UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF LOUISIANA

YOLANDE BURST, individually and as the legal representative of BERNARD ERNEST BURST, JR.	CIVIL ACTION
VERSUS	NO: 14-109
SHELL OIL COMPANY, ET AL.	SECTION: R

ORDER AND REASONS

Defendants Shell Oil Company, Chevron U.S.A. Inc., and Texaco, Inc. move to exclude the testimony of plaintiff's expert epidemiologist, Dr. Peter Infante.[1] The Court has reviewed the parties' submissions and has conducted a *Daubert* hearing on the admissibility of Dr. Infante's general causation opinion. The Court grants defendants' motion because it finds that Dr. Infante's general causation opinion is based on an unreliable methodology.

I. BACKGROUND

Plaintiff Yolande Burst filed this products liability action against defendants Shell, Chevron (as successor to Gulf Oil Corporation), and Texaco.[2] She alleges that her late husband, Bernard Burst, Jr., worked at various gas stations from 1958 through 1971, during which time he regularly used products

[1] R. Doc. 90.

[2] R. Doc. 1.

manufactured, supplied, distributed, and sold by defendants.[3] Specifically, she alleges that he regularly came into contact with gasoline containing benzene.

On June 20, 2013, physicians diagnosed Mr. Burst with acute myeloid leukemia (AML).[4] He was 71 years old. He passed away as a result of the leukemia on December 21, 2013.[5]

Plaintiff alleges that her husband's regular exposure to gasoline containing benzene during the years he worked as a gas station attendant and mechanic caused his leukemia.[6] She claims that defendants negligently manufactured and sold products containing benzene and that they negligently failed to warn foreseeable users about the health hazards associated with these products.[7] She also alleges strict products liability.[8]

To demonstrate that gasoline containing benzene can cause AML and that, in this case, it caused Mr. Burst's AML, plaintiff offers the testimony of epidemiologist Dr. Peter Infante. In his report, Dr. Infante seeks to answer whether "occupational exposure to benzene is a cause of myelodysplastic syndrome (MDS) and acute

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[3] *Id.* at 3.

[4] R. Doc. 28-5 at 18.

[5] R. Doc. 28-6.

[6] R. Doc. 1 at 5.

[7] *Id.* at 9.

[8] *Id.* at 10.

myelogenous leukemia (AML)."[9] Dr. Infante concludes that low-level benzene exposure from gasoline can cause AML and that Mr. Burst's exposure to gasoline containing benzene caused his AML. Defendants now move to exclude Dr. Infante's opinions arguing that they are unreliable and irrelevant.

II. LEGAL STANDARD

This is a toxic torts case where plaintiff alleges that gasoline containing benzene caused her husband's AML. Accordingly, plaintiff must show general causation--that gasoline containing benzene can cause AML--and specific causation--that defendants' products caused Mr. Burst's AML. *See Knight v. Kirby Inland Marine Inc.*, 482 F.3d 347, 351 (5th Cir. 2007) ("General causation is whether a substance is capable of causing a particular injury or condition in the general population, while specific causation is whether a substance caused a particular individual's injury.") (citation omitted). A court may admit specific-causation evidence only after the plaintiff has produced admissible evidence on general causation. *See id.* ("[I]f it concludes that there is admissible general-causation evidence, the district court must determine whether there is admissible specific causation evidence.").

A district court has considerable discretion to admit or

[9] R. Doc. 99, Ex. 1 at 1 ("Infante Report").

exclude expert testimony under Rule 702. *See Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 138-39 (1997); *Seatrax, Inc. v. Sonbeck Int'l, Inc*., 200 F.3d 358, 371 (5th Cir. 2000). Rule 702, which governs the admissibility of expert witness testimony, provides:

> A witness who is qualified as an expert by knowledge, skill, experience, training, or education may testify in the form of an opinion or otherwise if: (a) the expert's scientific, technical, or other specialized knowledge will help the trier of fact to understand the evidence or to determine a fact in issue; (b) the testimony is based on sufficient facts or data; (c) the testimony is the product of reliable principles and methods; and (d) the expert has reliably applied the principles and methods to the facts of the case.

Fed. R. Evid. 702.

In *Daubert v. Merrell Dow Pharms., Inc.*, the Supreme Court held that Rule 702 requires the district court to act as a gatekeeper to ensure that "any and all scientific testimony or evidence admitted is not only relevant, but reliable." 509 U.S. 579, 589 (1993); *see also Kumho Tire Co., Ltd. v. Carmichael,* 526 U.S. 137, 147 (1999) (clarifying that the *Daubert* gatekeeping function applies to all forms of expert testimony). The Court's gatekeeping function thus involves a two-part inquiry into reliability and relevance.

First, the Court must determine whether the proffered expert testimony is reliable. The party offering the testimony bears the burden of establishing its reliability by a preponderance of the evidence. *See Moore v. Ashland Chem. Inc.,* 151 F.3d 269, 276 (5th Cir. 1998). The reliability inquiry requires the Court to assess

whether the reasoning or methodology underlying the expert's testimony is valid. *See Daubert,* 509 U.S. at 592-93. The aim is to exclude expert testimony based merely on subjective belief or unsupported speculation. *See id.* at 590. The Court in *Daubert* articulated a flexible, non-exhaustive, five-factor test to assess the reliability of an expert's methodology: (1) whether the expert's theory can be or has been tested; (2) whether the theory has been subject to peer review and publication; (3) the known or potential rate of error of a technique or theory when applied; (4) the existence and maintenance of standards and controls; and (5) the degree to which the technique or theory has been generally accepted in the scientific community. *Id.* at 593-95. The Supreme Court has emphasized, however, that these factors "do not constitute a 'definitive checklist or test.'" *Kumho*, 526 U.S. at 150 (quoting *Daubert*, 509 U.S. at 593). Rather, district courts "must have considerable leeway in deciding in a particular case how to go about determining whether particular expert testimony is reliable." *Id.* at 152. Courts have also considered whether experts are "proposing to testify about matters growing naturally and directly out of research they have conducted independent of the litigation, or whether they have developed their opinions expressly for purposes of testifying." *Daubert v. Merrell Dow Pharms., Inc.*, 43 F.3d 1311, 1317 (9th Cir. 1995). They have examined whether the expert has adequately accounted for obvious alternative

explanations. *See Claar v. Burlington N.R.R.*, 29 F.3d 499, 502 (9th Cir. 1994). They have also asked whether the expert "is being as careful as he would be in his regular professional work outside his paid litigation consulting." *Sheehan v. Daily Racing Form, Inc.*, 104 F.3d 940, 942 (7th Cir. 1997).

A district court's gatekeeper function does not replace the traditional adversary system or the role of the jury within this system. *See Daubert*, 509 U.S. at 596. As the Supreme Court noted in *Daubert*: "Vigorous cross-examination, presentation of contrary evidence, and careful instruction on the burden of proof are the traditional and appropriate means of attacking shaky but admissible evidence." *Id.* The Fifth Circuit has held that, in determining the admissibility of expert testimony, district courts must accord proper deference to "the jury's role as the proper arbiter of disputes between conflicting opinions" and that, generally, "questions relating to the bases and sources of an expert's opinion affect the weight to be assigned that opinion rather than its admissibility." *United States v. 14.38 Acres of Land, More or Less Situated in Leflore Cnty., Miss.*, 80 F.3d 1074, 1077 (5th Cir. 1996) (quoting *Viterbo v. Dow Chem. Co.*, 826 F.2d 420, 422 (5th Cir. 1987)) (internal quotation marks omitted). Nonetheless, expert testimony "must be reliable at each and every step or else it is inadmissible," and "[t]he reliability analysis applies to all aspects of an expert's testimony: the methodology, the facts

underlying the expert's opinion, the link between the facts and the conclusion, et alia." *Knight*, 482 F.3d at 355 (internal quotation marks omitted). If the "expert's opinion is based on insufficient information, the analysis is unreliable." *Paz v. Brush Engineered Materials, Inc.*, 555 F.3d 383, 388 (5th Cir. 2009).

In *Joiner*, the Supreme Court explained that "nothing in either *Daubert* or the Federal Rules of Evidence requires a district court to admit opinion evidence that is connected to existing data only by the *ipse dixit* of the expert." 522 U.S. at 146. Rather, "[a] court may conclude that there is simply too great an analytical gap between the data and the opinion proffered." *Id.*; *see also LeBlanc v. Chevron USA, Inc.* 396 F. App'x 94, 98 (5th Cir. 2010).

The Court next considers whether the expert's reasoning or methodology is relevant. The question here is whether the reasoning or methodology "fits" the facts of the case and will thereby assist the trier of fact to understand the evidence. *See Daubert*, 509 U.S. at 591.

In fulfilling its role as a gatekeeper, the Court recognizes that "the courtroom is not the place for scientific guesswork, even of the inspired sort." *Rosen v. Ciba-Geigy Corp.*, 78 F.3d 316, 319 (7th Cir. 1996). Rather, "[l]aw lags science; it does not lead it." *Id.* The Court is mindful of the Supreme Court's guidance that

> there are important differences between the quest for truth in the courtroom and the quest for truth in the

> laboratory. Scientific conclusions are subject to perpetual revision. Law, on the other hand, must resolve disputes finally and quickly. The scientific project is advanced by broad and wide-ranging consideration of a multitude of hypotheses, for those that are incorrect will eventually be shown to be so, and that in itself is an advance. Conjectures that are probably wrong are of little use, however, in the project of reaching a quick, final, and binding legal judgment--often of great consequence--about a particular set of events in the past. We recognize that, in practice, a gatekeeping role for the judge, no matter how flexible, inevitably on occasion will prevent the jury from learning of authentic insights and innovations. That, nevertheless, is the balance that is struck by Rules of Evidence designed not for the exhaustive search for cosmic understanding but for the particularized resolution of legal disputes.

Daubert, 509 U.S. at 596-97.

III. DISCUSSION

A. Introduction

Defendants contend that there is no scientific basis for concluding that gasoline containing benzene causes AML. While benzene is a known human carcinogen, defendants assert that the scientific literature does not demonstrate that gasoline can cause AML.

As the record indicates, gasoline is a mixture of many substances including benzene. While the benzene content of gasoline varies depending on a number of factors, the record indicates that the benzene concentration of gasoline may have ranged from under 1% to as high as 4% or 5% between 1958 and 1971 when Mr. Burst worked as a service station attendant and mechanic.

To prove that gasoline containing benzene can cause AML, plaintiff offers the testimony of epidemiologist Dr. Infante. As to general causation, Dr. Infante concludes: "[I]t is my opinion that exposure to very low level benzene from gasoline can cause damage to the DNA of bone marrow cells as well as AML . . . . The data related to gasoline exposure and risk of AML are consistent with the epidemiological data on benzene exposure that demonstrate an elevated risk of MDS/AML . . . ."[10]

Under *Daubert*, the Court's focus is Dr. Infante's methodology. The reported basis for Dr. Infante's opinion is his "review of the epidemiological and toxicological literature, plus internal industry documents, related to benzene exposure and risk of developing blood diseases."[11] Dr. Infante states he "followed the methodology of the International Agency for Research on Cancer (IARC) and of the Occupational Safety and Health Administration (OSHA) in evaluating epidemiological studies, case reports and toxicological studies of benzene exposure and its effect on the hematopoietic system."[12] Dr. Infante provides no other explanation of his methodology.

Epidemiology provides the best evidence of general causation in toxic tort cases. *See Brock v. Merrell Dow Pharms., Inc.*, 874

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[10] *Id.* at 79.

[11] *Id.* at 4.

[12] *Id.*

F.2d 307, 311 (5th Cir. 1989), *modified by* 884 F.3d 166 (5th Cir. 1989); *Norris v. Baxter Healthcare Corp.*, 397 F.3d 878, 882 (10th Cir. 2005) (stating "that epidemiology is the best evidence of general causation in a toxic tort case"). This is not to say that epidemiologic evidence "is a necessary element in all toxic tort cases," but "it is certainly a very important element." *Brock*, 874 F.2d at 313.

Epidemiology is the study of "the incidence, distribution, and etiology of disease in human populations." Federal Judicial Center, Reference Manual on Scientific Evidence 551 (3d ed. 2011). As explained by the Fifth Circuit:

> Epidemiology attempts to define a relationship between a disease and a fact suspected of causing it . . . . To define that relationship, the epidemiologist examines the general population, comparing the incidence of the disease among those people exposed to the factor in question to those not exposed. The epidemiologist then uses statistical methods and reasoning to allow her to draw a biological inference between the factor being studied and the disease's etiology.

Brock, 874 F.2d at 311.

To determine whether a causal relationship exists between an agent and a disease, an epidemiologist must first identify an association. An association occurs when "two events (*e.g.*, exposure to a chemical agent and development of disease) . . . occur more frequently together than one would expect by chance." Reference Manual at 552 n.7. An association, by itself, is *not* equivalent to causation. *Id.* at 552. Unlike an association,

"[c]ausation is used to describe the association between two events when one event is a necessary link in a chain of events that results in the effect." *Id.* at 552 n.7. The Reference Manual indicates that "[a]ssesssing whether an association is causal requires an understanding of the strengths and weaknesses of a study's design and implementation, as well as a judgment about how the study's findings fit with other scientific knowledge." *Id.* at 553. Because "all studies have 'flaws' in the sense of limitations that add uncertainty about the proper interpretation of results," the key questions in evaluating epidemiologic evidence "are the extent to which a study's limitations compromise its findings and permit inferences about causation." *Id.* at 553.

Once an association is found, "researchers consider whether the association reflects a true cause-effect relationship;" that is, whether "an increase in the incidence of disease among the exposed subjects would not have occurred had they not been exposed to the agent." *Id.* at 597-98. Alternative explanations, "such as bias or confounding factors," should first be considered. *Id.* at 598. If alternative explanations are not present, researchers apply the Bradford Hill criteria to evaluate whether an agent could be a cause of a disease. *See In re Breast Implant Litig.*, 11 F. Supp. 2d 1217, 1233 (D. Colo. 1998). The Bradford Hill criteria are: (1) temporal relationship; (2) strength of the association; (3) dose-response relationship; (4) replication of findings; (5)

biological plausibility; (6) consideration of alternative explanations; (7) cessation of exposure; (8) specificity of the association; and (9) consistency with other knowledge. Reference Manual at 600. The Reference Manual cautions:

> There is no formula or algorithm that can be used to assess whether a causal inference is appropriate based on these guidelines. One or more factors may be absent even when a true causal relationship exists. Similarly, the existence of some factors does not ensure that a causal relationship exists. Drawing causal inferences after finding an association and considering these factors requires judgment and searching analysis, based on biology, of why a factor or factors may be absent despite a causal relationship, and vice versa. Although the drawing of causal inferences is informed by scientific expertise, it is not a determination that is made by using an objective or algorithmic methodology.

Id.

Under *Daubert*, "courts must carefully analyze the studies on which experts rely for their opinions before admitting their testimony." *Knight*, 482 F.3d at 355; *see also Brock*, 874 F.2d at 309-10 ("[C]ourts must critically evaluate the reasoning process by which experts connect data to their conclusions in order for courts to consistently and rationally resolve the disputes before them."); *Wagoner v. Exxon Mobil Corp.*, 813 F. Supp. 2d 771, 799 (E.D. La. 2011) ("Whether epidemiological studies support an expert's opinion on the question of general causation in a toxic tort case is critical to determining the reliability of the opinion."). Courts "may exclude expert testimony based on epidemiological studies where the studies are insufficient, whether considered individually

or collectively, to support the expert's causation opinion." *Baker v. Chevron USA, Inc.*, 680 F. Supp. 2d 865, 875 (S.D. Ohio 2010) (citing *Joiner*, 522 U.S. at 156-57). A court cannot exclude expert testimony simply because it disagrees with the expert's conclusions, but the Supreme Court has recognized that

> conclusions and methodology are not entirely distinct from one another. Trained experts commonly extrapolate from existing data. But nothing in either *Daubert* or the Federal Rules of Evidence requires a court to admit opinion evidence that is connected to existing data only by the *ipse dixit* of the expert. A court may conclude that there is simply too great an analytical gap between the data and the opinion offered.

Joiner, 522 U.S. at 146.

Courts have excluded expert opinions on causation based on epidemiologic and other scientific studies for a number of reasons. First, studies that "do not represent statistically significant results" may not provide a reliable foundation for an epidemiologist's general causation opinion in a toxic torts case. *LeBlanc*, 396 F. App'x at 99 (citing *Joiner*, 522 U.S. at 145 (holding that a study showing a statistically insignificant increase in disease incidence following exposure to the alleged causal chemical can properly be rejected by the district court as a foundation for the expert's opinion)). The results of epidemiologic studies are often expressed in terms of a relative risk (RR),[13] an odds ratio (OR),[14] or a standardized morality ratio

[13] "The relative risk is a number which describes the increased or decreased incidence of the disease in question in

(SMR).[15] An RR, OR, or SMR of 1.0 indicates that the number of observed incidences of disease/death equals that of expected cases. In contrast, a figure higher than 1.0 indicates that the number of observed incidences exceeds that of expected cases; in other words, it indicates a positive association. A study is considered statistically significant only when the results--*e.g.*, RR, OR, or SMR--are expressed with a 95% confidence interval,[16] and when that

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the population exposed to the factor as compared to the control population not exposed to the factor. . . . A relative risk of 1.0 means that the incidence of [the disease] in the two groups were the same. A relative risk greater than 1.0 means that there [was more disease in the group exposed to the factor]." *Brock*, 874 F.2d at 312.

[14] "A measure of association, often used in epidemiology. For example, if 10% of all people exposed to a chemical develop a disease, compared with 5% of people who are not exposed, then the odds of the disease in the exposed group are 10/90 = 1/9, compared with 5/95 = 1/19 in the unexposed group. The odds ratio is (1/9)/(1/19) = 19/9 = 2.1. An odds ratio of 1 indicates no association." Reference Manual at 291.

[15] "SMR, or standardized mortality ratio, in epidemiology is the ratio of observed deaths to expected deaths according to a specific health outcome in a population. The calculation used to determine the SMR is simple: number of observed deaths/number of expected deaths. The SMR may be quoted as either a ratio or a percentage. If the SMR is quoted as a ratio and is equal to 1.0, then this means the number of observed deaths equals that of expected cases. If higher than 1.0, then there is a higher number of deaths than would be expected under normal circumstances. Similarly, an SMR of 100 would mean that the risk in the study population is equal to that of the general population. For example, an SMR of 641 represents a relative risk of dying from a particular cancer that is 6.4 times greater than that of the general population." *Taylor v. Airco, Inc.*, 494 F. Supp. 2d 21, 25 n.4 (D. Mass. 2007).

[16] Studies may also employ a 90% confidence interval.

interval does not include the number 1.0. *See Brock*, 874 F.2d at 312. As the Fifth Circuit has explained:

> [I]f a study concluded that the relative risk for [a disease] was 1.30, which is consistent with a 30% elevated risk of harm, but the confidence interval was from 0.95 to 1.82, then no statistically significant conclusions could be drawn from this study because the relative risk, when adjusted by the confidence interval, includes 1.0. Again, it is important to remember that the confidence interval attempts to express mathematically the magnitude of possible error, due to the above mentioned sources as well as others, and therefore a study with a relative risk of greater than 1.0 must always be considered in light of its confidence interval before one can draw conclusions from it.

Id. Some courts require opinions on general causation to be grounded in studies demonstrating a statistically significant relative risk greater than 2.0. *See Daubert*, 43 F.3d at 1321 (requiring a relative risk of greater than 2.0 for an epidemiology study to show causation under a preponderance standard); *Siharth v. Sandoz Pharms. Corp.*, 131 F. Supp. 2d 1347, 1356 (N.D. Ga. 2001) ("[I]n the world of epidemiology, the threshold for concluding that an agent was more likely than not the cause of a disease is a relative risk greater than 2.0."). The Fifth Circuit has not adopted such a requirement.

Second, a study that provides merely "a suggestion or possibility of a relationship is insufficient for a causation opinion." *In re Breast Implant Litig.*, 11 F. Supp. at 1233; *see also Knight*, 482 F.3d at 353 ("Although the study's 'suggestion' could theoretically provide some basis for the conclusion that

diesel exhaust causes bladder cancer, it does not, as appellants argue, 'clearly support' that conclusion."). The same is true of a study that "only provides an arguable inferential starting point" for finding a causal relationship. *LeBlanc*, 396 F. App'x at 99. Studies that are inconclusive and merely recommend that further studies be done are likely to fall into this category. *See In re Breast Implant Litig.*, 11 F. Supp. at 1231. This is not to suggest that studies must unequivocally support a general causation opinion, but they must provide more than a hypothesis.

Third, a study that notes "that the subjects were exposed to a range of substances and then nonspecifically note[s] increases in disease incidence" can be disregarded. *LeBlanc*, 396 F. App'x at 99; *see also Joiner*, 522 U.S. at 146 (holding that an expert's reliance on a study was misplaced when the subjects of the study "had been exposed to numerous potential carcinogens"); *Knight*, 482 F.3d at 353 ("Of all the organic solvents the study controlled for, it could not determine which led to an increased risk of cancer . . . . The study does not provide a reliable basis for the opinion that the types of chemicals appellants were exposed to could cause their particular injuries in the general population."). Likewise, studies that do not examine the precise disease at issue may not provide good grounds for an expert's opinion. *See Henricksen v. Conoco Phillips Co.*, 605 F. Supp. 2d 1142, 1171-75 (E.D. Wa. 2009) (calling into question the relevance of studies

that did not study the specific disease at issue).

Fourth, when a study's authors expressly disclaim the causal relationship that the expert relies upon the study to prove, the study likely does not provide a reliable basis for the expert's opinion. *See Joiner*, 522 U.S. at 145 (holding that a study did not support an expert's opinion on causation when the study was "unwilling to say that PCB exposure had caused cancer"); *LeBlanc*, 396 F. App'x at 100 ("The district court properly rejected the studies as supporting causation because the authors of the studies concluded that there was no proof of causation."); *McClain v. Metabolife Int'l, Inc.*, 401 F.3d 1233, 1248 (11th Cir. 2005) (criticizing an expert for drawing "unauthorized conclusions from limited data--conclusions the authors of the study do not make").

Case reports, which anecdotally describe an occurrence, often on an individual basis, cannot establish general causation "because they simply describe[] reported phenomena without comparison to the rate at which the phenomena occur in the general population or in a defined control group; do not isolate and exclude potentially alternative causes; and do not investigate or explain the mechanism of causation." *Casey v. Ohio Med. Prods.*, 877 F. Supp. 1380, 1385 (N.D. Cal. 1995); *see also Siharath*, 131 F. Supp. 2d at 1361 (collecting cases).

As to the conclusions and guidance of regulatory and advisory bodies that a substance is carcinogenic, courts have cautioned that

they, alone, do not provide a reliable basis for establishing legal causation. The Fifth Circuit has explained:

> Regulatory and advisory bodies such as IARC, OSHA and EPA utilize a "weight of the evidence" method to assess the carcinogenicity of various substances in human beings and suggest or make prophylactic rules governing human exposure. This methodology results from the preventive perspective that the agencies adopt in order to reduce public exposure to harmful substances. The agencies' threshold of proof is reasonably lower than that appropriate in tort law, which "traditionally make[s] more particularized inquiries into cause and effect" and requires a plaintiff to prove "that it is more likely than not that another individual has caused him or her harm."

Allen v. Pa. Eng'g Corp., 102 F.3d 194, 198 (5th Cir. 1996) (quoting *Wright v. Williamette Indus., Inc.*, 91 F.3d 1105, 1107 (8th Cir. 1996)); *see also Baker*, 680 F. Supp. 2d at 880 ("The mere fact that Plaintiffs were exposed to benzene emissions in excess of mandated limits is insufficient to establish causation."); *Parker v. Mobil Oil Corp.*, 7 N.Y. 3d 434, 450 (N.Y. 2006) (finding that "standards promulgated by regulatory agencies as protective measures are inadequate to demonstrate legal causation"); David L. Eaton, *Scientific Judgment and Toxic Torts--A Primer in Toxicology for Judges and Lawyers*, 12 J. L. & Pol'y 5, 36 (2003) ("[R]egulatory levels are of substantial value to public health agencies charged with ensuring the protection of the public health, but are of limited value in judging whether a particular exposure was a substantial contributing factor to a particular individual's disease or illness.").

B. Analysis

The Court has performed an extensive review of the parties' briefings and submissions, Dr. Infante's report and testimony, and the relevant scientific literature. After this review, the Court finds that Dr. Infante's general causation opinion is not grounded in a reliable methodology. Dr. Infante's methodology is flawed because he relies on multiple studies that do not reliably support or do not otherwise "fit" his conclusion. Ultimately, there is simply too great an analytical gap between the underlying data and the opinion offered.

1. Dr. Infante's Reliance on Benzene Studies

The majority of the literature on which Dr. Infante relies in formulating his general causation opinion relates to studies examining the risks associated with exposure to benzene in general, not studies examining the risks associated with exposure to gasoline. Out of Dr. Infante's 102-page report, he devoted 54 pages to literature pertaining to benzene exposure generally and only 14 pages to literature pertaining specifically to gasoline exposure. But here, Mr. Burst allegedly sustained exposure to gasoline containing benzene, not pure benzene or any other substance containing benzene. The question here, therefore, is whether exposure to gasoline containing benzene can cause AML, not whether exposure to benzene generally can cause AML. *See Henricksen*, 605 F. Supp. 2d at 1156 ("This is a products liability

action and Defendant's product is gasoline."). Dr. Infante does discuss the gasoline literature and he does conclude that gasoline exposure can cause AML. But, contrary to Dr. Infante's contention, the data related to gasoline exposure is far from consistent with the data related to benzene exposure.

Because benzene is a known human carcinogen and because all gasoline contains benzene, the Court recognizes that literature pertaining to benzene is generally relevant to the causation question at issue. Still, there are important reasons to question the sufficiency of this knowledge as it relates to Dr. Infante's general causation opinion.

The parties do not dispute that, at certain levels of exposure, benzene can cause AML. Dr. David Pyatt, defendants' expert toxicologist, recognized that benzene is one of the most studied substances in the world, and that it is a carcinogen is widely accepted. The EPA, OSHA, IARC, Agency for Toxic Substances and Disease Registry (ATSDR), and other scientific bodies all categorize benzene as a human carcinogen. Despite this consensus, no scientific authority has classified gasoline as a human carcinogen. For example, IARC has concluded: "There is *inadequate evidence* for the carcinogenicity in humans of gasoline." IARC, Monographs on the Evaluation of Carcinogenic Risks to Humans, Vol. 45, Occupational Exposures in Petroleum Refining; Crude Oil and Major Petroleum Fuels (1989) (emphasis in original). Likewise, the

ATSDR Toxicological Profile for Gasoline (1995) concluded that there is no conclusive evidence to support a finding that gasoline causes cancer.[17] Specifically, the ATSDR report stated:

> Benzene, a component of gasoline, is a known human carcinogen that has been shown to cause an increased incidence of hematopoietic cancers (leukemia) in occupational exposed workers . . . . However, . . . the evidence for an association between increased incidence of cancer (including leukemia) and exposure to gasoline in humans is inadequate. Further, while there is sufficient evidence that benzene is carcinogenic in rats, causing an increased incidence of tumors at multiple sites . . . , gasoline has only been shown to cause increased incidences of renal cell tumors in male rats (a finding that is not considered relevant to humans) and liver tumors in female mice. Therefore, there is no conclusive evidence to support or refute the carcinogenic potential of gasoline in humans or animals based on the carcinogenicity of one of its components, benzene.[18]

To explain why gasoline has not been found to be carcinogenic, defendants proffer two explanations. First, defendants assert that because gasoline contains only small concentrations of benzene, individuals cannot be exposed to sufficient levels of benzene from gasoline to be at risk for AML. Second, defendants assert that because gasoline is a mixture of substances, including benzene and toluene, "competitive inhibition" between the different substances may impede the metabolism of benzene. For example, Dr. Pyatt,

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[17] Although the ATSDR published this report in 1995, it remains the current position of the agency. *See* ATSDR, Public Health Statement for Automotive Gasoline, http://www.atsdr.cdc.gov/PHS/PHS.asp?id=466&tid=83 (last visited June 16, 2015) ("[T]here is no evidence that exposure to gasoline causes cancer in humans.").

[18] Defense Ex. A-2 at 87.

citing multiple studies, hypothesizes that competitive inhibition occurs between toluene and benzene whereby co-exposure to the substances, as opposed to exposure to just benzene, results in the reduced metabolism of benzene.[19]

Consistent with defendants' contention that the literature pertaining to gasoline exposure is most relevant and that Dr. Infante's reliance on the benzene literature is improper, a district court, addressing the same general causation opinion offered by Dr. Infante, stated that while "evaluations of both gasoline and its toxic component benzene are obviously relevant to" plaintiff's case, "the court cannot simply presume that the qualitative toxic and carcinogenic effects of benzene from *any source* are the same." *Henricksen*, 605 F. Supp. 2d at 1156; *see also Rider v. Sandoz Pharm. Corp.*, 295 F.3d 1194, 1201 (11th Cir. 2002) ("Even minor deviations in chemical structure can radically change a particular substance's properties and propensities."). In *Henricksen*, the district court held that "[i]f it is possible to extrapolate from studies of benzene or other benzene-containing products conclusions regarding gasoline, then it will be incumbent upon [plaintiff] to explain and demonstrate why the extrapolation is scientifically proper." *Henricksen*, 605 F. Supp. 2d at 1156.

The Court finds that although evaluation of the benzene

[19] In contrast, Dr. Infante cites animal studies which he contends show that simultaneous exposure to toluene and benzene may enhance the toxicity of benzene. Infante Report at 42.

literature is generally relevant to Dr. Infante's ultimate opinion, *see Dickson v. Nat'l Maint. & Repair of Ky., Inc.*, No. 5:08-CV-00008, 2011 WL 12538613, at *6 (W.D. Ky. April 28, 2011) ("Benzene may be considered a causative agent despite only being a component of the alleged harm."), it, alone, cannot provide a reliable basis for Dr. Infante's opinion. While seemingly all scientific authorities recognize benzene as a carcinogen, none recognizes gasoline as a carcinogen, and defendants have offered several justifications for why exposure to benzene in gasoline should be evaluated differently than exposure to benzene generally. As such, while the Court recognizes the general relevance of these studies, they alone do not provide sufficient grounds to reliably support Dr. Infante's general causation opinion.

2. Dr. Infante's Reliance on the Gasoline Literature

The Court now turns to Dr. Infante's review of and reliance on the gasoline literature.[20] After an extensive review of the studies on which Dr. Infante relied, the Court concludes that Dr. Infante's methodology is deficient for a number of reasons. First, Dr. Infante relies on a number of studies that did not isolate exposure to gasoline, the relevant product at issue, or did not provide exposure metrics. Second, Dr. Infante relies on studies that did not exhibit statistically significant results or did not indicate

[20] While Dr. Infante cites numerous sources in his report, the Court primarily limits its discussion to the relevant literature discussed at the *Daubert* hearing.

a positive association between gasoline exposure and AML. Third, Dr. Infante relies on studies that did not specifically examine AML, the disease at issue, and instead examined leukemia generally or other types of leukemia. Finally, in several instances, Dr. Infante cherry-picked data from studies that did not otherwise support his conclusion, failed to explain contrary results, reached conclusions the authors of the study did not themselves make, and manipulated data without providing any evidence of his work. Exacerbating Dr. Infante's methodological failings is that even in light of the inconsistent and conflicting studies on which he relies and the paucity of scientific literature supporting his conclusion, he fails to provide a meaningful analysis in which he reconciles conflicting studies or applies the Bradford Hill criteria to the gasoline-specific studies.

a. Studies that Do Not Isolate Gasoline Exposure or that Do Not Provide Exposure Metrics

Dr. Infante's reliance on studies that did not isolate gasoline exposure from exposure to other substances cannot reliably support his opinion. *See LeBlanc*, 393 F. App'x at 99 (noting a study indicating "that the subjects were exposed to a range of substances and then nonspecifically not[ing] increases in disease incidence" can be disregarded); ATSDR Toxicological Profile on Gasoline (1995) (highlighting "concurrent exposure to other potentially carcinogenic substances (*i.e.*, service station attendants are also exposed to motor oils, diesel fuel oils, and

solvents as well as automobile and truck engine exhaust)" as a characteristic of studies containing "inherent limitations that preclude their use as evidence for an association between gasoline exposure and cancer in humans"). In other words, unless a study isolates exposure to gasoline from other products containing benzene, it cannot support the conclusion that the benzene in gasoline is the causative agent. As an example, Dr. Infante relied on Schwartz, E., *Proportionate Mortality Ratio Analysis of Automobile Mechanics and Gasoline Service Station Workers in New Hampshire*, 12 AM. J. INDUS. MED. 91 (1987).[21] In his report, without any notation or caution, Dr. Infante stated that the study demonstrated "[w]orkers in the gasoline service station industry experienced a leukemia mortality excess of more than 3-fold which was statistically significant (PMR = 3.28, $p < 0.05$)."[22] Dr. Infante failed to acknowledge that the workers in the study sustained potential exposure to gasoline vapor, benzene, solvents, lubricating oils, asbestos, welding fumes, and car and truck exhaust, or that Schwartz concluded that "the results of this analysis suggest that one or more of the exposures experienced by automobile mechanics and service station workers poses a carcinogenic risk." Likewise, Dr. Infante did not acknowledge the study's guidance that "[m]ore definitive epidemiologic studies are

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[21] Plaintiff's Ex. 8.

[22] Infante Report at 67.

required to determine if the leukemia excess is associated with exposure to benzene, gasoline, or other workplace substances." Dr. Infante's reliance on a number of other studies is similarly flawed. *See* Hunting, K., *et al.*, *Haematopoietic Cancer Mortality Among Vehicle Mechanics*, 52 OCCUP. ENVTL. MED. 673 (1995)[23] (noting that, in addition to gasoline, workers sustained potential exposures to degreasing agents, diesel fuel, asbestos from brake work, used motor oils, Varsol, spray cans of brake, battery, or carburetor cleaner, and that some workers also experienced other exposures during welding, spray painting, sheet metal work, carpentry, and tire repair operations); Lindquist, R., *et al.*, *Acute Leukemia in Professional Drivers Exposed to Gasoline and Diesel*, 42 EUR. J. HAEMATOL. 98 (1991)[24] (noting professional drivers were exposed to petroleum products, including gasoline, diesel, aircraft fuels, and their combustion products, and finding "an etiological relationship between the development of acute leukemia and exposure to petroleum products as fuel and exhaust"); Sathiakamur, N., *et al.*, *A Case Control Study of Leukemia Among Petroleum Workers*, 37 J. OCCUP. & ENVTL. MED. 1269 (1995)[25] (examining risks associated with exposure to crude oil).

Dr. Infante's reliance on studies that do not quantify

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[23] Plaintiff's Ex. 14.

[24] Plaintiff's Ex. 22.

[25] Plaintiff's Ex. 23A.

gasoline exposure is equally problematic. *See* ATSDR Toxicological Profile on Gasoline (1995) (highlighting studies' "lack of information on levels of exposure to gasoline vapor" as one of "several inherent limitations that preclude their use as evidence for an association between gasoline exposure and cancer in humans"). For example, many of the studies on which Dr. Infante relied examined workers in certain occupations, such as petroleum distribution workers or gasoline service station attendants, instead of examining gasoline exposure directly. *See* Terry, P., *et al.*, *Occupation, Hobbies, and Acute Leukemia in Adults*, 29 LEUKEMIA RES. 1117 (2005)[26] (examining the association between AML and employment as a gasoline station attendant and employment in the petroleum industry); Schnatter, A., *et al.*, *A Retrospective Mortality Study among Canadian Petroleum Marketing and Distribution Workers*, 101 ENVTL. HEALTH PERSP. 85 (1993)[27] (examining the association between truck drivers exposed to "finished hydrocarbons" and leukemia, but acknowledging that they had "no knowledge concerning the actual levels of benzene experienced by these truck drivers"); Schnatter, A., *et al.*, *Myelodysplastic Syndrome and Benzene Exposure Among Petroleum Workers: An International Pooled Analysis*, 104 J. NAT'L CANCER INST. 1724

[26] Plaintiff's Ex. 16.

[27] Plaintiff's Ex. 18.

(2012)[28] (examining the association between AML and ever working as a tanker truck driver without any elaboration as to the substances to which the drivers were exposed). While such professions may serve as an imprecise proxy for gasoline exposure, it is impossible to tell, and the studies do not indicate, to what substances and at what levels the workers were actually exposed. As stated, even gasoline service station attendants, the most relevant group of workers in this case, may be exposed to numerous substances in addition to gasoline. *See* ATSDR Toxicological Profile on Gasoline (1995) (noting that "service station attendants are also exposed to motor oils, diesel fuel oils, and solvents as well as automobile and truck engine exhaust"). In one of the few gasoline studies reviewed by Dr. Infante that actually made quantitative exposure estimates, Wong, O., *et al.*, *Health Effects of Gasoline Exposure. II. Mortality Patterns of Distribution Workers in the United States*, 101 ENVTL. HEALTH PERSP. SUPPL. 6 (1993),[29] the authors observed no statistically significant increased risk for AML in workers exposed to gasoline.

b. Studies that Do Not Exhibit Statistically Significant Results

Dr. Infante's reliance on studies exhibiting results that are not statistically significant does not reliably support his

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[28] Plaintiff's Ex. 27.

[29] Plaintiff's Ex. 19.

opinion. *See Joiner*, 522 U.S. at 145; *LeBlanc*, 396 F. App'x at 99. While Dr. Infante's report generally acknowledges when a study did not demonstrate statistically significant results, he testified that such studies provide "some evidence" of an association thereby exhibiting his reliance upon them. For example, Rushton, L., *A 39-Year Follow-up of the U.K. Oil Refinery and Distribution Center Studies: Results for Kidney Cancer and Leukemia*, 101 ENVTL. HEALTH PERSP. SUPPL. 77 (1993),[30] did not observe a statistically significant increased risk of AML in workers employed at oil refineries. Nevertheless, Dr. Infante testified that this study provides "some evidence" that gasoline causes AML. The Court recognizes, as explained by Dr. Infante, that studies that do not demonstrate statistically significant results may be relied upon within the epidemiologic community in certain instances, but the guidance of the Supreme Court and the Fifth Circuit instructs that such studies do not reliably support epidemiologists' general causation opinions in the context of toxic tort litigation. Many of the studies on which Dr. Infante relied did not produce statistically significant results and his reliance on them is therefore questionable. *See* Wong, O., *et al.*, *Health Effects of Gasoline Exposure. II. Mortality Patterns of Distribution Workers in the United States*, 101 ENVTL. HEALTH PERSP. SUPPL. 6 (1993);[31]

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[30] Plaintiff's Ex. 17.

[31] Plaintiff's Ex. 19.

Sorahan, T., *et al.*, *Mortality of United Kingdom Oil Refinery and Petroleum Distribution Workers, 1951-1998*, 52 OCCUP. MED. 333 (2002);[32] Wong, O., *et al.*, *A Hospital-Based Case-Control Study of Acute Myeloid Leukemia in Shanghai: Analysis of Environmental and Occupational Risk Factors by Subtypes of the WHO Classification*, 184 CHEMICO-BIOLOGICAL INTERACTIONS 112 (2010);[33] Lynge, E., *et al.*, *Risk of Cancer and Exposure to Gasoline Vapors*, 145 AM. J. EPID. 449 (1997) (Dr. Infante relied on the non-significant results pertaining to the Swedish cohort); Lagorio, S., *et al.*, *Mortality of Filling Station Attendants*, 20 SCAND. J. WORK ENVTL. HEALTH 331 (1994).[34]

c. Studies that Do Not Examine AML Specifically

Third, many of the studies on which Dr. Infante relied did not examine the risk for AML specifically, and instead examined the risk of leukemia generally or other specific types of leukemia. Because Mr. Burst's physicians diagnosed him with AML, not some other type of leukemia, and because the specific type of leukemia is relevant to the general causation question at issue, Dr. Infante's reliance on such studies does not reliably support his opinion that gasoline causes AML. *See* ATSDR Toxicological Profile on Gasoline (1995) ("It is very difficult to draw any definitive

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[32] Plaintiff's Ex. 24.

[33] Plaintiff's Ex. 42.

[34] Plaintiff's Ex. 9.

conclusions from" a study where "several different types of leukemia were reported."); Wong, O., *et al.*, *Health Effects of Gasoline Exposure. II. Mortality Patterns of Distribution Workers in the United States*, 101 ENVTL. HEALTH PERSP. SUPPL. 6 (1993)[35] ("Several previous epidemiologic studies indicate that exposure to benzene or petroleum products containing benzene may result in an increased risk of acute myeloid leukemia but not other cell types."). For example, Schwartz, E., *Proportionate Mortality Ratio Analysis of Automobile Mechanics and Gasoline Service Station Workers in New Hampshire*, 12 AM. J. INDUS. MED. 91 (1987), did not examine AML, but, instead, leukemia generally. Likewise, a significant number of studies on which Dr. Infante relied did not examine AML specifically. *See* Spivey, unpublished Union Oil internal report (1983)[36] (examining leukemia generally); Naizi, GA, Fleming, AF, *Blood Dyscrasia in Unofficial Vendors of Petrol and Heavy Oil and Motor Mechanics in Nigeria*, 19 TROP. DOCT. 55 (1989) (examining anemia, microcytosis, hypocromia, thrombocyotopenia, and neutropenia); Hunting, K., *et al.*, *Haematopoietic Cancer Mortality Among Vehicle Mechanics*, 52 OCCUP. ENVTL. MED. 673 (1995)[37] (examining leukemia and aleukemia and, while noting one case of AML, not providing any separate analysis for the risk of AML);

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[35] Plaintiff's Ex. 19.

[36] Plaintiff's Ex. 7.

[37] Plaintiff's Ex. 14.

Schnatter, AR, *et al.*, *A Retrospective Mortality Study among Canadian Petroleum Marketing and Distribution Workers*, 101 ENVTL. HEALTH PERSP. 85 (1993)[38] (examining leukemia generally); Lindquist, R., *et al.*, *Acute Leukemia in Professional Drivers Exposed to Gasoline and Diesel*, 42 EUR. J. HAEMATOL. 98 (1991)[39] (examining acute leukemia generally); Brandt, P., *et al.*, *Occupational Exposure to Petroleum Products in Men with Acute Non-Lymphocytic Leukaemia*, 1 BRITISH MED J 553 (1978)[40] (examining acute non-lymphocytic leukemia (ANLL), which Dr. Infante testified is not strictly limited to AML); Australian Health Watch, 10th (1998)[41] and 11th (2000)[42] Reports (examining leukemia generally).

d. Dr. Infante Cherry-Picks Data and Fails to Explain Contrary Results

Dr. Infante cherry-picks data from studies in several significant instances and fails to explain contrary results in a manner that belies the reliability of his methodology. For example, Dr. Infante cites Sandler, DP, *et al.*, *Exposure to Chemical and Risk for Myelodoysplastic Syndrome*, Abstract # S60, 28th Annual Meeting, Society for Epidemiologic Research, Snowbird,

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[38] Plaintiff's Ex. 18.

[39] Plaintiff's Ex. 22.

[40] Plaintiff's Ex. 6.

[41] Plaintiff's Ex. 44.

[42] Plaintiff's Ex. 25.

Utah (1995),[43] for its examination of the risk of myeldodysplastic syndrome (MDS) from exposure to gasoline, kerosene, and petroleum distillates. Absent from Dr. Infante's report is any acknowledgment that this study separately examined the risk for AML and did not find a statistically significant increased risk. The Court can only speculate as to why Dr. Infante neglected to discuss this pertinent finding in his report.

Similarly, at the hearing, Dr. Infate cited Wong, O., *et al.*, *A Hospital-Based Case-Control Study of Acute Myeloid Leukemia in Shanghai: Analysis of Environmental and Occupational Risk Factors by Subtypes of the WHO Classification*, 184 CHEMICO-BIOLOGICAL INTERACTIONS 112 (2010),[44] for its observation of an increased risk of AML in "unloading workers" and workers involved in home/workplace renovations. Dr. Infante explained that these workers were likely exposed to benzene and gasoline, and, therefore, concluded that the study supported his opinion. This same study, however, separately examined the relationship between gasoline exposure and AML and did not observe a statistically significant association (OR 1.07 95% CI 0.72-1.61).[45] That Dr.

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[43] Plaintiff's Ex. 15.

[44] Plaintiff's Ex. 42.

[45] Notably, despite not finding a statistically significant association between gasoline and AML, the study observed a statistically significant increased risk between benzene exposure and AML (OR 1.43 95% CI 1.05-1.93).

Infante disregards this directly applicable result in favor of other data involving workers with exposures to unidentified substances is problematic and suggests a methodology driven by an attempt to achieve a particular result.

Finally, Dr. Infante cites Lynge, E., *et al.*, *Risk of Cancer and Exposure to Gasoline Vapors*, 145 AM. J. EPID. 449 (1997), the largest study of service station workers occupationally exposed to gasoline and gasoline vapors. The authors studied cancer incidence in a cohort of 19,000 gasoline service station workers from Denmark, Norway, Sweden, and Finland. The authors identified workers from the 1970 censuses and followed them for 20 years. According to the authors, the benzene content in gasoline in Nordic countries at this time ranged from 2% to 6%. The study observed "no excess risk of leukemia or specifically of acute myeloid leukemia." Despite this finding, Dr. Infante stated that the study provides "some evidence in support of an association"[46] because one of the cohorts demonstrated a non-statistically significant increased risk of AML (8 cases observed versus 3.86 expected in the Swedish cohort). Dr. Infante relied on this result despite the authors' conclusion that the attendants' gasoline exposure posed "no excess risk of leukemia or specifically of acute myeloid leukemia."

[46] Infante Report at 70.

e. Dr. Infante Does Not Justify His Manipulation of Data

In other instances, Dr. Infante manipulated data in a manner not performed by the authors of the study. Even if, as Dr. Infante urges, this practice is common in the field of epidemiology, Dr. Infante repeatedly failed to show that he performed these manipulations in a reliable manner or that they are even appropriate. For example, Rushton, L., Romaniuk, H., *A Case-Control Study to Investigate the Risk of Leukaemia Associated with Exposure to Benzene in Petroleum Marketing and Distribution Workers in the United Kingdom*, 54 OCCUP. ENVTL. MED. 152 (1997),[47] examined petroleum distribution workers exposed to low levels of benzene. Dr. Infante relied on Table 5 of the study, which presented results based on cumulative exposure to benzene. There, the authors observed no statistically significant increased risk of acute myeloid or monocytic leukemia whether the workers were exposed to less than 0.45 ppm-years benzene, 0.45-4.49 ppm-years benzene, or 4.5-44.9 ppm-years benzene. While not statistically significant, the study observed an increased risk for the two lower exposure groups. Dr. Infante testified that the non-statistically significant increased risk for the two lower exposure groups "in and of itself provides evidence that low cumulative exposure to benzene is associated with an elevated risk of AML." Dr. Infante

[47] Plaintiff's Ex. 50.

also stated that if one combines the data from the 0.45-4.49 ppm-years group and the 4.5-44.9 ppm-years group, a positive association is observed. Dr. Infante stated that he did not perform an analysis for statistical significance on this figure, but asserted that the result would be statistically significant if he had. Unfortunately, the authors themselves did not perform this calculation, and Dr. Infante provides no indication of how he performed this calculation or whether it is appropriate. At the hearing, Dr. Infante explained that he performed the calculation on a "sticky note." The Court cannot credit Dr. Infante's calculations which involve calculating different results from separate data sets from this study without, at the very least, evidence of his calculations, let alone some indication of why this calculation is appropriate when the authors of the study chose not to perform it themselves. Dr. Infante's combination of two separate data sets from the Spivey study, an unpublished Union Oil internal report from 1983,[48] suffers from the same problem.[49]

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[48] Plaintiff's Ex. 7.

[49] There, Dr. Spivey examined the risk of leukemia associated with work as a garage and gas station attendant, fork lift and tow motor operator, petroleum engineer, painter, and auto mechanic. The study did not demonstrate a statistically significant excess risk of leukemia and did not specifically examine the risk of AML. In his report, Dr. Infante purports to combine the data from the garage and gas station attendants and the auto mechanics to produce a statistically significant result. Notably, Dr. Infante's calculation was not performed by the author of the study, and Dr. Infante does not provide any evidence of his own calculations. Without this, the Court is

Similarly, Dr. Infante adjusted the results of Wong, O., *et al.*, *Health Effects of Gasoline Exposure. II. Mortality Patterns of Distribution Workers in the United States*, 101 ENVTL. HEALTH PERSP. SUPPL. 6 (1993).[50] There, the authors studied a cohort of 18,135 gasoline distribution workers with potential exposure to gasoline for at least one year at land-based terminals or on marine vessels between 1946 and 1985. "[U]nlike most previous studies in the petroleum industry," the authors made "quantitative exposure estimates" as to the workers' exposures. This, the authors noted, permitted an analysis of whether a dose-response relationship existed, "one of the most important criteria in determining causation." The authors concluded:

> The results of this study indicate that there was no increased mortality from . . . leukemia among marketing and marine distribution employees in the petroleum industry, who were exposed to gasoline, when compared to the general population. Furthermore, based on internal comparisons, there was no association between mortality from . . . leukemia and various indices of gasoline exposure. In particular, neither duration of gasoline exposure, cumulative exposure, frequency of peak exposures, nor average intensity of exposure had any effect on . . . leukemia mortality.

The study observed a non-significant mortality increase from AML in land-based terminal employees, "but no trend was detected when the data were analyzed by various gasoline exposure indices." The

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unable to evaluate Dr. Infante's methodology.

[50] Plaintiff's Ex. 19.

authors noted that "[t]his nonsignificant excess was limited to land-based terminal employees hired before 1948" when benzene levels in the industry were likely higher.

Because the overall mortality of the cohort was only half of what was expected, Dr. Infante adjusted the land-based terminal employees results of this study for the "healthy worker effect." The healthy worker effect describes a phenomenon that can occur when studying occupational disease: "Workers usually exhibit lower overall death rates than the general population because the severely ill and chronically disabled are ordinarily excluded from employment." Last, J., *A Dictionary of Epidemiology* (3d ed. 1995). Because the workers may be healthier than the general population, comparing the incidence of disease or death in the workers to that of the general population may result in a bias. By adjusting for the healthy worker effect, Dr. Infante concluded that the excess rate of AML was in fact statistically significant, contrary to what Wong found.

Dr. Infante's adjustment for healthy worker effect is problematic in this instance. First, Dr. Infante provides no indication of how he adjusted for the healthy worker effect. Thus, the Court has no basis to evaluate his methodology to determine whether it is reliable. Second, Wong expressly acknowledged the impact of a healthy worker effect and chose not to adjust for it. Wong explained: "[B]ecause internal comparisons do not involve an

external comparison population [*e.g.*, the general population, which is presumably less healthy than the working population under study], our analyses and interpretation based on these internal comparisons would not be affected by the choice of an external comparison population." In other words, Wong explained that by comparing the data to both the general population and to internal subgroups, they accounted for potential bias created by healthy worker effect.[51] Dr. Infante provides no acknowledgment of this discussion or explanation of why his adjustment is appropriate in lieu of it.

Dr. Infante also adjusted the results of Sorahan, T., *et al.*, *Mortality of United Kingdom Oil Refinery and Petroleum Distribution Workers, 1951-1998*, 52 OCCUP. MED. 333 (2002),[52] for healthy worker effect. There, the authors performed a cohort study of 28,630 oil refinery workers and 16,480 petroleum distribution workers. The authors observed a SMR of 1.51 (95% CI 0.97-2.24) for AML and distribution workers, but the result was not statistically significant. The authors themselves recognized that "there is evidence of a healthy worker effect," but did not adjust their results. In two instances, the authors stated that "[i]t is

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[51] Referring to another study, Dr. Infante separately noted at the hearing that one would not observe much of a healthy worker effect if a cohort is compared to other workers instead of the general population.

[52] Plaintiff's Ex. 24.

important to gauge the size of this effect." According to Dr. Infante, "the SMR for all causes demonstrated a significant" healthy worker effect, so he adjusted the results accordingly.[53] Dr. Infante provided no explanation of how he adjusted for the bias or to what extent he did so, and instead, simply stated: "When this adjustment is made, the SMRs for total leukemia and for AML specifically are both statistically significant. For AML, SMR = 1.61 (95% CI = 1.03-2.39)."[54] The Court has no basis from which to evaluate whether Dr. Infante performed the adjustment correctly, or, for example, whether he reliably gauged the size of the effect.

The Court emphasizes that it does not question whether combining data sets and adjusting for bias such as that arising from the healthy worker effect is accepted in the field of epidemiology. In such instances, however, when an expert performs after-the-fact manipulations of published data, it is particularly important for the expert to provide not only a justification for doing so, but also some evidence of his work and the reliability of his method. An expert's solitary assurances do not allow the Court to ensure that the methodology is reliable.

f. Summary

In light of the Court's examination of the studies on which Dr. Infante relied, it is clear that Dr. Infante relied on a

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[53] Infante Report at 73.

[54] *Id.*

universe of divergent studies that either did not examine the substance at issue, did not examine the disease at issue, or did not exhibit statistically significant results. Moreover, Dr. Infante exhibited a willingness to ignore or disregard contrary results, and to manipulate data in a manner not supported by any evidence of his work or independent justification and, in one instance, inconsistent with the authors' own discussion.

Compounding Dr. Infante's methodological failings is that, despite analyzing a collection of studies inconsistent in both subject matter and results, Dr. Infante did not present a meaningful analysis in which he reconciled this conflicting group of studies. Instead of providing a rigorous analysis explaining how he came to his conclusion from the gasoline literature, Dr. Infante simply provides a literature review, at times supplemented by his own commentary, and states a conclusion. Notably, Dr. Infante employs no overall application of the Bradford Hill criteria, a bedrock of epidemiological methodology for determining issues of general causation, in analyzing the gasoline literature. While this approach may suffice in cases where numerous consistent studies produce similar results, this is not the case here. It bears emphasis that an expert's extrapolation from studies that are not directly on point or that do not unequivocally support his conclusion is not necessarily grounds to exclude the opinion as unreliable. Such practice may be appropriate in certain instances,

particularly when combined with other supporting information. But, as is the case here, when an expert exhibits wholesale reliance on such studies without any differentiation or attempt to explain why the studies remain relevant in light of their inconsistency with the facts of the case, the methodology is unreliable.

The Court's focus is Dr. Infante's underlying methodology, but the Court also notes that there is a paucity of scientific literature supporting Dr. Infante's opinion that gasoline can cause AML. *See Henricksen*, 605 F. Supp. 2d at 1175 ("None of the studies relied upon have concluded that gasoline has the same toxic effect as benzene, and none have concluded that the benzene component of gasoline is capable of *causing* AML."); *Castellow v. Chevron USA*, 97 F. Supp. 2d 780, 796 (S.D. Tex. 2000) ("Plaintiffs here have not shown that the relevant scientific or medical literature supports the conclusion that workers exposed to benzene, as a component of gasoline, face a statistically significant risk of an increase in the rate of AML."); *Parker*, 7 N.Y. 3d at 450 ("[N]o significant association has been found between gasoline exposure and AML. Plaintiff's experts were unable to identify a single epidemiologic study finding an increased risk of AML as a result of exposure to gasoline."). Moreover, no regulatory or advisory body has concluded that gasoline can cause AML, *see Henricksen*, 605 F. Supp. 2d. at 1151 (noting that "no authoritative source (organization or regulatory agency) has identified gasoline as cancer-causing"),

even though, as noted by the Fifth Circuit, regulatory bodies apply a lower threshold of proof in determining issues of causation than is "appropriate in tort law." *Allen*, 102 F.3d at 198. The dearth of supporting literature renders a significant void that makes Dr. Infante's methodological failings even more problematic.

Further, even if the Court's sifting of the literature yielded a few studies that could plausibly support Dr. Infante's opinion,[55] the vast majority of studies do not fit Dr. Infante's conclusion

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[55] For example, Jakobsson, R., *et al.*, *Acute Myeloid Leukemia Among Petrol Station Attendants*, 48 ARCH. ENVTL. HEALTH 255 (1993), studied the risk of AML within different occupations using occupational information obtained from the Swedish census of 1970. The study observed 10 cases of AML in male petrol station attendants versus 2.8 expected, yielding a statistically significant odds ratio of 3.6 (95% CI 1.7-6.6). The authors posited that "[a] reasonable hypothesis was that exposure to benzene from petrol had contributed to the excess risk of AML, given that petrol in Sweden has contained up to 5% of benzene for several decades." The authors later noted, however, that two of the ten workers with AML had handled other petroleum products. Further, the district court in *Henricksen* recognized that "[t]his study has been criticized for various reasons by other scientists, including for the discovery that [three] of the reported AML cases never worked as petrol service attendants and three others only did so for a short time." *Henricksen*, 605 F. Supp. at 1173.

Talbot, EO, *et al.*, *Risk of Leukemia as a Result of Community Exposure to Gasoline Vapors: A Follow-Up Study*, 111 ENVTL. RES. 597 (2011), examined the risk of leukemia and AML in residents of a Pennsylvania community affected by a gasoline spill in the 1990s. The study produced statistically significant SIRs of 7.69 and 11.54 for leukemia and AML, respectively, in the highest exposure area, which the authors concluded "suggest[s] a possible association between chronic low level benzene exposure and increased risk of leukemia among residents" of the gasoline spill site. The authors noted that "[t]he lack of specific individual level exposures . . . is a limitation of the study."

and his reliance on them makes his opinion unreliable. *See Knight*, 482 F.3d at 355 ("Even if one of the studies relied on by [the expert] provided a plausible basis for general causation, the district court, after weighing the 'reliability' and 'relevance' of such evidence, finding one or the other lacking, could still reach the conclusion that the evidence was inadmissible."). The Court must examine an expert's overall methodology to determine whether it is reliable, and not simply accept an otherwise deficient methodology because there is a scintilla of material that might arguably support the expert's opinion. This is especially the case here because "[i]t is important that a study be replicated in different populations and by different investigators before a causal relationship is accepted by epidemiologists and other scientists." Reference Manual at 604.

Because the Court excludes Dr. Infante's opinion on general causation and there is no other admissible general causation evidence in this case, his specific causation testimony is also inadmissible. *See Knight*, 482 F.3d at 351 (stating that a court may admit specific-causation evidence only after the plaintiff has produced admissible evidence on general causation).

IV. CONCLUSION

For the foregoing reasons, the Court GRANTS defendants' motion to exclude Dr. Peter Infante.

New Orleans, Louisiana, this 16th day of June, 2015.

SARAH S. VANCE

UNITED STATES DISTRICT JUDGE