

Exhibit 500

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May 16, 2025

Re: Robert Arnold Kidd
DOB: █████ 1960
Rebuttal to report of Dr. Richard F. Ambinder

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. Robert Kidd'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. Robert Kidd 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, 3rd full 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 8, 4th full paragraph: Dr. Ambinder states that *"The oversimplification that all lymphomas or all NHL share the same causation leads to serious errors. See Expert Report of Michael McCabe (February 2025) at pp. 26-27."*
Response: Dr. Goldstein, a senior hematologist and toxicologist, noted in a 2010 commentary² and follow-up summary published by the International Agency for Research on Cancer (IARC)³ that studies of the mechanism of benzene toxicity are consistent with a relatively non-specific mechanism capable of producing multiple chromosomal changes, and that evidence indicates that benzene (and its toxic metabolites) target the early hematopoietic stem cell, which is the progenitor of myeloid cell types as well as lymphocytic cell types. In other words, it is the same pluripotential stem cell that is at risk for the well-recognized causal relationship between benzene and acute myelogenous leukemia (AML) that differentiates into both lymphocytic cell lines, which are the cell lines that eventually produce NHL, as well as myelocytic cell lines. Goldstein also stressed the

¹ Affiliation listed for identification purposes only.

² Goldstein BD. Benzene as a cause of lymphoproliferative disorders. *Chem Biol Interact.* 2010 Mar 19;184(1-2):147-50. doi: 10.1016/j.cbi.2009.12.021. Epub 2009 Dec 24. PMID: 20035727.

³ Goldstein BD, Smith MT. Benzene and haematological cancers. In: Baan RA, Stewart BW, Straif K, editors. *Tumour Site Concordance and Mechanisms of Carcinogenesis.* Lyon (FR): International Agency for Research on Cancer; 2019. Chapter 8. PMID: 33979086.

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relevance of recent research demonstrating genotoxic effects of benzene in circulating lymphocytes of exposed humans or experimental animals. This is important, since in reaching conclusions about the chemical causation of cancer, there has been an increase in the reliance on mechanistic information. This is evident in the criteria used by IARC and by the U.S. National Toxicology Program (NTP) in classifying a chemical as a Group 1 or known human carcinogen. In short, I agree with Dr. Ambinder that it is an oversimplification that all lymphomas or all NHL share the same causation for all possible carcinogens given the possibility that some carcinogens only exert their effects at post-differentiation lymphocytic line level. However, given that the evidence for benzene specifically supports that it produces multiple chromosomal changes at the pluripotential level, genotoxic effects in circulating lymphocytes, AND in a substantial body of rigorously conducted epidemiological studies, is associated with NHL, in my opinion, it is reasonable to conclude that benzene can cause each of the NHL subtypes, all of which stem from the same pluripotential cell type.

- (3) Page 8, last paragraph: Dr. Ambinder quotes an article by Wang (2023⁴) from which he also reproduced a Table that lists “established risk factors” for Diffuse Large B-Cell Lymphoma (DLBCL). The list does not include any chemical toxicants.
Comment: I note that, as stated in the abstract of this same article, the author conclude that “*There is strong evidence for multiple environmental exposures in DLBCL etiology, including exposure to trichloroethylene, benzene, and pesticides and herbicides, with recent associations noted with glyphosate*”.
- (4) Page 13, 5th paragraph: Here, Dr. Ambinder referred to the estimates of Mr. Kidd’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 “...at the highest potential exposure for Mr. Kidd, and applying conservative, health-protective assumptions, Mr. Kidd’s exposures to chemicals in the Camp Lejeune drinking water did not increase his overall cancer risk by more than 8×10^{-5} (i.e., 0.008% or 8 cancer cases in 100,000 exposed people).”
Comment: In my specific causation report, I noted that Mr. Kidd’s status as a Marine living in Camp Lejeune and the timing of his exposure profile very closely aligns with the exposure profile discussed in the ATSDR report of an adult (age above 16 years) living on-base for 3-years exposed to drinking contaminants from the Hadnot WTP (i.e., PCE, TCE, and benzene) that ATSDR estimated was associated with a lifetime cancer risk, beginning in the late 1970’s, of over 1 per 10,000 until around 1982, with a peak of 1.4 per 10,000 (i.e., 14 per 100,000) for exposures surrounding 1981. This is somewhat higher than the estimate made by Dr. Bailey.
- (5) Page 13 through 15: In these pages, Dr. Ambinder offers a critique of the discussion of differential etiology in my specific causation report of Mr. Kidd.
- 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 most DLBCL, rules them out, and then concludes that exposures at Camp Lejeune, however limited, must be the cause.*”
 - b. Dr. Ambinder then reviews my discussion of various risk factors as they pertain to Mr. Kidd, and then states that “*However, as reviewed above, the “known causes” of DLBCL don’t*

⁴ Wang SS. Epidemiology and etiology of diffuse large B-cell lymphoma. *Semin Hematol.* 2023 Nov;60(5):255-266. doi: 10.1053/j.seminhematol.2023.11.004. Epub 2023 Nov 27. PMID: 38242772; PMCID: PMC10962251.

account for the vast majority of DLBCL in the United States. Eliminating these known and relatively rare causes of DLBCL doesn't make it at all plausible that minimal exposures at Camp Lejeune had anything to do with the development of DLBCL in Mr. Kidd. The approach suggested by Dr. Hu is inherently flawed and is not appropriately applied in situations where most of the potential causes remain unknown as is the case with DLBCL."

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 Mr. Kidd's exposure to TCE, PCE, and benzene from Camp Lejeune increased the risk of and constituted the cause or a substantial contributing cause to his Non-Hodgkins Lymphoma (NHL)."*

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 DLBCL cannot explain most cases of DLBCL, tying a case of DLBCL 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) factors⁵. In depth reviews of mechanistic research have indicated that environmental carcinogenesis occurs through multiple mechanisms, reflecting what Smith and colleagues⁶ 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 cancer⁷. 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^{8,9} (rather than as a result of exposure to external factors, genetic

⁵ 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.

⁶ 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, Coglianò 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.

⁷ 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.

⁸ 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.

⁹ 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.

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 Cancer¹⁰ in 2016 and Goldstein and Patel in 2019¹¹. In short, the Vogelstein and Tomasetti theory fails to account for the known effects of 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.

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

Sincerely,



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¹⁰ 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.

¹¹ 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.

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