Exhibit 494

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Re: Ronald Lee Carter
DOB: [redacted]/1948; DOD: 5/9/2022
Rebuttal to report of Dr. Richard F. Ambinder

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I am writing in response to your request for a response to the April 8, 2025 expert report provided by Richard F. Ambinder, M.D., Ph.D. that relate to Mr. Carter's cancer and its relationship to exposures incurred at Camp Lejeune. My rebuttal report does not contain a response to all of the points that Dr. Ambinder makes in his report with which I disagree, nor should my rebuttal to some portions of his report and not others be viewed as agreement with the portions of his report that I do not rebut below.

Please refer to my February 7, 2025 report on Mr. Carter for a summary of my background and qualifications as well as my general causation report of December 9, 2024.

I offer the following comments, each preceded by a reference to the associated location in Dr. Ambinder's report:

(1) Page 8, 5th paragraph, Dr. Ambinder states that "*With regards to studies of environmental exposures to benzene, trichloroethylene, perchloroethylene, and vinyl chloride, I have relied on the expert report prepared by Dr. Goodman,";*
Comment: I refer to my own general causation report on benzene, TCE, and PCE.

(2) Page 11, 4th full paragraph: Dr. Ambinder notes that: "*I must differ with Dr. Hu's assessment of the cause of Mr. Carter's death. He notes, '…Mr. Carter experienced an acute cerebrovascular event; work-up revealed occlusion of the right posterior cerebral artery with suspected intravascular lymphoma that was untreatable.' Intravascular lymphoma is a rare entity that is distinct from MCL. The diagnosis requires a biopsy or autopsy to diagnose…"*
Comment: My statement that Mr. Carter had a work-up that "…revealed occlusion of the right posterior cerebral artery with suspected intravascular lymphoma that was untreatable," was simply a re-statement of what was written in his medical record. I was not expressing an independent opinion of Mr. Carter's cause of death. I nevertheless make the following two observations: (A) intravascular lymphoma was raised as a possibility; the only way to have firmly determined if it was, or was not, in fact, a direct precipitating factor in his stroke or not would have been through an autopsy. His death certificate makes it clear that an autopsy was not performed; (B) even without the presence of an intravascular lymphoma, it is well-documented that cancer is associated with a significantly increased risk of stroke either directly or via coagulation disorders that establish a state of hypercoagulation, with NHL being specifically associated with an increased risk of both ischemic

[1] Affiliation listed for identification purposes only.

and hemorrhagic stroke[2],[3]. I would agree with Dr. Ambinder that Mr. Carter likely had a higher risk of stroke given his family history of myocardial infarctions and strokes. However, the risks for stroke and other cardiovascular events typically increase with each additional risk factor, making choosing one risk factor or another as "the single cause" both an unrealistic and arbitrary exercise. In my opinion, Dr. Ambinder errs by not acknowledging the known increased risk that his NHL presented in relationship to the stroke that ended Mr. Carter's life.

(3) Page 11-12: Here, Dr. Ambinder referred to the estimates of Mr. Carter's risk of cancer from exposure to chemicals in the water at Camp Lejeune that were produced by Bailey, which, in turn, were based on an exposure assessment conducted by Dr. LaKind. Dr. Ambinder quoted the Bailey report in stating that "*…Mr. Carter's exposures to chemicals in the Camp Lejeune drinking water increased his overall cancer risk by 0.01% (i.e., 1 × 10-4, or 1 cancer case in 10,000 exposed people) over his background cancer risk*."
Comment: In my specific causation report, I noted that Mr. Carter's status as a civilian worker at Camp Lejeune and the timing of his exposure profile very closely aligns with, and, in fact, exceeds, the exposure profile of "15-years of exposure to workers on-base who lived off-base to all chemical contaminants from Hadnot Point (i.e., PCE, TCE, and benzene)" that ATSDR estimated was associated with a lifetime cancer risk of over 1 per 10,0000 for exposures between the mid-1960's to around 1982, with a peak of 2.6 per 10,000 for exposures surrounding 1970. This is somewhat higher than the estimate made by Dr. Bailey.

(4) Page 12 through 14: In these pages, Dr. Ambinder offers a critique of the discussion of differential etiology in my specific causation report of Mr. Carter.
   a. He begins by noting that "*Dr. Hu relies on elimination rather than evidence based causation. He considers a variety of etiologies that have not been linked to MCL, rules them out, and then concludes that exposures at Camp Lejeune must be the cause*."
   b. Dr. Ambinder then reviews my discussion of various risk factors as they pertain to Mr.Carter, and then states that "*Dr. Hu reviews possible suspects for NHL in his differential etiology review as though there are only a handful and having eliminated all the suspects that there is general agreement are not contributors to MCL, he attributes the cancer to exposures at Camp Lejeune. However, as reviewed above, the causes of MCL are almost entirely unknown, so eliminating things that are not known to cause MCL doesn't make it at all plausible that exposures at Camp Lejeune had anything to do with the development of MCL in Mr. Carter*…."

Comment: The first comment by Dr. Ambinder overstates my opinion. I stated my conclusion in my report as follows: "*Thus, given my general causation assessment and the factors reviewed above, it is my opinion, to a reasonable degree of medical certainty, that the combination of Mr. Carter's exposures to TCE, PCE, and benzene from Camp Lejeune more likely than not was a substantial contributing factor to the causation of his mantle cell lymphoma*."

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[2] Dardiotis E, Aloizou AM, Markoula S, Siokas V, Tsarouhas K, Tzanakakis G, Libra M, Kyritsis AP, Brotis AG, Aschner M, Gozes I, Bogdanos DP, Spandidos DA, Mitsias PD, Tsatsakis A. Cancer-associated stroke: Pathophysiology, detection and management (Review). Int J Oncol. 2019 Mar;54(3):779-796. doi: 10.3892/ijo.2019.4669. Epub 2019 Jan 2. PMID: 30628661; PMCID: PMC6365034.

[3] Zöller B, Ji J, Sundquist J, Sundquist K. Risk of haemorrhagic and ischaemic stroke in patients with cancer: a nationwide follow-up study from Sweden. Eur J Cancer. 2012 Aug;48(12):1875-83. doi: 10.1016/j.ejca.2012.01.005. Epub 2012 Jan 30. PMID: 22296948.

The second comment by Dr. Ambinder essentially implies two positions (A) that any particular cancer caused by external factors must only have a single cause, and that since the set of risk factors identified for MCL cannot explain most cases of MCL, tying a case of MCL to any particular risk factor (such as TCE, PCE, and benzene) is inherently flawed; and (B) that the vast majority of cancers are NOT related to external causes, and are, instead, related to random events (e.g., mutations). These are both fallacious arguments.

The first position, (A), ignores the fact that as research on the process of carcinogenesis continues to make progress, it has become clear that cancer causation is a multistep and multifactorial phenomenon that is heavily influenced by extrinsic (i.e., environmental) factors[4]. In depth reviews of mechanistic research have indicated that environmental carcinogenesis occurs through multiple mechanisms, reflecting what Smith and colleagues[5] have identified as 10 basic mechanisms (acting as an electrophile either directly or after metabolic activation; genotoxicity; altering DNA repair or cause genomic instability; inducing epigenetic alterations; inducing oxidative stress; inducing chronic inflammation; being immunosuppressive; modulating receptor-mediated effects; causing immortalization; and altering cell proliferation, cell death, or nutrient supply). Combinations of carcinogenic factors (e.g., chemical mixtures, as well as chemical carcinogens interacting with genetic susceptibility factors) are likely to play a role in most cancers, with the accumulation of a number of complementary causes required to produce cancer[6]. Metaphorically-speaking, cancer can be thought of as a homicide caused by an assassination team, e.g., plotters, look-outs, the get-away-car driver, the shooter, etc.. Dr. Ambinder's opinion would be akin to stating that only a single member of the team could be held responsible for the homicide.

The second position implied by Dr. Ambinder's comment (B) mirrors an argument made by Tomasetti and Vogelstein, who published research with an interpretation suggesting that most cancers occur at random[7],[8] (rather than as a result of exposure to external factors, genetic susceptibility factors, and the interaction of genetic susceptibility factors with external factors such as chemical carcinogens). However, these studies, including their methodology and their interpretation, have been roundly criticized and rejected, with contradictory evidence discussed by, for example, the International Agency for Research on Cancer[9] in 2016 and Goldstein and Patel in 2019[10]. In short, the Vogelstein and Tomasetti theory fails to account for the known effects of

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[4] Wu S, Powers S, Zhu W, Hannun YA. Substantial contribution of extrinsic risk factors to cancer development. Nature. 2016 Jan 7;529(7584):43-7. doi: 10.1038/nature16166. Epub 2015 Dec 16. PMID: 26675728; PMCID: PMC4836858.

[5] Smith MT, Guyton KZ, Gibbons CF, Fritz JM, Portier CJ, Rusyn I, DeMarini DM, Caldwell JC, Kavlock RJ, Lambert PF, Hecht SS, Bucher JR, Stewart BW, Baan RA, Cogliano VJ, Straif K. Key Characteristics of Carcinogens as a Basis for Organizing Data on Mechanisms of Carcinogenesis. Environ Health Perspect. 2016 Jun;124(6):713-21. doi: 10.1289/ehp.1509912. Epub 2015 Nov 24. PMID: 26600562; PMCID: PMC4892922.

[6] Goodson WH, Lowe L, Gilbertson M, Carpenter DO. Testing the low dose mixtures hypothesis from the Halifax project. Rev Environ Health. 2020 Aug 24;35(4):333-357. doi: 10.1515/reveh-2020-0033. PMID: 32833669.

[7] Tomasetti C, Vogelstein B. Cancer etiology. Variation in cancer risk among tissues can be explained by the number of stem cell divisions. Science. 2015 Jan 2;347(6217):78-81. doi: 10.1126/science.1260825. PMID: 25554788; PMCID: PMC4446723.

[8] Tomasetti C, Li L, Vogelstein B. Stem cell divisions, somatic mutations, cancer etiology, and cancer prevention. Science. 2017 Mar 24;355(6331):1330-1334. doi: 10.1126/science.aaf9011. PMID: 28336671; PMCID: PMC5852673.

[9] IARC. Most types of cancer not due to "bad luck". IARC responds to scientific article claiming that environmental and lifestyle factors account for less than one third of cancers. Available at: https://www.iarc.who.int/wp-content/uploads/2018/07/pr231_E.pdf ; accessed February 5, 2023.

[10] Goldstein BD, Patel V. Controversy about the "Bad Luck" Cancer Hypothesis Could Lead to a Useful Tool for Planning Primary Prevention Cancer Research. Chem Res Toxicol. 2019 Jun 17;32(6):949-951. doi: 10.1021/acs.chemrestox.8b00390. Epub 2019 Apr 17. PMID: 30995013.

environment carcinogens on cells/cellular structures, differences in the incidence rates of various cancers between regions, and changes in the rates of multiple cancers that have been documented both in the U.S. as well as other countries. Overall, in my opinion and those of others, cancers, including NHL, are largely caused by and/or contributed to by non-random factors.

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This ends my rebuttal of Dr. Ambinder's report.

Sincerely,

Howard Hu, M.D., M.P.H., Sc.D.