE. Some animal studies show that immunomodulation—either immune suppression or immune stimulation—occurs in rodents typically dosed with very high concentrations of TCE. Collectively, these human and animal studies do not establish that TCE modulates the immune system at levels of exposure that are relevant to purported Camp Lejeune exposures. As such, they do not inform that the levels of exposure to TCE at Camp Lejeune caused kidney cancer by affecting the immune system or inflammatory processes.

In her Opinion 5, Dr. Gilbert opines that TCE-induced kidney cancer was augmented by cumulative co-exposure to the other VOCs. Other experts have been tasked with addressing of Dr. Gilbert's fifth opinion (i.e., Dr. John Lipscomb, etc.). I note, however, as was the case with Dr. Gilbert's fourth opinion, Dr. Gilbert's fifth opinion is not linked to her second and third opinions. That is, Dr. Gilbert failed to demonstrate that the postulated, but

unquantified, cumulative effects of co-exposure to TCE, PCE, benzene, and vinyl chloride caused kidney cancer through their additive effects on the immune system, inflammatory processes or oxidative stress. In fact, Dr. Gilbert's analysis is largely disputed by my own analysis concerning potential effects of PCE, benzene, and vinyl chloride individually on these mechanisms.

Finally, other Plaintiffs' experts (e.g., Drs. Bird, Hatten, Freeman, and Mallon), none of whom are immunologists, opined superficially that there is an intersection between Camp Lejeune VOCs, immunotoxicity, and kidney cancer etiology in their respective reports. Their analyses were not sufficiently detailed to reliably support the opinions they asserted. They fail to critically analyze the data and experimental studies concerning TCE, PCE, benzene, and vinyl chloride, with respect to their posited effects on the immune system and inflammatory responses. Their comments on the potential immunotoxicity of Camp Lejeune VOCs do little to advance Plaintiffs' arguments that altered immunity by these chemicals is involved in the etiology of kidney cancer.

8.0 Findings and Opinions

There is scientific literature concerning the immunotoxicity of TCE in animals and, to a lesser extent, humans. None of the animal studies or human observations concerning TCE and the immune system have been done or made within the contexture of any cancer—including kidney cancer. There is little doubt that the tumor microenvironment in kidney cancer can be shaped by immune and inflammatory processes, which under various circumstances can either have a positive effect (i.e., anti-tumor) or, conversely, an unfavorable outcome (i.e., tumor progression leading to clinical disease). In short, the intersection between the immune system and the etiology of kidney cancer is complex. This inherent complexity in the immunobiology of kidney cancer, with its associated variability, makes drawing any conclusions about potential immunotoxic contributions to kidney cancer causation in the absence of direct experimental proof fraught with problems requiring scientifically unmeritorious leaps in logic.

At best, the existing literature concerning TCE immunotoxicity provides a conceptual framework (i.e., background) for formulating a hypothesis that TCE causes kidney cancer through mechanisms that involve perturbations of the immune response or inflammatory processes. Intellectually honest scientists can debate whether such a hypothesis is sufficiently compelling enough to warrant experimental testing aimed at obtaining findings that support or refute the proposition that myriad effects of TCE on the immune system mechanistically cause kidney cancer. However, leapfrogging over the necessity to test by adopting the mere hypothesis itself as being conclusive belies the sanctity of the Scientific Method.

Based on the foregoing, my professional opinions, all of which I hold within the bounds of reasonable scientific certainty are as follows:

Opinion 1: My independent analysis demonstrates that relevant animal and human studies do not show that modulation of the immune system is a plausible mechanistic pathway by which TCE, PCE, benzene, and vinyl chloride cause kidney cancer.

Opinion 2: Plaintiffs' expert, Dr. Kathleen Gilbert, has opined that TCE causes immunotoxicity that can promote kidney cancer development. It is my opinion that Dr. Gilbert's novel opinion is without support and is merely a hypothesis that heretofore has not been adequately tested. The existing data and available scientific studies do not show that perturbations of the immune system or inflammatory processes by TCE, PCE, benzene, or vinyl chloride, alone, or in combination with one another, are operant mechanistically as causes of kidney cancer. Leapfrogging over the necessity to test a hypothesis, by adopting the mere hypothesis itself as being conclusive as Dr. Gilbert does, belies the purpose of engaging in the scientific method.

Opinion 3: Other plaintiffs' experts (e.g., Dr. Timothy M. Mallon, Dr. Benjamin Hatten, Dr. Michael D. Freeman and Dr. Steven B. Bird), none of whom are immunologists, opined superficially that there is an intersection between Camp Lejeune VOCs, immunotoxicity and kidney cancer etiology in their respective reports. Their analyses were not sufficiently detailed to reliably support the opinions asserted. They fail to critically analyze the data and experimental studies concerning TCE, PCE, benzene, and vinyl chloride, with respect to their positive effects on the immune system and inflammatory responses. Again, relevant studies show no effects on the immune system and inflammatory responses to support plaintiffs' experts' opinions that TCE, PCE, benzene, and vinyl chloride can cause kidney cancer.

I reserve the right to supplement the basis or modify these opinions should additional information be made available to me.

9.0 COMPENSATION

Currently, since April 2024, I am employed as a Principal Scientist by Intertox, Inc. I am a salaried employee and have no ownership interest in Intertox. As such, my compensation is not directly tied to time invoiced for my work on this case. The hourly rate for my work on the Camp Lejeune cases is $575.

10.0 EXHIBITS TO TESTIMONY

As exhibits to illustrate my testimony, I may use any or all documents referenced in Section 2.0 of this report, any or all documents and materials referenced at the end or footnoted in this report, and any and all material referenced in plaintiffs' expert reports.

10.1 Case-Specific Documents Reviewed

1. Plaintiffs' Master Complaint No. 7:23-CV-897
2. United States' Answer to the Master Complaint
3. Notice of Submission by the Plaintiff Leadership Group Regarding Disease Counts
4. Scheduling Order
5. Expert Report of Remy J.-C Hennet, December 9, 2024
6. Expert Report of Alexandros Spiliotopoulos, December 9, 2024
7. Expert Report of Jay L. Brigham, December 9, 2024
8. Expert Report of Jay L. Brigham, February 7, 2025
9. Expert Report of Ari Kelman, February 7, 2025
10. Expert Report of Peter G. Shields, February 7, 2025
11. Expert Report on Bladder Cancer of Julie E. Goodman, February 7, 2025
12. Expert Report on Kidney Cancer of Julie E. Goodman, February 7, 2025
13. Expert Report on Non-Hodgkin's Lymphoma of Julie E. Goodman, February 7, 2025
14. Expert Report on Leukemia of Julie E. Goodman, February 7, 2025.
15. Expert Report on Parkinson's Disease of Julie E. Goodman, February 7, 2025
16. Expert Report of John C. Lipscomb, February 7, 2025
17. Expert Report of Morris L. Maslia, October 25, 2024
18. Expert Report of Mustafa M. Aral, October 25, 2024
19. Expert Report of Norman L. Jones and R. Jeffery Davis, October 25, 2024
20. Rebuttal Expert Report of Leonard F. Konikow, January 14, 2025
21. Rebuttal Expert Report of Kyle Longley, January 14, 2025
22. Rebuttal Expert Report of David Sabatini, January 14, 2025
23. Rebuttal Expert Report of Norman L. Jones and R. Jeffery Davis, January 14, 2025
24. Rebuttal Expert Report of Morris L. Maslia, January 14, 2025
25. Expert Report on Kidney Cancer of Dr. Steven B. Bird, December 5, 2024.
26. Expert Report on Kidney Cancer of Dr. Michael D. Freeman, December 5, 2024.
27. Expert Report on Kidney Cancer of Dr. Kathleen M. Gilbert, December 5, 2024.
28. Expert Report on Kidney Cancer of Dr. Benjamin Hatten, December 5, 2024.
29. Expert Report on Kidney Cancer of Dr. Timothy Mallon, December 5, 2024.
30. Expert Report on Bladder Cancer of Dr. Steven B. Bird, December 5, 2024.
31. Expert Report on Bladder Cancer of Dr. Stephen H. Culp, December 5, 2024.
32. Expert Report on Bladder Cancer of Dr. Kathleen Gilbert, December 5, 2024.
33. Expert Report on Bladder Cancer of Dr. Benjamin Hatten, December 5, 2024.
34. Expert Report on Bladder Cancer of Dr. Laura Plunkett, December 5, 2024.
35. Expert Report on Leukemia and Non-Hodgkin Lymphoma of Dr. Steven B. Bird, December 5, 2024.
36. Expert Report on Leukemia and Non-Hodgkin Lymphoma of Dr. Dean W. Felsher, December 5, 2024.
37. Expert Report on Leukemia and Non-Hodgkin Lymphoma of Dr. Kathleen Gilbert, December 5, 2024
38. Expert Report on Leukemia of Dr. Lukasz P. Gondek, December 5, 2024
39. Expert Report on Leukemia of Dr. Timothy M. Mallon, December 5, 2024
40. Expert Report on Non-Hodgkin Lymphoma of Dr. Howard Hu, December 5, 2024

41. Expert Report on Parkinson's Disease of Dr. Steven B. Bird, December 5, 2024
42. Expert Report on Parkinson's Disease of Dr. Amelia K. Boehme, December 5, 2024
43. Expert Report on Parkinson's Disease of Dr. Jason Cannon, December 5, 2024
44. Expert Report on Parkinson's Disease of Dr. Lucio Costa, December 5, 2024
45. Expert Report on Parkinson's Disease of Dr. Briana DeMiranda, December 5, 2024
46. Expert Report on Parkinson's Disease of Dr. Michael Freeman, December 5, 2024
47. Expert Report on Parkinson's Disease of Dr. Gary Miller, December 5, 2024
48. Expert Report of Kyle Longley, December 5, 2024
49. Supplemental Report of Dr. Jason Cannon, January 10, 2025
50. Supplemental Report of Dr. Howard Hu, January 31, 2025
51. Bove, FJ. "Videotaped & videoconferenced deposition of Dr. Frank J. Bove [re: Camp Lejeune Water Litigation re: All cases]." Submitted to US District Court, Eastern District of North Carolina, Southern Division. Case No. 7:23-cv-00897, October 17, 18, 2024
52. Savitz, DA. "Videotaped & videoconferenced deposition of Dr. David A. Savitz [re: Camp Lejeune Water Litigation re: All cases]." Submitted to US District Court, Eastern District of North Carolina, Southern Division. Case No. 7:23-cv-00897, June 10, July 17, 2024
53. Maslia, M. "Videotaped & videoconferenced deposition of Morris Maslia [re: Camp Lejeune Water Litigation re: All cases]." Submitted to US District Court, Eastern District of North Carolina, Southern Division. Case No. 7:23-cv-00897, September 26, 2024
54. Martel, SNJ. "Videotaped & videoconferenced deposition of Susan N.J. Martel [re: Camp Lejeune Water Litigation re: All cases]." Submitted to US District Court, Eastern District of North Carolina, Southern Division. Case No. 7:23-cv-00897, September 26, 2024
55. Agency for Toxic Substances and Disease Registry (ATSDR). 2017a. "Public Health Assessment Camp Lejeune Drinking Water, U.S. Marine Corps Base Camp Lejeune, North Carolina." January 20, 2017.
56. Agency for Toxic Substances and Disease Registry (ATSDR). 2017b. "ATSDR Assessment of the Evidence for the Drinking Water Contaminants at Camp Lejeune and Specific Cancers and Other Diseases." January 13, 2017.
57. Agency for Toxic Substances and Disease Registry (ATSDR). 2007. "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: Chapter A." July 2007.
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11.0 LITERATURE RESOURCES REVIEWED, CONSIDERED AND RELIED UPON

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APPENDIX A: CV OF MICHAEL J. MCCABE, JR.

Michael J. McCabe, Jr., Ph.D.
Toxicologist/Immunologist

PROFESSIONAL EXPERIENCE

2024 – Intertox, Inc., Seattle, Washington - Harleysville*, Pennsylvania

- **Principal Scientist, Toxicology and Immunology Expert**
  National expert performing technical investigations, analyses, research, written reports and testimony aimed at supporting opinions directed toward the resolution (e.g., settlement or verdict) of litigation or insurance matters involving alcohol, cannabinoids, drugs of abuse or misuse, medical devices, vaccines, and environmental or occupational exposures to chemical (i.e., toxicants) or biological (i.e., pathogens) agents and their effects on human health, behavior and performance.

2017 – Temple University, Philadelphia, Pennsylvania

- **Department of Chemistry; College of Science and Technology**
  Adjunct Associate Professor, Lecturer Forensic Toxicology; Master's level graduate students

2019 – 2024 Exigent Group Limited, Cape Town, South Africa

2023 – 2024 Morae Global Corporation, Houston, Texas

- **Executive Director Exigent Forensic Consulting**
  Had operational and technical oversight of a team of scientists and professionals who functioned as testifying experts in various disciplines including toxicology & pharmacology, liquor liability, human factors, clinical psychology, premises safety, biomechanics, etc.

- **Toxicology and Immunology Expert**
  Provided technical investigations, analysis, reports, and testimony involving the application of fundamental principles of toxicology and environmental medicine toward the resolution of torts and other litigation involving exposures to drugs, chemicals, xenobiotics and other environmental agents and stressors affecting human health and/or performance. Case examples involved the following:

  - alcohol
  - dram shop
  - cannabinoids/marijuana
  - opioids
  - other drugs of abuse/misuse (e.g., benzodiazepines, cocaine)
  - carbon monoxide and other gases (e.g., hydrogen sulfide, chlorine, methane)
  - metals (e.g., lead, mercury, cobalt, zinc, nickel, arsenic, aluminum, etc.)
  - asbestos
  - pesticides and herbicides
  - solvents (e.g., BTEX, VOCs)
  - medical devices
  - vaccines
  - carcinogens
  - food poisoning
  - skin/eye irritants
  - allergens
  - adverse drug reactions

* Dr. McCabe works from an office located in the greater Philadelphia area.

2009 – 2019 **Robson Forensic, Inc., Lancaster and Philadelphia, Pennsylvania**

- **Toxicology and Immunology Expert, 2009 - 2019**

- **Director of Practice Groups, 2014 - 2019**
  Accountable for technical oversight of expert work within all RFI Practice Groups (~100 experts). Responsibilities included recruiting, training, mentoring and quality assurance (peer review).

- **Science Practice Group Leader, 2012 - 2015; 2019**
  Responsible for case assignment, technical oversight and peer review of expert work within scientific disciplines including toxicology, pharmacology, immunology, pharmacy, liquor liability, arboriculture, animal (equine) science, environmental health and safety, industrial hygiene, water quality, blood spatter, food safety and questioned documents.

2000 – 2017 **University of Rochester Medical Center, Rochester, New York**

- **Department of Environmental Medicine; School of Medicine and Dentistry**

  Adjunct Associate Professor 2009 - 2017
  Associate Professor 2003 - 2009
  Assistant Professor 2000 - 2003

- **Research, Teaching and Administrative duties as follows:**

  Research - function as a Principal Investigator responsible for operational and fiscal management and oversight of an NIH-funded scientific research program centered on mechanistic metal toxicology and immunotoxicology. Supervised technical and intellectual efforts of approximately 25 scientists (Ph.D., M.S., B.S. levels) working on lab-based and epidemiological research projects.

  Teaching - instructional responsibilities within and across university-wide medical and graduate curricula including lecturing (topics included metal toxicity, cell signaling, immunity, ethics), course development (e.g., Course Director, Target Organ Toxicology), and laboratory supervision and mentoring of postdoctoral, graduate (Ph.D. and M.S.) and undergraduate trainees.

  Administrative - committee service in various capacities within the Environmental Health Sciences Center *"Environmental Agents as Modulators of Human Disease and Dysfunction"* (e.g., Director Immunomodulators and Immunopathogenesis Research Core), Toxicology Training Program (e.g., Deputy Director Toxicology Training Program, Curriculum Committee Chairman, Thesis Committee member on > 20 Ph.D. and M.S. dissertations), and appointments to various committees within the School of Medicine and the College (e.g., University Flow Cytometry Oversight Committee, Task Force to establish an Undergraduate Public Health Major).

1992 – 2000 Wayne State University, Detroit, Michigan

- **Institute of Chemical Toxicology, Graduate School of Health Sciences**

  Assistant Professor 1997 - 2000
  Adjunct Assistant Professor, Department of Pharmaceutical Sciences 1994 - 2000
  Research Assistant Professor 1992 – 1997
  Established an extramurally-funded research program centered on mechanistic metal immunotoxicity. Responsible for teaching immunology and cellular biochemistry to graduate level students (Master's, Ph.D. and PharmD).

  Director, Imaging and Cytometry Facility Core, Environmental Health Sciences Center in Molecular and Cellular Toxicology with Human Applications 1997 - 2000
  Responsible for establishing and operating a state-of-the-art flow cytometry facility serving the needs of ~20 scientists engaged in molecular cell biology research projects requiring immunophenotyping, cell cycle analysis, apoptotic marker analysis, intracellular cytokine analysis, etc.

1990 – 1992 Karolinska Institute, Stockholm, Sweden

- **Institute of Environmental Medicine, Postdoctoral Research Associate**
  Training and research in mechanisms of toxicity, cell death, cell signaling, metal toxicology

1985 – 1990 Albany Medical Center Hospital, Albany, New York

- **Pathology and Laboratory Medicine, Medical Technician, Serology and Blood Bank**

EDUCATION

1991 Ph.D., Biomedical Studies (Microbiology and Immunology), Albany Medical College
1990 M.S., Biomedical Studies (Microbiology and Immunology), Albany Medical College
1984 B.S., Biology, Siena College, Loudonville, New York
1984 *In Vitro* Cell Biology and Biotechnology, State University of New York at Plattsburgh and the W.H. Miner Agricultural Research Center, Chazy, New York

Continuing Education and Certifications

- An Introduction to Clinical and Medical Toxicology; Society of Toxicology Continuing Education Course; Nashville, TN, March 2023
- Certified as a Diplomate of the American Board of Toxicology; 2012 - 2021
- Fellow of the Academy of Toxicological Sciences (ATS); 2012 - 2018
- Ethics, Opioids and America's Drug Overdose Crisis; Society of Toxicology Webinar, December 2019
- TIPS Instructor Certification Training; TIPS/Health Communications, Inc., April 2018
- Ocular Toxicology. Pharmacology and Drug Delivery: An Eye to the Future. Society of Toxicology Contemporary Topics in Toxicology; San Francisco CA, June 2016

- New Horizons in Chemical Carcinogenesis: Advances in Mode of Action and Mechanism of Cancer Pathogenesis. Society of Toxicology Continuing Education Course; San Diego CA March 2015
- Toxicology and Regulatory Considerations for Combination Products. Society of Toxicology Continuing Education Course; San Diego CA, March 2015
- Advances in Safety Assessment of Medical Devices. Society of Toxicology Continuing Education Course; San Diego CA, March 2015
- 17th Annual Toxicology Teaching Day, Department of Emergency Medicine, Upstate Medical University/Upstate New York Poison Control Center; Syracuse NY, November 2013
- The Changing Faces of Antidotes. American College of Medical Toxicology; San Juan PR, March 2013
- Alcohol Abuse Academy: Current Perspectives on Impairment, Dependence and Withdrawal. American College of Medical Toxicology; San Juan PR, March 2013
- Basic Principles of Human Risk Assessment. Society of Toxicology Continuing Education Course; San Antonio TX, March 2013
- The REACH Regulation and Safety Assessment Approaches for Chemicals that Come in Contact with the Skin. Society of Toxicology Continuing Education Course; San Antonio TX, March 2013
- 16th Annual Toxicology Teaching Day, Department of Emergency Medicine, Upstate Medical University/Upstate New York Poison Control Center; Syracuse NY, November 2012
- Prescription Opioid Misuse Academy: The Dark Side of Prescription Opioids. American College of Medical Toxicology; San Diego CA, March 2012
- The Robert F. Borkenstein Course on The Effects of Drugs on Human Performance and Behavior. Indiana University: Center for Studies of Law in Action; Bloomington IN, April 2010
- The Robert F. Borkenstein Course on Alcohol and Highway Safety; Testing, Research and Litigation. Indiana University: Center for Studies of Law in Action; Bloomington IN, December 2009
- First Forensic Course: Ethanol and Marijuana. American College of Medical Toxicology; Baltimore MD, November 2009
- Servers and Managers Alcohol Responsibility Training (S.M.A.R.T.); Certified, 2009
- New Frontiers in Metal Toxicology; Genetic Susceptibility, Early Diagnosis, and Related Biological Indices. Society of Toxicology Continuing Education Course; Baltimore MD, March 2009
- Faculty Development Medical Education Leadership Series. University of Rochester School of Medicine and Dentistry; Rochester NY, 2007 - 2008
- Essentials of Metal Toxicology. Society of Toxicology Continuing Education Course; San Diego CA, March 2006
- Radiation and Radioisotope Safety Training. University of Rochester Medical Center Radiation Safety Unit; August 2000
- Certified Key Operator, Becton Dickinson Immunocytometry Systems FACSCalibur Cell Analyzer and Sorter, Training Course; Mansfield MA, December 1997

PROFESSIONAL MEMBERSHIPS

- Society of Toxicology, 1989 - present
- American Chemical Society, 2012
- American Association of Immunologists, 2003 - 2008

HONORS AND AWARDS

- Best Paper of the Year Award, Society of Toxicology, Immunotoxicology Specialty Section, 2009
- Outstanding Young Investigator Award, Society of Toxicology, Immunotoxicology Specialty Section, 2000
- Who's Who among Students at American Colleges & Universities, 1990
- Dean's Award for Excellence in Research, Albany Medical College, 1990
- Dean's Award for Excellence in Research, Albany Medical College, 1989
- Graduate Student Award for Excellence in Research, Society of Toxicology, Metals Specialty Section, 1989

EDITORIAL ASSIGNMENTS

- Associate Editor, Toxicology and Applied Pharmacology, 2001 - 2013
- Editorial Board Member, Toxicology and Applied Pharmacology, 1999 - 2001
- Editorial Board Member, Toxicological Sciences, 2008 - 2015
- Editorial Board Member, Toxicology Letters, 2009 - 2013
- Editorial Board Member, Journal of Immunotoxicology, 2003 - 2013

Peer-reviewer for the following journals (selected list):

Environmental Health Perspectives
Toxicology
Journal of Immunology
Carcinogenesis
Critical Reviews in Toxicology
Chemical Research in Toxicology
Journal of Inorganic Biochemistry
Nutrition and Cancer
Cell Proliferation
Apoptosis
Cellular Microbiology
Journal of Pharmacy and Pharmacology
Journal of Biochemical and Molecular Toxicology
Journal of Applied Toxicology

INTERNATIONAL/NATIONAL ADVISORY HEALTH COUNCILS AND RESEARCH AND REGULATORY REVIEW COMMITTEES

- ENVIRON International Corp., Environmental Exposures to Nickel and its Relationship to Disease: Respiratory Disease, Asthma and Cardiovascular Toxicity, Panelist, Arlington, VA, October 2012
- Department of Defense, U.S. Army Medical Research and Materiel Command, Congressionally Directed Medical Research Programs, Gulf War Illness Research Peer-Review Panel Chairman, October 2011
- National Institutes of Environmental Health Sciences, Division of Extramural Research and Training, Superfund Basic Research and Training Program Review Panel, 2011
- National Institute of Environmental Health Sciences, Expert Panel Workshop to Examine the Role of Environment in the Development of Autoimmune Disease, Expert Panelist and White Paper Co-Author, 2010
- U.S. Environmental Protection Agency - Workshop on Policy-Relevant Science to Inform and Plan for Review of the National Ambient Air Quality Standards for Lead, Expert Panelist, 2010
- World Health Organization/International Programme of Chemical Safety, Harmonization Project – Guidance Document for Risk Assessment of Mercury Immunotoxicity, 2009 - 2010
- Congressionally-Directed Medical Research Program (Department of Defense), Peer-Reviewed Medical Research Program Panel, (Gulf War Injury Proposals), 2000 - 2010, 2012, 2013
- National Research Council of the National Academies of Science, Committee on Beryllium Alloy Exposures, Managing Health Effects of Beryllium Exposure, The National Academy Press, 2007 - 2008
- National Institutes of Environmental Health Sciences, Division of Extramural Research and Training, Special Emphasis Review Panel, Interdisciplinary Partnerships in Environmental Health Sciences, 2006
- Center for Scientific Review, NIH Division of Research Grants, Skeletal Biology Structure and Regeneration Study Section, *Ad hoc* member, 2006
- Center for Scientific Review, NIH Division of Research Grants, Hypersensitivity, Autoimmune and Immune-mediated Disease Review Panel, *Ad hoc* member, 2006
- National Institute of Dental and Craniofacial Research, Special Emphasis Review Panel, Sjogren's Syndrome, 2006
- Environmental Protection Agency, External Reviewer, Air Quality Criterion for Lead, 2005
- Center for Scientific Review, NIH Division of Research Grants, Integrative and Clinical Endocrinology and Reproduction Study Section, *Ad hoc* Member, 2005
- Center for Scientific Review, NIH Division of Research Grants, ZRG1 MOSS Musculoskeletal R01 and Small Business Review Panel, 2005
- National Institutes of Environmental Health Sciences, Division of Extramural Research and Training, Special Emphasis Review Panel, Centers of Biomedical Research Excellence (COBRE), 2005
- National Workshop Research Asthma Disparities, 2005
- National Institutes of Environmental Health Sciences, Division of Extramural Research and Training, Superfund Basic Research and Training Program Review Panel, 2004-2005

- ALTX-4 (2) Special Emphasis Panel, Small Business Incentive Research Applications, 1999-2004
- Center for Scientific Review, NIH Division of Research Grants, Alcohol and Toxicology (ALTX-4) Study Section, *Ad hoc* Member, 1999 - 2003
- ALTX-4 (2) Special Emphasis Panel, Postdoctoral Fellowships, 2001
- ALTX-4 (2) Special Emphasis Panel, Minority Pre-doctoral Fellowships, 1999
- National Institutes of Environmental Health Sciences Special Review Panel, Biological Effects of Power Frequency Electromagnetic Fields (EMF), 1996

PROFESSIONAL SERVICE ASSIGNMENTS

National

- Society of Toxicology Ethics, Legal, Forensic and Societal Issues Specialty Section (2022 – present); Vice President (2022); President (2023/2024); Past-President (2024/2025)
- Society of Toxicology, Education Career Development Committee; Committee member, 2019 - 2021
- Society of Toxicology, Career Resources and Development Committee; Committee member, 2018 - 2019
- Society of Toxicology Metals Specialty Section; Councilor (2001 - 2004); Vice President-elect (2004); Vice President (2005); President (2006); Past-President (2007)
- Society of Toxicology Immunotoxicology Specialty Section; Program Committee (1999 - 2001), Executive Committee (1999 - 2000), Awards Committee (1999), Membership Committee Chairman (1997 - 2000); Councilor (2004 - 2006)

University

- Deputy Director, Toxicology Training Program, University of Rochester, 2004 - 2008
- Chairman, Curriculum Committee, Toxicology Training Program, U. Rochester, 2006 - 2008
- Director, Immunomodulators and Immunopathogenesis Research Core, Environmental Health Sciences Center, University of Rochester, 2003 - 2008
- Member, Flow Cytometry Oversight Committee, University of Rochester, 2003 - 2009
- Fenn Award Committee (review/select best Ph.D. thesis), University of Rochester, 2006 - 2008
- Member, Admissions Committee, Toxicology Training Program, U. Rochester, 2001 - 2008
- Member, Policy Committee, Toxicology Training Program, U. Rochester, 2001 - 2008
- *Ad hoc* Member, Task Force on Public Health Undergraduate Major for the College, 2007
- Facilitator, Ethics and Professional Integrity Core Course, 2004 - 2008
- Member, Toxicology Training Program Retreat Committee, 2002 - 2007
- Coordinator, Environmental Health Sciences Center Seminar Series, 2000 – 2007

INVITED PRESENTATIONS (Does not include CLE presentations)

- Over 25 invited seminars at universities and government agencies across the country including (2019) Wayne State University; (2018) Wright State University; (2009) St. John's University; U.S. Food and Drug Administration; (2008) Texas A&M University, New York University; (2005) West Virginia University; (2004) Karolinska Institute, University of Louisville, (2000) Boston University, University of Connecticut; (1999) New York University; (1998) Pennsylvania State University, University of Texas at Austin, Medical College of Virginia, Rutgers University

- Society of Toxicology Annual Meeting – Workshop Session, Complex Interpretations of Substance Detection and Impairment. Sins of Our Fathers: *Lessons Learned from the Evolution of Alcohol per se Limits to Driving Under the Influence of Drugs Policy*, Salt Lake City UT, March 2024.

- Society of Toxicology Annual Meeting – Ethics, Legal, Forensic and Society Issues Specialty Section, Inaugural Keynote Address, San Antonio TX, March 2018

- Society of Toxicology Annual Meeting – Informational Session, Lead: Children's Exposures and Current Regulatory Standards. *Current State of Lead Research and Children's Issues*, Baltimore MD, 2009

- Society of Toxicology Annual Meeting – Continuing Education Course, New Frontier in Metal Toxicology: Genetic Susceptibility, Early Diagnosis, and Related Biological Indices. *Cell Signal Pathways Targeted by Toxic Metals*, Baltimore MD, 2009

- Ohio Valley Society of Toxicology Annual Meeting – *Attenuation of Apoptosis by Heavy Metals: Signaling Pathways Involved and Potential Importance in Autoimmunity*, Lexington KY, 2004

- Society of Toxicology Annual Meeting – Symposium, Arsenic Disruption of Cell Cycle: Mechanisms and Effects on Apoptosis, Differentiation and Carcinogenesis. *Cell Cycle Dysregulation by Arsenite: Implications for Its Chemotherapeutic Actions*, Baltimore MD, 2004

- National Institute of Environmental Health Sciences, – Workshop, Environmental Factors in Autoimmune Disease. *Attenuation of Activation-Induced Cell Death: A Potential Mechanism Contributing to Mercury-Induced Autoimmunity*, Durham, NC, 2003

- Society of Toxicology Annual Meeting – Symposium, Molecular Mechanisms of Xenobiotic-Induced Autoimmunity, San Francisco CA, 2001

- Society of Toxicology Annual Meeting – Symposium, Metals and Disorders of Cell Accumulation: Modulation of Apoptosis and Cell Proliferation. *Mechanisms Contributing to Systemic Autoimmune Disease: Mercury-Induced Tyrosine Phosphorylation and Disruption of the CD95/Fas Apoptotic Death Pathway*, New Orleans LA, 1999

EXTRAMURAL GRANT FUNDING

- NIH ROI ES029484, Understanding the connection between exposure to mercury, auto immunity and tolerance in B cells, Consultant, 09/09/2018 - 08/31/2024
- NIH R21 ES024476, Understanding the Role of Mercury Exposures in Disrupting Central Tolerance in B cells, Consultant, 08/01/2014 - 07/31/2016
- NIH R21 ES021285, Understanding the Influence of n-3-Polyunsaturated Fatty Acids on Pro-inflammatory Aspects of Mercury, Consultant, 08/01/2012 - 07/31/2014
- NIH R21 ES019228, Analysis of B Cell Receptor Signals Modified by Mercury, Consultant, 07/15/2010 - 06/30/2012
- NIH R01 ES012403, Death Receptor Signaling and Mercury Immunotoxicity, Principal Investigator, 04/01/2003 - 03/31/2008
- NIH R01 ES11000, Disruption of Lymphocyte Signal Transduction by Mercury, Co-Principal Investigator, 12/01/2001 - 11/30/2007
- NIH R21 ES10351, Mechanisms Contributing to Mercury-Induced Autoimmunity, Principal Investigator, 10/01/1999 - 09/30/2003
- NIH R25 RR123711, Environmental Cyberschoolhouse, Co-Principal Investigator, 09/01/1998 - 08/31/2002
- NIH P30 ES06639-S, Shared Instrument Grant-Analytical Flow Cytometer System, Co-Principal Investigator, 09/01/1997 - 08/31/1998
- NIH R29 ES07365, Mechanisms and Consequences of Immunomodulation by Lead, Principal Investigator, 08/01/1996 - 07/31/2002
- NIH R01 ES04040, Cellular and Molecular Toxicity of Lead, Co-Investigator, 08/01/1995 - 07/30/1999
- NIH R01 CA49935, Immunomodulation and Chemically Induced Carcinogenesis, Co-Principal Investigator, 12/01/1994 - 11/30/1997

PEER-REVIEWED PUBLICATIONS

- Gill R., McCabe, Jr., M.J. and Rosenspire A.J. Low level exposure to inorganic mercury interferes with B cell receptor signaling in transitional type 1 B cells. *Toxicol. Appl. Pharmacol.* 330:22-29, 2017 PMID: 28668464.
- Gill R., Jen K.L., McCabe, Jr., M.J. and Rosenspire A.J. Dietary n-3 PUFAs augment caspase 8 activation in Staphylococcal aureus enterotoxin B stimulated T-cells. *Toxicol. Appl. Pharmacol.* 309:141-8, 2016 PMID: 27614254.
- Gill R., Lanni L., Jen K.L., McCabe, Jr., M.J. and Rosenspire A.J. Docosahexaenoic acid counteracts attenuation of CD95-induced cell death by inorganic mercury. *Toxicol. Appl. Pharmacol.* 282:61-7, 2015 PMID: 25461680.
- Gill R.F., McCabe Jr., M.J. and Rosenspire A.J. Elements of the B cell signalosome are differentially affected by mercury intoxication. *Autoimmun. Dis.* 2014:1-10, 2014 PMID: 239358.

- Songdej, N., Winters, P.C., McCabe, Jr., M.J., and van Wijngaarden E. A population-based assessment of blood lead levels in relation to inflammation. *Environ. Res.* 110:272-277, 2010. PMID: 20116055
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- McNeely, S.C., Belshoff, A.C., Taylor, B.F., Fan, T.M., McCabe, Jr., M.J., Pinhas, A.J. and States, J.C. Sensitivity to sodium arsenite depends upon susceptibility to arsenite-induced mitotic arrest. *Toxicol. Appl. Pharmacol.* 229:252-261, 2008.
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- McCabe, Jr., M.J., Laiosa, M.D., Li, L., Menard, S.L., Mattingly, R.R., and Rosenspire, A.J. Low and non-toxic inorganic mercury burdens attenuate BCR-mediated signal transduction. *Toxicol. Sci.* 99:512-521, 2007.
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- Waalkes, M. P., Fox, D. A., States, J. C., Patierno, S. R., and McCabe, Jr., M. J. Forum: Metals and Disorders of Cell Accumulation: Modulation of Apoptosis and Cell Proliferation. *Toxicol. Sci.* 56:255-261, 2000.
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BOOK CHAPTERS

- Lynes, M.A., Pietrosimone, K., Marusov, G., Donaldson, D.V. Tarracciano, C., Yin, X., Lawrence, D.A. and McCabe, Jr., M.J. Metal Influences on Immune Function. In, Cellular and Molecular Biology of Metals, J. Koropatnick and R. Zalups (eds), Taylor & Francis, pp. 379 – 414, 2010.

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- McCabe, Jr., M. J. and Lawrence, D. A. Aspects of Lead Potentiation of B Lymphocyte Responses and Their Relationship to Immune Dysregulation. In, Metal Ions in Biology and Medicine, P. Collery, L. A. Poirer, M. Manfait, and J. C. Etienne (eds), John Libbey Eurotext, Paris, pp. 271-276, 1990.
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LETTERS, EDITORIALS, SHORT ARTICLES AND OTHER CONTRIBUTIONS

- Waalkes, M. P., Fox, D. A., States, J. C., Patierno, S. R., and McCabe, Jr., M. J. Forum: Metals and Disorders of Cell Accumulation: Modulation of Apoptosis and Cell Proliferation. Toxicol. Sci. 56: 255-261, 2000.
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TEACHING

Lecturing:

- Adjunct Associate Professor, Temple University, Philadelphia, PA; Department of Chemistry, Course Director – Forensic Toxicology, 2017, 2018, 2019, 2020, 2021, 2022, 2023
- Forensic Immunotoxicology; New York University School of Medicine, 3 hours/year, 2020
- Principles of Toxicology, New York University School of Medicine, Lecturer – Overview of Forensic Toxicology; 1.5 lecture hours/year, 2011 - 2013; 2017, 2018
- Society of Toxicology Undergraduate Diversity Program. Fundamentals of Forensic Toxicology, Society of Toxicology Annual Meeting, Baltimore, MD, Presenter, March 12, 2017
- CJFI410, Advanced Crime Scene Forensics, Colorado Technical University, undergraduate, "Overview of Forensic Toxicology," 2015
- TOX-501, Forensic Pathology, University of Rochester School of Medicine, Toxicology Training Program, Course Co-Director, 2012, 2014
- Environmental Immunotoxicology, New York University School of Medicine, Lecturer – Signal Transduction Mechanisms; 3 lecture hours/year, 2010, 2012
- Forensic Science, University of New Haven, Lecturer – Alcohol & Drug Toxicology, March 2011
- TOX-590, Reproductive Toxicology, University of Rochester School of Medicine, Toxicology Training Program, Lecture – Reproductive Immunotoxicology; 2 lecture hours/year, 2007
- TOX-522, Target Organ Toxicology, University of Rochester, Toxicology Training Program, Lecturer – Metal Toxicology; 2 lecture hours/year, 2007
- TOX-521, Molecular Toxicology, University of Rochester School of Medicine, Toxicology Training Program, Lecturer – Apoptosis; 2 lecture hours/year, 2006 - 2008
- TOX-595, Current Topics in Immunotoxicology, University of Rochester, Toxicology Training Program, Course Director, 1.5 hours/week/semester, 2005 - 2009
- IND-501, Ethics and Professional Integrity in Research, University of Rochester School of Medicine, Graduate Education Curriculum, Group Facilitator; 6 lecture hours/year, 2005 - 2008
- TOX-521 & 522, Molecular Toxicology, University of Rochester School of Medicine, Toxicology Training Program, Course Director, 2005 - 2007
- TOX-595, Seminars in Toxicology, University of Rochester School of Medicine, Toxicology Training Program, Course Director, 2005 – 2007
- TOX-522, Target Organ Toxicology, University of Rochester School of Medicine, Toxicology Training Program, Lecturer; Innate Immunity; 2 lecture hours/year, 2008 – 2010; Autoimmune Diseases; 2 lecture hours/year, 2007 – 2009; Metal Toxicology; 2 lecture hours/year, 2007; Immunotoxicology; 8 lecture hours/year, 2004 - 2008

- Year Two Case Seminars, HD- Emerging Diseases and The Environment, University of Rochester School of Medicine, Medical Student Curriculum, Lecturer – Lead Poisoning, 2004 - 2007
- Workshop Leader, University of Rochester School of Medicine, Toxicology Training Program, How to Write a Research Paper, 2004 - 2007

Thesis Adviser – Graduate Students and Post-doctoral Fellows Trained

- Michael A. Laiosa, Ph.D. (2006 - 2008) University of Rochester, Toxicology Training Program, Postdoctoral Fellow
- David Farrer, Ph.D. (2002 - 2006) University of Rochester, Toxicology Training Program, Thesis: Target Cells and Key Mediators in Lead-Induced Immune Modulation
- Geniece McCollum, Ph.D. (2001 - 2006) University of Rochester, Toxicology Training Program; Thesis: Mechanism of Arsenic-Induced Growth Inhibition of a Myeloid Leukemia Cell Line
- Michael J. Whitekus, Ph.D. (1996 - 2000), Wayne State University, Multidisciplinary Program in Molecular and Cellular Toxicology. Thesis: Inorganic Mercury and Dysregulation of Fas-Mediated Apoptosis
- Parto Guity, Ph.D. (1993 - 1998), Wayne State University, Department of Pharmaceutical Sciences. Thesis: Effect of Lead on Vitamin-D-Induced Osteocalcin Secretion: Involvement of Protein Kinase C
- Philip Pokorski, Ph.D. (1993 - 1997), Wayne State University, Department of Pharmaceutical Sciences. Thesis: Effects of Lead on Renal Proximal Tubule Cells and the Restorative Effects of Dimercaptosuccinic Acid in Treatment of Lead Poisoning

Member of more than 25 Ph.D. and M.S. thesis dissertation committees and qualifying examinations over the past 30 years.

APPENDIX B: LIST OF PRIOR TESTIMONY FOR MICHAEL J. MCCABE, JR.

4/8/2021	State of Utah vs. William Travis Fryer Seventh District Juvenile Court, Grand County, Utah Case No. 1183385 Trial Defendant
6/24/2021	KRISTA GENO, as Personal Representative of the Estate of JOSEPH KENT TWYMAN, Deceased v. TYLER WYATT GILLILAND, WAL-MART STORES, EAST, L.P. and SHIKI 2, LLC, d/b/a Shiki Japanese Restaurant Case No: CJ-2014-6041 District Court of Oklahoma City Trial Plaintiff
8/18/2021	Stephen Blighton, as personal representative of the Estate of Victoria Christine Blighton, Plaintiff v. Family Fun and Sports of Marianna, LLC, d/b/a Beef 'O' Brady's 14th Judicial Circuit in and for Jackson County, Florida Case No.: 2019 CA 514 Deposition Defendant
8/19/2021	Darren Findling, Personal Representative for the Estate of Junior Clifford Martin, Deceased, Plaintiff v. Douglas Augustyniak and Nutrien AG Solutions, Inc. Defendants, et al. Circuit Court for the County of Van Buren, Michigan Case No.: 2020-070145-NI Deposition Plaintiff
9/15/2021	Constance Christopher, Plaintiff v. Wal-Mart Stores East I, LP et al. Circuit Court of Buchanan County, Missouri Case No. 20BU-CV-00950 Deposition Plaintiff
10/21/2021	Stephen Blighton, as personal representative of the Estate of Victoria Christine Blighton, Plaintiff v. Family Fun and Sports of Marianna, LLC, d/b/a Beef 'O' Brady's 14th Judicial Circuit in and for Jackson County, Florida Case No.: 2019 CA 514 Deposition Defendant

12/9/2021	Stephen Blighton, as personal representative of the Estate of Victoria Christine Blighton, Plaintiff v. Family Fun and Sports of Marianna, LLC, d/b/a Beef 'O' Brady's 14th Judicial Circuit in and for Jackson County, Florida Case No.: 2019 CA 514 Trial Defendant
1/12/2022	Taronica L. McCormick, Administrator of the Estate of Dwayne K. McCormick, Plaintiff, v. Robert D. Huang, M.D.; Jose Sarao, M.D.; Ear Nose and Throat Group of New Jersey; Union Surgery Center Superior Court of New Jersey, Middlesex County Docket No. MID-L-2720-20 Deposition Plaintiff
4/26/2022	Harvey Mahler, Plaintiff, vs. Vitamin Shoppe Industries, Inc., d/b/a The Vitamin Shoppe, Defendants Case No. 19-CV-03848 United States District Court for the Northern District of Illinois Eastern Division Deposition Defendant
5/9/2022	Travis S. Sweigart, Plaintiff, vs. Voyager Trucking Corp. and Kevin J. Patten, Defendants Case No. 5:21-CV-00922-EGS United States District Court for the Eastern District of Pennsylvania Deposition Defendant
5/10/2022	Gae Guagenti, Administrator of the Estate of John Guagenti, Deceased, Plaintiff, vs. Bobcat of Lima, Inc., et al., Defendants Case No. CV 2021 0018 State of Ohio, County of Allen, In the Court of Common Pleas Deposition Defendant
5/12/2022	Juan Gonzalez, et al. Plaintiffs vs. Uno Chicago Grill, et al. Defendants Docket No. Mid-K-7308-16 Superior Court of New Jersey Law Division: Middlesex County Deposition Defendant

5/16/2022	Todd and Lindsay Powers, Plaintiffs, vs. City of Geneva, Defendant Index No. 116046-2017 State of New York Supreme Court, County of Ontario Trial Defendant
6/3/2022	Louis A. Boni, III and Kasie Boni, Plaintiffs, vs. Tios Lak, LLC, Defendants Case No. 2020-CP-07-01436 State of South Carolina, County of Beaufort Court of Common Pleas, 14th Judicial Circuit Deposition Defendant
6/6/2022	Mandy Sturmur and Cole Sturmur (A minor), Martha Brice & Gary Brice vs. Felicia Wallace, The Whistle Stop Inn, Inc & Westfield Insurance Company, Defendants Cause No: 49D03-1802-CT-008019 State of Indiana, County of Marion Marion Superior Court Deposition Defendant
6/8/2022 9/23/2022	Deborah Monnahan, et al., Plaintiffs v. Modine Manufacturing Company, et al., Defendants Case No. 18CM-CC00218 Circuit Court of Camden County, Missouri Deposition Plaintiff
6/10/2022	Louis A. Boni, III and Kasie Boni, Plaintiffs, vs. Tios Lak, LLC, Defendants Case No. 2020-CP-07-01436 State of South Carolina, County of Beaufort Court of Common Pleas, 14th Judicial Circuit Trial Defendant
7/15/2022	Karolina Twarowski, et al., Plaintiffs, vs. Heart's Desire, DCL, LLC, et al., Defendants Civil Action: 1:20-cv-00815-SAG United States District Court for the District of Maryland Northern District – Civil Division Deposition Plaintiff

8/16/2022	Ellis Morganfield Plaintiff, And Shamron Henry-Murray Plaintiff, vs. Francis Marion Barnett, IV, Elevated Restaurant Group, LP And KCI USA, Inc. Defendants Cause No. 2019CII05163 Consolidated With Cause No. 2019CI08623 District Court of Bexar County, Texas; 285th Judicial District Deposition Defendant
9/21/2022	Lynn Sharp, Plaintiff vs. Heitzenrater's Hideout, LLC d/b/a The Hideout and John Heitzenrater, Defendants No. GD-16-000945 Court of Common Pleas of the Fifty-Ninth Judicial District; Elk County, Pennsylvania Trial Defendant
9/27/2022	Wendy Landree, Plaintiff, vs. Christopher Schweikert, The Park Tap & Grill, Heilongjiang Barn, LLC, et al. Defendants Docket No.: MID-L-7897-18 Superior Court of New Jersey Law Division: Middlesex County Trial Defendant
11/9/2022	Denise Bradshaw, As Administratrix of the Estate of David Bradshaw III and Amanda Gordon, as Guardian for David Bradshaw IV and Denise Bradshaw, Plaintiffs vs. India Thompson, Individually and in her Official Capacity and Lexington-Fayette Urban County Government, Defendants Civil Action No. 19-CI-03277 Commonwealth of Kentucky; Fayette Circuit Court Deposition Plaintiff
11/15/2022	Michael Broderick and Ilene Broderick, Plaintiffs, against Edgewater Park Owners Cooperative, Inc., Edgewater Park Athletic Assoc., Inc., Edgewater Park Volunteer Hose Co. No. 1, Inc. and Edgewater Park Athletic Association Corp., Defendants Supreme Court of the State of New York, County of Bronx Trial Plaintiff
11/17/2022	Isaac Flowers, as Successor Personal Representative of the Estate of Cedar Flowers, Deceased, Plaintiff, v. Medicine Wheel, Inc., D/B/A Milburn Family Medicine Clinic, Paul Weathers, Heather Workman, RJRX, LLC, D/B/A Sooner Pharmacy of Tishomingo, Parks Family Dental, PC and Justin Parks, Defendants Case No. CJ-2019-00020 District Court of Johnston County, State of Oklahoma Deposition Plaintiff

11/29/2022	William Traylor, Plaintiff; v. Apache Corporation and Pioneer Energy Services Corp., Defendants Cause No. 2018-21167 District Court of Harris County, Texas; 164th Judicial District Deposition Defendant
1/20/2023	Alison S. Inga v. Nature's Bounty Company Case Number: 9:2020cv81513 US District Court for the Southern District of Florida Deposition Plaintiff
4/24/2023	Michael T. Powell, John M. Yarbough, Sheila D. Yarbough and Gabriel C. Fells vs. Tequllas, Inc., Tequilas, Inc. d/b/a Tequila's Mexican Restaurant Bar & Grill, Richard Ceja, New Punjab Ltd. Co., New Punjab Ltd. Co, d.b.a Fuel Point, Nakaash Ali, Shahrukh Ali, Fahad Momin and Luis Fernando Torres Cause No. E-206286 District Court of Jefferson County, Texas Hearing Plaintiff
6/14/2023	Ronnie Trigg, et al. v. Justin Eberle, Field Box St. Peters LLC, and Hattrick's Irish Sports Pub, LLC Case No. 21SL-CC00813 Circuit Court of the Twenty-First Judicial Circuit. St. Louis County, Missouri Deposition Defendant
6/15/2023	Stephen F. Pekach and Kimberly N. Pekach, H/W Plaintiffs, v. Kelly's Seafood, Inc. d/b/a Kelly's Seafood d/b/a Kelly's Seafood Restaurant d/b/a Kelly's Seafood Restaurant and Bar and Brett William Kelly, Defendants No. 01812 Court of Common Pleas, Philadelphia County Trial Defendant
7/13/2023	Estate of Michael A. Hanfeld, c/o Tracey M. Hanfeld, Special Administrator, Tracy M. Hanfeld, Plaintiff, Medical Associates/Mercy Family Care Network, LLC, Involuntary Plaintiff, vs. Commercial Recreation Specialists, Inc., Hawkeye Boat Sales, Inc. North Sports, Inc. (d/b/ Aquaglide), Connelly Skis HoldCo, Inc. Guangzhou Asia Inflatables, Co. Limited, et al. Defendants Case No. 21-CV-272 State of Wisconsin, Circuit Court Grant County Deposition Plaintiff

7/19/2023	Kellie and Forrest Benner, Plaintiffs, vs. Tacky Jacks; Estate of Shannon Clark; Matt Harris; et al. Case Number: CV-2020-901029 Circuit Court of Baldwin County, Alabama Deposition Plaintiff
8/3/2023	William Byrne, as Administrator of the Estate of Margaret Leja, deceased, Plaintiff, vs. Mark Burak, as Special Administrator of the Estate of Paul C. Burak, deceased, the Catholic Bishop, a corporation sole, d/b/a Archdiocese of Chicago, and Square Celt, LLC, an Illinois Limited Liability Company, d/b/a Square Celt Ale House & Grill, Defendants No. 19 L 4088 Circuit Court of Cook County, Illinois Deposition Plaintiff
8/8/2023	Willie Smith, Plaintiff, vs., Rite Aid, Walgreen Co., Walgreen Boots Alliance, et al., Defendants Docket No. ESX-L-3355-20 Superior Court of New Jersey: Essex County Deposition Defendant
8/22/23	Deborah Monnahan, et al., Plaintiffs v. Modine Manufacturing Company, et al., Defendants Case No. 18CM-CC00218 Circuit Court of Camden County, Missouri Trial Plaintiff
9/7/2023	Amritpaul Singh Athwal, and Harprit Kaur Athwal, Plaintiffs, v Volvo Trucks North America, Inc., Volvo Group North America, LLC, and Webasto Thermo & Comfort North America, Inc., Defendants Case No. 1:22-cv-00044-HAB-SLC United States District Court for the Northern District of Indiana; Fort Wayne Division Deposition Plaintiff
9/25/2023	Kristen Pym Plaintiff, v. Ford Motor Company and Robert Armstrong Defendants Cause No: 19SL-CC00857 Circuit Court of Missouri; Twenty First Judicial Circuit (St. Louis County) Deposition Plaintiff

Michael J. McCabe, Jr., Ph.D.

History of Expert Testimony

10/26/2023	Ruth Halpine, Plaintiff, vs. Gulf Shores Tacky Jack's LLC; et al., Defendants Civil Action No. CV-22-901088 Circuit Court of Baldwin County, Alabama Deposition Plaintiff
3/29/2024	Joanne M. Moitoza and John R, Souza, Individually and as Co-Administrators of the Estate of John J. Souza, Plaintiffs, vs. Sarah E. Bergbenholtz, a/k/a Sarah Becker, Ivan, Inc. d/b/a Federal Taphouse and Kitchen, et al. Civil Action No. PC 2019-6835 Superior Court, Providence, Rhode Island Deposition Defendant
4/9/2024	Donald Beckerdite, Plaintiff, v. Bar Three LLC D/B/A Brewbakers, MCBCO Brewery, LLC D/B/A Martin City Brewing Company, and Delbert Hannah, by and through Kevin Jones, Defendant *ad litem* Case No. 22CA-CC00299 The Circuit Court of Cass County, Missouri Deposition Plaintiff
5/29/2024	Lukas T. Udris, Plaintiff, vs. Brandon H. Christianson, and Kansas City Bier Company, LLC, Defendants Case No.: 2216-CV10212, Div. 12 Circuit Court of Jackson County, Missouri at Independence Deposition Plaintiff
8/27/2024	Caroline Patton Griffin, Individually and as Surviving Spouse and Executor of the Estate of Lee Dixon Griffin, Jr., Plaintiff, v. Toyota Motor Corporation, Toyota North America, Inc.; Toyota Motor Sales, U.S.A., Inc.; Toyota Motor Engineering & Manufacturing North America, Inc.; Toyota Manufacturing, Texas, Inc.; and Jim Ellis Automotive Holdings, Inc., Defendants Civil Action File No.: 1:23-cv-03107-TWT, United States District Court for the Northern District of Georgia Atlanta Division Deposition Plaintiff
12/16/2024	Daron L. Glenn Plaintiff v. Ford Motor Company; McMahon Associates, Inc.; Ramos & Associates, Inc.; Armour & Sons Electric; Obafemi Taiwo; Autoliv; PennDOT; City of Philadelphia; Tyreese Wheeler, Defendants No. 01479 Court of Common Pleas County of Philadelphia Trial Defendant