IN THE SUPREME COURT OF THE STATE OF DELAWARE

IN RE ZANTAC (RANITIDINE) LITIGATION	§	No. 255, 2024
	§	Court Below:
	§	Superior Court of the State of Delaware
	§	C.A. No. N22C-09-101

Submitted: April 16, 2025
Decided: July 10, 2025

Before **SEITZ**, Chief Justice; **VALIHURA**, **TRAYNOR**, **LEGROW**, and **GRIFFITHS**, Justices, constituting the Court *en Banc*.

Upon appeal from the Superior Court of the State of Delaware. **REVERSED.**

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LEGROW, Justice:

This Court accepted an interlocutory appeal from the Superior Court's decision denying a series of motions that sought to exclude several expert reports proffered by the plaintiffs in support of their position that Zantac containing ranitidine—or its generic—is capable of causing the ten types of cancers at issue in this case. In their motions, the defendants raised several objections to the methodologies that the plaintiffs' experts employed to support their general causation conclusions. The Superior Court, however, concluded that all those objections amounted to disputes that were questions for the jury, not the trial judge. In so doing, the court referred to the "liberal thrust" of Delaware's evidentiary rules as favoring the admissibility of expert testimony, concluded that Delaware's rule is distinct from the analogous federal rule, and held that the expert's general causation conclusions could be based on the alleged disease-causing agent, rather than the product at issue in this case.

We reverse. First, the Superior Court erred in adopting a standard that favored or presumed the admissibility of expert testimony. Under our rules and existing precedent, the proponent of an expert opinion bears the burden of establishing that the opinion is based on sufficient facts or data and on dependable principles and methods that are reliably applied to the facts of the case. Unless these sufficiency and reliability elements are established by a preponderance of the evidence, the opinion is not admissible. Delaware's evidentiary rules governing expert testimony

are consistent with federal law. A trial judge must act as the gatekeeper of expert testimony and should not dismiss challenges to the sufficiency or reliability of an expert opinion by viewing the disputes as questions for the jury to weigh.

Second, the trial court erred in framing the general causation question at issue in this case. General causation addresses whether the substance at issue is capable of causing the harm alleged. The court concluded that the experts could base their conclusions on studies regarding the alleged disease-causing agent rather than the product at issue in the case, without establishing a reliable bridge between the product at issue and the scientific data regarding the toxic agent. In so holding, the trial court failed to require the experts to apply a reliable scientific methodology to reach their conclusion that the exposure to the toxic agent in the studies on which the experts relied was comparable to the exposure to the toxic agent caused by the product. That holding was inconsistent with Delaware law.

I. FACTUAL AND PROCEDURAL BACKGROUND[1]

This interlocutory appeal arises out of personal injury claims filed in the Superior Court. Nearly 75,000 plaintiffs (the "Plaintiffs") alleged that their ingestion of the molecule ranitidine, marketed under the brand name Zantac—in

[1] Unless otherwise stated, the facts are adopted from the *In re Zantac (Ranitidine) Litig.*, 2024 WL 2812168 (Del. Super. May 31, 2024) (footnotes and record citations omitted) [hereinafter the "Order at __"].

which N-Nitrosodimethylamine ("NDMA"), a likely carcinogen, may be found—caused the cancer with which they were diagnosed (the "Zantac Litigation").[2]

A. Zantac's History

The Defendants-below, Appellants are GlaxoSmithKline LLC ("GSK"); Boehringer Ingelheim Pharmaceuticals, Inc., Boehringer Ingelheim Corporation, and Ingelheim U.S.A. Corporation (collectively, "B.I."); Sanofi US Services Inc., Sanofi-Aventis U.S. LLC, and Chattem, Inc. (collectively, "Sanofi"); Pfizer Inc. ("Pfizer") (together with GSK, B.I., and Sanofi, the "Brand Defendants"); and Patheon (together with the Brand Defendants, the "Defendants").

Ranitidine is a histamine-2 receptor blocker used to "treat heartburn and many other gastro-intestinal disorders, including duodenal ulcers, gastroesophageal reflux disease ("GERD") and esophagitis."[3] In 1983, the FDA approved ranitidine for prescription use to treat ulcers and later approved it to treat other stomach and esophageal conditions. In 1995, the FDA approved ranitidine for low dose over-the-counter ("OTC") use, and by 2004, the FDA had approved higher doses of ranitidine for OTC use.

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[2] Ranitidine has not been sold in the United States since the U.S. Food and Drug Administration issued a voluntary recall of the product in the spring of 2020. All manufacturers complied with the voluntary recall. Ranitidine was sold under the brand name Zantac during the pendency of the events of the litigation, and we therefore use ranitidine and Zantac interchangeably in this opinion, as do the parties to this litigation.

[3] *In re Zantac (Ranitidine) Prods. Liab. Litig.*, 644 F. Supp. 3d 1075, 1094-95 (S.D. Fla. 2022) [hereinafter the "MDL Order" at ___].

During the more than 35 years that ranitidine was on the market, four brand pharmaceutical companies and generic manufacturers sold versions of the product.[4] GSK developed the medication and initially marketed it in prescription form. In 1995, GSK marketed it as an OTC medication in a joint venture with a predecessor of Pfizer. In 1998, GSK transferred its rights to sell OTC Zantac in the U.S. to that Pfizer predecessor. In 2006, B.I. acquired the rights to sell OTC Zantac. In 2017, Defendant Sanofi began selling OTC Zantac after acquiring the brand from B.I.

In September 2019, a citizen petition submitted to the FDA sparked a recall of ranitidine. A private company and online pharmacy called Valisure theorized that ranitidine had the potential to degrade into NDMA. To evaluate this theory, Valisure tested batches of ranitidine under various conditions and found high levels of NDMA. Based on those findings, Valisure submitted a citizen petition to the FDA asserting that ranitidine contains "extremely high levels of [] NDMA."[5] Valisure reported that its study found NDMA at levels in excess of three million nanograms per tablet, exceeding the limit of 96 nanograms per day that the FDA had set for NDMA ingestion in the context of an unrelated class of medications.

"NDMA is an N-nitrosamine impurity," and multiple health agencies in the United States and other countries "consider NDMA to be [either] a probable human

[4] Patheon was a contract manufacturing organization ("CMO") for Zantac.

[5] Order at *2.

carcinogen" or "a reasonably anticipated human carcinogen."[6] But "NDMA is a ubiquitous substance found in trace amounts in air, water, and food."[7] "Studies have [] shown that NDMA increases the risk of cancer in humans and animals. As a result of findings like these, the FDA had set an acceptable daily intake ("ADI") limit for NDMA at 96 nanograms."[8]

After reviewing Valisure's petition, the FDA raised concerns about the study's testing methodology.[9] The FDA also voiced concerns with Valisure's findings which, when replicated, did not produce the same results.[10] Despite those inconsistencies, the FDA and ranitidine manufacturers studied NDMA in ranitidine

[6] MDL Order at 1095.

[7] *Id.* at 1106.

[8] *Id.* at 1095.

[9] *See id.* at 1092 ("To achieve a test result of 3,000,000 ng, however, Valisure had to heat the ranitidine to a temperature well above the 98 degrees Fahrenheit found in the human body; Valisure used a temperature of 266 degrees Fahrenheit. When Valisure tested ranitidine with a temperature of 98 degrees Fahrenheit, Valisure detected no NDMA. Valisure's testing, however, extended beyond just temperature-based tests. Using the human body's base temperature, Valisure tested ranitidine's reaction with salt in an artificial stomach. Once ranitidine was mixed with salt, Valisure detected NDMA in excess of 300,000 ng. The amount of salt Valisure used, however, is worth noting. According to a Plaintiffs' expert in this MDL, the amount of salt Valisure used to generate 300,000 ng of NDMA was so great that it was close to the level where, upon consumption, the salt intake would cause death. When Valisure tested ranitidine with salt concentrations more closely approximating what a human could safely ingest, Valisure detected no NDMA.").

[10] *See id.* ("The FDA did not immediately act on Valisure's information, however, for at least two reasons. First, the FDA concluded that the laboratory equipment that Valisure used to test for NDMA actually created NDMA. In other words, Valisure's laboratory equipment created the very substance for which it was testing. Second, the FDA wanted to conduct its own tests using laboratory equipment that did not create NDMA. Using its own laboratory equipment, the FDA tested ranitidine pills from several different manufacturers. Some of the ranitidine pills tested showed no NDMA or almost no NDMA. Others showed NDMA, but the NDMA was below the FDA's limit of 96 ng.").

and examined whether ranitidine use increased cancer risks in patients. Over the next month, tests revealed NDMA amounts lower than what Valisure reported. Some of the lots tested contained amounts below the acceptable daily intake ("ADI"). "Some ranitidine pills did show NDMA above 96 ng, but even the highest-tested pill showed NDMA at a tiny fraction of the level reported by Valisure."[11]

In the fall of 2019, the manufacturers who were then selling ranitidine voluntarily recalled their products.[12] By April 2020—after further testing confirmed that the NDMA levels in some samples continued to exceed the ADI—the FDA requested that manufacturers initiate a withdrawal of all remaining batches on the market.

B. Procedural History

After the ranitidine recall, litigation ensued nationwide. The plaintiffs in those cases allege that the ranitidine they consumed degraded into NDMA and caused them to develop various types of cancer. Before the claims in Delaware were filed, a Multidistrict Litigation in Florida was formed to address similar claims that ranitidine caused the plaintiffs to develop cancer.

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[11] *Id.*

[12] *See id.* ("Why then did the FDA initiate a voluntary recall of ranitidine? Although the FDA's tests revealed NDMA levels far below Valisure's, and although many of the FDA's tests showed NDMA levels that were acceptable, the fact remained that some of the FDA's tests showed ranitidine samples that eclipsed the 96 ng daily limit. Based upon the potential of some ranitidine pills to eclipse the 96 ng limit, the FDA initiated its voluntary recall of ranitidine.").

i. National Procedural History—The "MDL"

To address the claims filed in federal court, the United States Judicial Panel on Multidistrict Litigation established a multidistrict litigation process (the "MDL") in February 2020 in the U.S. District Court for the Southern District of Florida in West Palm Beach for all pretrial purposes. The Judicial Panel ordered federal lawsuits for personal injury and economic damages from the purchase or use of Zantac to be transferred to the MDL.

The claims in the MDL narrowed over time. First, the plaintiffs notified the MDL court that they had decided not to pursue general causation expert reports for breast and kidney cancers and had narrowed their initial list of cancers purportedly caused by ranitidine ingestion from ten to eight. In January 2022, the MDL plaintiffs again notified the court that they were not pursuing claims related to certain cancers, and further narrowed the list of associated cancers to five. Shortly after the MDL plaintiffs notified the MDL court that they would not provide general causation opinions for five cancers,[13] many of the MDL claimants with those cancers refiled their claims in Delaware.

In early 2022, the MDL court held a *Daubert* hearing to examine plaintiffs' experts' general causation opinions that Zantac caused five types of cancer in the

[13] The MDL court noted that the plaintiffs in the MDL intended to "prove that ranitidine causes bladder, esophageal, gastric, liver, and pancreatic cancers (the 'Designated Cancers'), as opposed to other cancers ('Non-Designated Cancers.')." *Id.* at 1098.

patients who ingested it. On December 6, 2022, the MDL court issued its opinion on the pending *Daubert* and summary judgment motions ("MDL Order"). In its 200-page opinion, the MDL court, in pertinent part, excluded the plaintiffs' experts' general causation opinions and granted summary judgment for Defendants. The court found that the MDL plaintiffs' experts improperly supported their general causation opinions by extrapolating data "not on the conclusions of any ranitidine-based study author, but instead (for the most part) upon the raw data found in studies that analyzed NDMA-rich food and NDMA-rich air . . . [including] studies focused on the consumption of processed meats and the inhalation of fumes in rubber factories."[14]

The MDL court made three findings of significance to the issues before us on appeal, each of which formed the bases for its *Daubert* ruling. First, the court addressed the issue of threshold dose and held that "Plaintiffs must identify a threshold dose range at which ranitidine can cause cancer . . . ."[15] The MDL court reasoned that case law in that circuit requires a plaintiff to identify either a threshold dose or a range of doses, and "the Plaintiffs minimize the importance of the concept of the amount of any potential risk from ranitidine consumption."[16] The MDL court

[14] *See id.* at 1093–94.

[15] *See id.* at 1109.

[16] *See id.*

noted that "[t]he question of general causation is not satisfied simply because an infinitesimal risk of cancer is more than zero risk."[17]

Second, the MDL court addressed the experts' reliance on NDMA studies to form their opinions about ranitidine. The MDL court held that a general causation inquiry must focus on ranitidine, not extrapolations from studies about an allegedly harmful component of the medication.[18] The MDL court held that "the Plaintiffs must show that ranitidine consumption can result in sufficient NDMA ingestion to cause their alleged injuries."[19] The court went on to admonish the MDL plaintiffs' experts' focus on NDMA because, among other reasons, "[t]he amount of NDMA in ranitidine is uncertain" and "[a] critical, important benefit of the ranitidine epidemiology is that it removes this question from the estimate of cancer risk."[20] The MDL court noted that a focus on epidemiological studies on ranitidine was essential, explaining that

> Regardless of how much NDMA was formed in ranitidine products through exposure to heat in the supply chain, people consumed them. Did that consumption, regardless of how much NDMA was in the ranitidine over time, result in cancer? Relatedly, did anyone who consumed ranitidine get cancer, regardless of how long their ranitidine consumption lasted? These are the narrowed (and highly relevant)

[17] *See id.*

[18] *See id.* at 1104–06.

[19] *See id.* at 1106.

[20] *See id.* at 1218.

questions that ranitidine epidemiology attempts to answer.[21] Third, the MDL court discussed its gatekeeping function "to ensure that speculative and unreliable opinions do not reach the jury."[22]

The MDL court focused its analysis on whether the plaintiffs' general causation opinions on ranitidine could be submitted to the jury despite there being "no published conclusion or finding, outside of this litigation, that concludes that ranitidine causes cancer of any kind."[23] In contrast, the court noted, "there is a large amount of evidence for the Defendants' position—evidence that there is no link between ranitidine consumption and cancer."[24] Further, the MDL court noted that the plaintiffs' "lack of independent scientific support is a valid ground for the Court to grant the Defendants' Epidemiology [*Daubert*] Motion because it is a valid ground for the Court to question the reliability of the Plaintiffs' experts' methodologies."[25]

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[21] *See id.*

[22] *See id.* at 1167.

[23] *See id.* at 1191–92.

[24] *See id.* at 1188, 1191–92 ("Because ranitidine, an immensely successful and popular drug, has been consumed by the public for almost forty years, and because ranitidine has been sold for much of that time as an over-the-counter drug, the public health consequences, if ranitidine causes cancer, would be significant. Given that risk to the public health, it is unsurprising that the FDA's initiation of a voluntary recall of ranitidine in the spring of 2020 resulted in 10 epidemiological studies that investigated the link between ranitidine and cancer.").

[25] *See id.* at 1191–92.

ii. The Superior Court Action

In September 2022, nearly 75,000 ranitidine-related personal injury complaints were filed in the Delaware Superior Court. Plaintiffs allege that Defendants collectively bear responsibility for their cancer and the related injuries or deaths allegedly caused from their ingestion of ranitidine. The Plaintiffs' claims relate to ten specific types of cancer: bladder, esophageal, gastric, liver, pancreatic, breast, colorectal, kidney, lung, and prostate. Almost 80% of the Delaware Plaintiffs originally registered their claims in the MDL, and almost 90% of the Delaware Plaintiffs allegedly suffered from one of the five types of cancer for which the MDL plaintiffs acknowledged there was insufficient evidence of causation.[26]

Under a Superior Court case management order, the Zantac Litigation is proceeding simultaneously on two tracks. The first track is intended to address "general causation"—that is, whether the ingestion of Zantac is capable of causing the types of cancer alleged by Plaintiffs. To carry their burden under this first track, Plaintiffs retained ten experts to offer general causation opinions for each of the ten cancers at issue in the case. The second track is designed to identify representative cases for bellwether discovery and trial.

[26] Appellants' Opening Br. at 11.

a. Plaintiffs' Experts

In the Superior Court action, Plaintiffs proffered a new slate of experts, who were not presented in the MDL; eight of those experts opined that ranitidine causes ten types of cancer. In November 2023, Defendants moved to exclude the general causation experts' testimony under Delaware Uniform Rule of Evidence 702 and *Daubert v. Merrell Dow Pharmaceuticals, Inc.*[27] Defendants argued to the Superior Court that all Plaintiffs' experts' reports and conclusions suffered from the same methodological flaws identified by the MDL court in its decision to exclude the expert reports in that litigation. The Delaware Defendants contended that those flaws should command the same result in this case. Specifically, Defendants argued that Plaintiffs' experts did not opine on threshold dose—most asserted that NDMA is unsafe at any level. Further, Defendants posited that the methodologies used by Plaintiffs' experts were outcome-driven and unreliable and therefore could not satisfy *Daubert* and Rule 702.

Plaintiffs' ten experts are doctors and scientists whose education and qualifications were not challenged in the Superior Court or on appeal. To help contextualize the *Daubert* motions resolved by the Superior Court, we briefly summarize the experts' proffered opinions.

(1) Dr. Charles Jameson opined that ranitidine produces NDMA both exogenously (outside the body) and endogenously (inside the body); that

[27] 509 U.S. 579 (1993).

NDMA meets five characteristics of the generally accepted characteristics of a carcinogen; and that it is generally accepted among cancer science researchers that NDMA is capable of causing cancer in animals and humans.[28]

(2) Dr. William Sawyer opined on a single issue: that an inhaled dose of NDMA observed in a particular study (the Hidajat study)[29] was equivalent to an oral dose of NDMA. Sawyer relied on a study that followed rubber workers. He did not opine on ranitidine.[30]

(3) Dr. Alfred I. Neugeut looked at peer-reviewed literature on NDMA, ranitidine, and bladder cancer; prepared a forest plot synthesizing the studies; and opined that there is a causal association between ranitidine and urinary bladder cancer.[31]

(4) Dr. Vinod K. Rustgi was asked by Plaintiffs to provide an expert opinion regarding the role of high levels of NDMA found in ranitidine in the risk of developing of Hepatocellular carcinoma ("HCC"), a type of liver cancer. In conducting his analysis, Dr. Rustgi relied on in-vitro data, in-vivo data, tissue culture and animal models, as well as epidemiological evidence in humans. Dr. Rustgi conceded, however, that ranitidine or NDMA is not generally accepted by the community of liver specialists as a cause of liver cancer.[32]

(5) Dr. Ioannis Hatzaras was designated by Plaintiffs to evaluate whether NDMA exposure from ranitidine can cause esophageal, stomach, and colorectal cancer. Dr. Hatzaras reviewed studies demonstrating that NDMA is a carcinogen and looked into the relationship between ranitidine-containing NDMA and development of foregut/colorectal cancer.[33]

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[28] Order at *14–15.

[29] The Hidajat study was "a study of 36,441 men who worked in a rubber factory in the United Kingdom in 1967." Appendix to Appellants' Opening Br. at A148 [hereinafter A__].

[30] Order at *17–18.

[31] *Id.* at *18–20.

[32] *Id.* at *20–21.

[33] *Id.* at *21–22.

(6) Dr. Dan J. Raz was asked by Plaintiffs to opine as to the causal relationship between ranitidine and lung cancer. Dr. Raz used a review of electronic databases to provide sources for his opinions and also looked to public health authorities, including the FDA, WHO, and IARC. Dr. Raz's ultimate opinion relied primarily on two studies and data points to support his opinion.[34]

(7) Dr. Pablo Leone was asked by Plaintiffs to offer a general causation opinion as to whether NDMA exposure from ranitidine causes breast cancer based upon epidemiological evidence. Dr. Leone acknowledged that medical and scientific associations do not identify a link between ranitidine and breast cancer. Dr. Leone considered studies of ranitidine epidemiology, NDMA dietary studies, draft and non-peer reviewed studies, and animal studies, and gave all the sources he considered equivalent weight.[35]

(8) Dr. Vitaly Margulis prepared a report that discussed how ranitidine breaks down into NDMA, how NDMA metabolizes in the body, and the mechanism by which NDMA can cause kidney cancer. Based on his review of data and studies, including dietary and occupational studies of NDMA, Dr. Margulis concluded that NDMA in ranitidine likely causes kidney cancer.[36]

(9) Dr. George Miller provided an opinion regarding whether NDMA exposure from ranitidine causes pancreatic cancer. In preparing that opinion, Dr. Miller first analyzed whether ranitidine contains a cancer-causing agent and found that NDMA is a toxic degeneration byproduct of ranitidine. Dr. Miller also relied upon testing outlined in the expert report by Emery Pharma—discussed below—and he analyzed studies that showed a link between dietary sources of NDMA and pancreatic cancer. Dr. Miller then compared the studies with others that did not show an association between ingestion of nitrates and pancreatic cancer, finding flaws with those that did not show an association. Dr. Miller also analyzed

[34] *Id.* at *22–23.

[35] *Id.* at *23–25.

[36] *Id.* at *26–27.

studies showing a link between occupational exposure to NDMA and pancreatic cancer.[37]

(10) Dr. Bruce J. Trock was asked to give a general causation opinion regarding whether NDMA exposure from ranitidine causes prostate cancer. Dr. Trock relied on evidence from animal and occupational studies of NDMA in reaching his opinion.[38]

Additionally, Plaintiffs retained Emery Pharma (hereinafter "Emery") to (i) conduct further testing on the levels of NDMA in ranitidine provided by Defendants and specifically the levels in Plaintiffs' own pills, and (ii) opine on ranitidine's ability to degrade and transform into NDMA. Defendants offered nine challenges to the admissibility of the Emery Pharma Opinion.[39]

b. The Superior Court's Order

On May 31, 2024, the Superior Court denied Defendants' motions to exclude the experts' testimony (the "Order"). The court addressed Defendants' challenges to each of Plaintiffs' ten experts and reached legal conclusions applicable to all the experts. Relevant to the claims on appeal, the Superior Court found that: (1) the "general causation" question in the case "focuses on NDMA,"[40] and the experts' general causation opinions therefore could be based on studies relating to the

[37] *Id.* at *27–29.

[38] *Id.* at *29–30.

[39] *Id.* at *31.

[40] *Id.* at *7.

ingestion of NDMA, rather than ranitidine itself;[41] (2) Delaware law does not "recognize a 'threshold dose' requirement as part of the general causation analysis";[42] and (3) in performing its role as a gatekeeper and conducting a *Daubert* analysis, the trial court should rule "with a 'liberal thrust' favoring admission."[43] Consistent with its "liberal thrust" standard, the court repeatedly dismissed each of Defendants' legal arguments by stating that they went to weight rather than admissibility, concluding that the issues Defendants raised were questions for a jury.

c. Interlocutory Appeal

Defendants asked the Superior Court to certify its order for an interlocutory appeal. The Superior Court denied certification, but this Court reviewed Defendants' application and granted the request.[44] Although evidentiary rulings are rarely appropriate for interlocutory review, this Court noted that: "a ruling on the issues regarding the Plaintiffs' general causation experts could be dispositive for some or all of the almost 75,000 claims filed in Delaware . . . and, importantly, the Superior Court's decision raises substantial issues regarding the *Daubert* standard generally and mass tort litigation specifically[.]"[45] The two guiding questions this

[41] *See id.* at *8–10.

[42] *Id.* at *7.

[43] *Id.* at *5.

[44] *In re Zantac (Ranitidine) Litig.*, 2024 WL 3271976 (Del. Super. July 1, 2024); D.I. 17 at 5 (Order Accepting Interlocutory Appeal).

[45] D.I. 17 at 5 (Order Accepting Interlocutory Appeal).

Court identified in its order were "whether (i) experts may base their causation opinions on studies regarding the cancer-causing agent or must focus on the product at issue in the litigation, and (ii) Delaware law requires experts to identify a threshold dose for purposes of establishing general causation."[46]

d. Parties' Contentions on Appeal

Appellants raise three claims on appeal. First, they argue that the Superior Court erred in holding that Plaintiffs' experts did not need to identify the threshold dose required to cause the cancers at issue.[47] Appellees argue in response that threshold dose is not required to reach an opinion on general causation.[48] Specifically, Appellees contend that threshold dose is not applicable to a carcinogen and as such is not relevant to the claims in this case.[49] Further, Appellees maintain that "there is no legal basis to disturb the Superior Court's holding that 'threshold dose' is one non-dispositive consideration under *Daubert*."[50]

Next, Appellants contend that the Superior Court erred in focusing its general causation analysis on NDMA, rather than ranitidine.[51] Appellants argue that "[t]he Court gave no tenable justification for [its] holding, which takes an approach

[46] *Id.*

[47] Appellants' Opening Br. at 18–27.

[48] Appellees' Answering Br. at 17–33.

[49] *Id.* at 23–27.

[50] *Id.* at 27–33.

[51] Appellants' Opening Br. at 28.

contrary to that of every independent scientist who has investigated whether there is a relationship between ranitidine and cancer."[52] Appellees respond that the Superior Court correctly considered each expert's reliance on NDMA and ranitidine data in assessing admissibility.[53] Appellees contend that "[w]hether [] exposure [to NDMA] comes from food, or from taking a pill every day, does not matter."[54] Further, Plaintiffs argued in the Superior Court that because it is "undisputed that [] NDMA is found in ranitidine *and* that NDMA causes cancer . . . it would seem obvious then, that if a person ingested ranitidine with NDMA, they could develop cancer."[55]

Finally, Appellants contend that the Superior Court applied an unduly lenient standard and wrongly held that all methodological critiques went to weight, not admissibility.[56] Specifically, Appellants argue that an analysis under Delaware Uniform Rule of Evidence ("DRE") 702 should not be conducted with a "liberal thrust favoring admission" and that it is a trial court's duty to ensure that an expert applies his or her methodology reliably.[57]

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[52] *Id.*

[53] Appellees' Answering Br. at 34.

[54] *Id.* at 12.

[55] Order at *8.

[56] Appellants' Opening Br. at 38.

[57] *Id.* at 38–47.

Appellees respond that the Superior Court applied the correct *Daubert* standard in reviewing the admissibility of Appellees' general-causation experts.[58] They note that after finding each expert's opinion methodologically reliable and reasonable under *Daubert*, the Superior Court was right to leave challenges to the "correctness" of those opinions to the jury.[59]

II. STANDARD OF REVIEW

We review questions of law, including a trial court's interpretations of rules of evidence or burdens of proof, *de novo*.[60] We review a trial court's decision to admit or exclude evidence for abuse of discretion.[61] "To find an abuse of discretion, there must be a showing that the trial court acted in an arbitrary and capricious manner."[62] "That standard applies as much to the trial court's decisions about how to determine reliability as to its ultimate conclusion."[63]

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[58] Appellees' Answering Br. at 42.

[59] *Id.* at 45.

[60] *Clark v. Clark*, 47 A.3d 513, 517 (Del. 2012); *Kahn v. Kolberg Kravis Roberts & Co., L.P.*, 23 A.3d 831, 836 (Del. 2011)*; see also State v. Kelly*, 947 A.2d 1123 (Del. 2008) ("We review interpretations of court rules and statutes *de novo*."); *Hopkins v. State*, 893 A.2d 922, 927 (Del. 2006) ("[W]e review a trial judge's interpretation of the Superior Court Rules relating to discovery *de novo*.").

[61] *Tumlinson v. Advanced Micro Devices, Inc.*, 81 A.3d 1264, 1268 (Del. 2013); *Gen. Motors Corp. v. Grenier*, 981 A.2d 531, 536 (Del. 2009) ("*Grenier II*"); *M.G. Bancorporation, Inc. v. Le Beau*, 737 A.2d 513, 522 (Del. 1999), *as modified on denial of reargument* (May 27, 1999).

[62] *Spencer v. Wal-Mart Stores E., LP*, 930 A.2d 881, 887 (Del. 2007) (citing *Chavin v. Cope*, 243 A.2d 694, 695 (Del. 1968)).

[63] *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 139 (1999).

III. ANALYSIS

DRE 702 governs the admissibility of expert opinion testimony. The Rule allows a party to rely on expert testimony that will assist the trier of fact, provided that the opinion meets the Rule's express admissibility requirements: the opinion must have a sufficient basis and be based on reliable principles and methods that are applied reliably to the facts of the case. Specifically, the Rule states:

> 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.[64]

The United States Supreme Court's holding in *Daubert* further explains the standard governing the admissibility of expert testimony. Delaware has adopted *Daubert*, and a well-developed body of caselaw explains how DRE 702 and *Daubert* are to be applied. This Court explained in *Tumlinson v. Advanced Micro Devices, Inc.*:

> In *Daubert*, the United States Supreme Court held that Federal Rule of Evidence 702—the nearly identical federal counterpart to [DRE] 702—displaced *Frye v. United States's* "general acceptance" test for determining the admissibility of expert opinion testimony. This Court, in *M.G. Bancorporation, Inc. v. Le Beau*, adopted *Daubert* and its

[64] D.R.E. 702.

progeny, as the "correct interpretation of Delaware Rule of Evidence 702."[65]

More specifically, under *Daubert*, "[i]n order for expert testimony to be admissible, the trial judge must act as a gatekeeper and determine that the evidence is both (1) reliable and (2) relevant."[66] To determine reliability under *Daubert*, a trial court may consider a non-exhaustive list of factors, including: (1) whether the expert opinion testimony "can be (and has been) tested"; (2) whether it "has been subjected to peer review and publication"; (3) its "known or potential rate of error"; and (4) whether it has attracted widespread acceptance within the scientific community.[67] "The inquiry is a flexible one, and its focus must be solely on principles and methodology, not on the conclusions that they generate."[68] "The party seeking to introduce the expert testimony bears the burden of establishing its admissibility by a preponderance of the evidence."[69]

We have interpreted DRE 702 to be consistent with its analogue, Federal Rule of Evidence ("FRE") 702, and we look to the federal rule and judicial application of

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[65] *Tumlinson*, 81 A.3d at 1269 (citing and quoting *Frye v. United States*, 293 F. 1013 (D.C. Cir. 1923); *M.G. Bancorporation*, 737 A.2d at 513).

[66] *Tumlinson v. Advanced Micro Devices, Inc.*, 106 A.3d 983, 990 (Del. 2013) (citing *Daubert*, 509 U.S. at 597).

[67] *Daubert*, 509 U.S. at 580, 593–94.

[68] *Id.* at 594.

[69] *Bowen v. E.I. DuPont de Nemours & Co.*, 906 A.2d 787, 795 (Del. 2006).

it as persuasive authority.[70] Because Delaware follows FRE 702 and views the official comments to the rule as helpful authority in construing DRE 702,[71] Delaware courts appropriately look to federal caselaw and commentary in discharging their gatekeeping function regarding expert testimony.

FRE 702 was recently amended to clarify the rule without changing its substance. The 2023 amendments to the federal rule confirmed that trial courts are required to vigorously exercise their gatekeeping function.[72] In a May 2022 report, the Judicial Conference Advisory Committee on Evidence Rules (the "Advisory Committee") wrote that judicial decisions treating expert opinions as presumptively admissible and dismissing challenges to the sufficiency or reliability factors as

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[70] *Scottoline v. Women First, LLC*, __ A.3d __, 2025 WL 1707364, at *4 (Del. June 18, 2025); *Tumlinson*, 106 A.3d at 989–90 ("In *M.G. Bancorporation, Inc. v. Le Beau*, we adopted the United States Supreme Court's holdings in *Daubert v. Merrell Dow Pharmaceuticals, Inc.* and *Kumho Tire Co. v. Carmichael* as 'the correct interpretation of Delaware Rule of Evidence 702.'"); *M.G. Bancorporation*, 737 A.2d at 523 ("Delaware Rule of Evidence 702, like its federal counterpart, 'establishes a standard of evidentiary reliability.'"); *see also* Del. Unif. R. Evid. 702 cmt. (stating D.R.E. 702 was amended in 2001 and 2017 to track F.R.E. 702); *Ricketts v. State*, 488 A.2d 856, 857 n.2 (Del. 1985) ("The Delaware Study Committee, which drafted the D.R.E., has stated that the historical materials surrounding the promulgation of the Federal Rules and the F.R.E. official notes and comments, 'should be considered as being part of the comments prepared by the Delaware Study Committee and a court should refer to these materials in construing these rules.'") (quoting D.R.E., Delaware Study Committee Prefatory Note); *see also, e.g.*, *Manna v. State*, 945 A.2d 1149, 1154 (Del. 2008) (looking to the F.R.E. to help interpret the D.R.E.).

[71] *Ricketts*, 488 A.2d at 857 n.2.

[72] Fed. R. Evid. 702 Advisory Committee's note to the 2023 amendments ("Rule 702(d) has also been amended to emphasize that each expert opinion must stay within the bounds of what can be concluded from a reliable application of the expert's basis and methodology. Judicial gatekeeping is essential because just as jurors may be unable, due to lack of specialized knowledge, to evaluate meaningfully the reliability of scientific and other methods underlying expert opinion, jurors may also lack the specialized knowledge to determine whether the conclusions of an expert go beyond what the expert's basis and methodology may reliably support.").

questions of "weight" rather than "admissibility" consistently misapplied the rule and failed to perform the court's gatekeeping function with fidelity. Specifically, the Advisory Committee stated:

> the Committee resolved to respond to the fact that many courts have declared that the reliability requirements set forth in Rule 702(b) and (d) --- that the expert has relied on sufficient facts or data and has reliably applied a reliable methodology --- are questions of weight and not admissibility, and more broadly that expert testimony is presumed to be admissible. These statements misstate Rule 702, because its admissibility requirements must be established to a court by a preponderance of the evidence. The Committee concluded that in a fair number of cases, the courts have found expert testimony admissible even though the proponent has not satisfied the Rule 702(b) and (d) requirements by a preponderance of the evidence --- essentially treating these questions as ones of weight rather than admissibility . . . .[73]

The Advisory Committee further explained that the change to FRE 702 emphasized the preponderance-of-the-evidence standard and "specifically was made necessary by the courts that have failed to apply correctly the reliability requirements of [Federal Rule 702]."[74] The Advisory Committee explained that this change would confirm that FRE 104(a) applies to FRE 702, noting that

> [U]ltimately the Committee unanimously agreed that explicitly weaving the Rule 104(a) standard into the text of Rule 702 would be a substantial improvement that would address an important conflict among the courts. While it is true that the Rule 104(a) preponderance of the evidence standard applies to Rule 702 as well as other rules, it is with respect to the reliability requirements of expert testimony that

[73] COMM. ON RULES OF PRAC. & PROC. OF THE JUD. CONF. OF THE U.S., REPORT OF THE ADVISORY COMMITTEE ON EVIDENCE RULES at 6 (May 15, 2022), https://perma.cc/PK3B-Q8G5.

[74] Fed. R. Evid. 702 Advisory Committee's note to the 2023 amendments.

> many courts are misapplying that standard. Moreover, it takes some effort to determine the applicable standard of proof --- Rule 104(a) does not mention the applicable standard of proof, requiring a resort to case law.[75]

The Advisory Committee went on to reiterate that "many courts have held that the critical questions of the sufficiency of an expert's basis, and the application of the expert's methodology, are questions of weight and not admissibility. These rulings are an incorrect application of Rules 702 and 104(a)."[76] In other words, the Advisory Committee eschewed a presumption of admissibility in favor of a carefully applied gatekeeping function.

DRE 702 has not been amended at the present time to mirror the 2023 amendments to FRE 702. But, because the Advisory Committee has explained that the 2023 amendments are not substantive and instead only clarified the existing federal standard, we view the committee's recent guidance as important material to consider in reviewing our trial courts' decisions and providing guidance to litigants.[77] Nothing in the recent amendments conflicts with our existing precedent, and the commentary accompanying those amendments offers additional guidance as

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[75] COMM. ON RULES OF PRAC. & PROC. OF THE JUD. CONF. OF THE U.S., REPORT OF THE ADVISORY COMMITTEE ON EVIDENCE RULES at 6, https://perma.cc/PK3B-Q8G5.

[76] Fed. R. Evid. 702 Advisory Committee's note to the 2023 amendments.

[77] *Id.*

trial courts confront the difficult task of evaluating the admissibility of an expert opinion.[78]

A. The trial court erred in interpreting DRE 702 as liberally favoring admissibility and adopting a standard distinct from FRE 702.

A trial court faces significant challenges in evaluating scientific testimony, particularly when a judge is asked to determine the sufficiency and reliability of an expert's conclusions on scientific causation. "Experts may rely upon different types of evidence to prove or disprove general causation, including as bases for an inference of general causation, including epidemiological studies, toxicological studies (dose-response relationship), and physiological-mechanism evidence."[79] "[T]hese types of evidence are not all afforded the same weight"[80] and require the judge to act as gatekeeper. But these challenges underscore the need for the court to faithfully apply DRE 702 so that the jury does not receive unreliable evidence.

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[78] Delaware is not the only state to grapple with these issues or to consider its state rule in light of the clarification to FRE 702. For example, the Maryland Supreme Court recently observed that the post-FRE 702 amendment "confirms our understanding of meaningful gatekeeping" and broadly affirmed the trial court's exclusion of expert testimony. *Katz, Abosch, Windesheim, Gershman & Freedman, P.A. v. Parkway Neuroscience & Spine Inst., LLC*, 301 A.3d 42, 68 (Md. 2023). The Maryland Supreme Court reversed the intermediate appellate court's decision to admit unreliable expert testimony, finding that the intermediate court recited the erroneous "weight and not admissibility" aphorism in making its decision. *Id.*

[79] MDL Order at 1104 (citing *In re Denture Cream Prods. Liab. Litig.*, 795 F. Supp. 2d 1345, 1351 (S.F. Fla. 2011)).

[80] *Id.*

The trial court undertook substantial effort to resolve the numerous motions in this case, which incorporated a significant factual and scientific record. Nevertheless, we conclude that the court erred in interpreting DRE 702 and the Plaintiffs' burden by: (1) stating that DRE 702 should be applied with a "liberal thrust" favoring admission; (2) concluding that Delaware's standard for admissibility is different from the analogous federal standard; and (3) dismissing any argument regarding the experts' application of methodology as going to weight rather than admissibility. Correctly understood, DRE 702 and its interpretive precedent required exclusion of the challenged expert opinions.

1. The Superior Court's "liberal thrust" standard

The Superior Court, before engaging in its *Daubert* analysis, noted that courts are directed to "conduct their *Daubert* analyses 'with a liberal thrust favoring admission.'"[81] The phrase "liberal thrust" is taken from *Daubert* itself, but the Superior Court adopted the phrase in a manner that divorced it from its context.[82]

In *Daubert*, the United States Supreme Court explained that the *Frye* test that previously governed expert testimony had imposed a "rigid 'general acceptance' requirement" on admissibility that was not consistent with the "liberal thrust" of the

[81] Order at *5 (quoting citing *Messick v. Novartis Pharmaceuticals Corp.*, 747 F.3d 1193, 1196 (9th Cir. 2014)).

[82] *See Messick*, 747 F.3d at 1196 ("Although Rule 702 should be applied with a 'liberal thrust' favoring admission . . . it requires that '[e]xpert testimony . . . be both relevant and reliable . . . .'") (quoting *Daubert*, 509 U.S. at 588).

federal rules of evidence.[83] The Supreme Court concluded that the "permissive backdrop" of the federal rules was inconsistent with the use of the *Frye* test as the exclusive test for admitting expert scientific testimony.[84]

The *Daubert* Court did not, however, adopt a "liberal thrust" or presumption favoring admissibility. Although *Daubert* recognized the limitations inherent in *Frye's* general acceptance test, Rule 702 and *Daubert* establish the sufficiency and reliability elements and the threshold that a proponent of expert testimony must meet to establish admissibility. Unless that threshold is met, expert testimony is not admissible, and trial courts should not approach a challenge to expert testimony with any presumption toward admissibility.

"[W]hen it comes to making preliminary determinations about admissibility, the judge *is* and *always has been* a factfinder."[85] Under Delaware's rules of evidence, the court must resolve any preliminary questions of admissibility, and the proponent of an expert opinion must prove its admissibility by a preponderance of the evidence.[86] The Superior Court's holding to the contrary, applying a "liberal

[83] *Daubert*, 509 U.S. at 588.

[84] *Id*. at 588–89.

[85] COMM. ON RULES OF PRAC. & PROC. OF THE JUD. CONF. OF THE U.S., REPORT OF THE ADVISORY COMMITTEE ON EVIDENCE RULES 6, https://perma.cc/PK3B-Q8G5.

[86] D.R.E. 104(a) ("The court must decide any preliminary question about whether a witness is qualified, a privilege exists, or evidence is admissible."); *Bowen*, 906 A.2d at 795 ("The party seeking to introduce the expert testimony bears the burden of establishing its admissibility by a preponderance of the evidence."); *Minner v. Am. Mortgage & Guar. Co.*, 791 A.2d 826, 843 (Del. Super. 2000) (citing *Nat'l Bank of Com. v. Dow Chem. Co.*, 965 F. Supp. 1490, 1497 (D. Ark.

thrust" that favors admissibility in the manner it did here, failed to hold Plaintiffs to their burden of proof.

2. Delaware follows the federal standard

"The Delaware Rules of Evidence are modeled after, and in many instances, track the Federal Rules of Evidence."[87] DRE 702's comment explicitly notes that it "was amended in 2001 to track [FRE] 702" as well as "amended in 2017 in response to the 2011 restyling of the Federal Rules of Evidence."[88]

Nevertheless, the Superior Court concluded that there were differences between Delaware law and federal law that required the court to apply standards distinct from those used by the MDL court. The Superior Court drew several broad conclusions as to why Delaware law required the court to part ways with the MDL court's decision and federal law. For instance, the Superior Court held that "Delaware law holds that statistical significance is 'not necessary to prove causality,'"[89] citing *Barrera v. Monsanto Company*[90] and *In re Zoloft*.[91] But

1996), *aff'd* 133 F.3d 1132 (8th Cir. 1998)); *see also Daubert*, 509 U.S. at 592 n.10 (citing F.R.E. 104(a)); *Oddi v. Ford Motor Co.*, 234 F.3d 136, 145 (3d Cir. 2000) ("The proponent must satisfy this burden 'by a preponderance of proof.'").

[87] *Nelson v. State*, 628 A.2d 69, 74 n.7 (Del. 1993); *Atkins v. State*, 523 A.2d 539, 542 (Del. 1987); *Ricketts*, 488 A.2d at 857 n.2.

[88] D.R.E. 702, cmt.

[89] Order at *6.

[90] *Barrera v. Monsanto Co.*, 2019 WL 2331090, at *5 (Del. Super. May 31, 2019).

[91] *In re Zoloft (Sertraline Hydrochloride) Prods. Liab. Litig.*, 858 F.3d 787, 793 (3d Cir. 2017).

although statistical significance may not be a prerequisite in every case, it remains an important consideration, and its absence should, at a minimum, require the expert to explain why it is not necessary under the particular facts of the case. Although the United States Court of Appeals for the Third Circuit in *In re Zoloft* cautioned that "[a] court should not . . . usurp the role of the fact-finder," the court reiterated that "plaintiffs ultimately must prove a causal connection between [the product] and [the injury]."[92]

Similarly, the Superior Court held that "Delaware does not recognize a 'threshold dose' requirement as part of the general causation analysis,"[93] again citing its decision in *Barrera v. Monsanto Company*.[94] *Barrera* involved whether the herbicide product known as "Roundup" caused the plaintiffs' cancer.[95] Unlike the Superior Court's holding here, *Barrera* did not hold that there is no "threshold dose" requirement in Delaware law. Instead, the court in *Barrera* made findings about the admissibility of epidemiological studies and noted that there is no "bright-line rule requiring statistical significance to prove causality."[96] Although we do not reach the

[92] *Id.*

[93] Order at *6–7.

[94] *Barrera*, 2019 WL 2331090, at *5.

[95] *Id.* at *1.

[96] *Id.* at *5.

"threshold dose" question in this appeal, we note that *Barrera* does not address threshold dose, and there is no consensus in Delaware law as to "threshold dose."

We do not suggest that the Superior Court should have simply adopted the MDL court's conclusions. The trial court correctly undertook an independent analysis of the admissibility of Plaintiffs' experts' opinions. But the Superior Court's dismissal of the significant methodological flaws identified by the MDL court—flaws that also appeared in the expert reports in Delaware—on the basis that Delaware has a different standard, was error.[97] The Superior Court was free to reach a different conclusion from the MDL court concerning whether to admit evidence under Rule 702, but it was required to faithfully apply the sufficiency and reliability standards set forth in Delaware and pertinent federal law.

3. The court's "weight, not admissibility" conclusions

As a result of its belief that Delaware applies a "liberal thrust" favoring admissibility that is distinct from the federal rule, the trial court applied the wrong standard to its gatekeeping function. In denying Defendants' motions to exclude Plaintiffs' general causation experts, the Superior Court abdicated its gatekeeping role by passing crucial questions of sufficiency and reliability to the jury.[98] The

[97] Order at *7.

[98] *See id.* at *16–17 ("Defendants' challenges to the reliability of Dr. Jameson's methodology are as follows: he cherry picked his evidence; did not rank or weigh his studies; the tests do not imitate conditions in humans; his reliance on non-peer reviewed studies; reliance on bad science and improperly rejecting or favoring unreliable studies; and, generally, relying on unreliable

Superior Court repeatedly dismissed Defendants' arguments regarding the admissibility of Plaintiffs' experts' opinions by finding that the arguments went to "weight, not admissibility."[99] As explained above, this is inconsistent with a trial court's gatekeeping function, DRE 702 and its federal analogue, and Delaware caselaw.

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exogenous studies. These challenges are for the jury."); *id.* at *18 ("Defendants reject his science. Perhaps, as presented during oral arguments, his science may be a bridge too far. But at this juncture, the criticisms go to weight and do not preclude admission."); *id.* at *20 ("Every case is different. In this early phase of the litigation, the Court is more compelled to its conclusion by the legal concepts that animate *Daubert* proceedings, especially as they recognize and uphold the distinct roles of the Court as gatekeeper and that of the jury as the ultimate fact finder, and by the encouragement of *In re Asbestos Litig*. and *Long* to allow the jury to consider debatable scientific approaches. Defendants can take up their challenges before the jury on cross examination."); *id.* at *21 ("This Court will not inject itself into a dispute over which party has the better science. Defendants' quarrel with Dr. Rustgi's reading of the Wang study is also unavailing, as the balance of Defendants' challenges to admissibility sound in areas reserved in the first instance to the expert witness's discretion and, ultimately, the jury's wisdom (i.e., cherry picking evidence, improper rejection of relevant data, vagueness in describing methodology, inconsistent testimony, etc.) These issues present a classic battle of the experts. Resolution of those disputes lies with the jury."); *id.* at *22 ("Defendants' arguments may undermine Dr. Hatzaras' opinion and be fodder for cross examination, but they cannot exclude that opinion. These expert battles are to be fought before the factfinders."); *id.* at *23 ("These decisions, made within the framework constructed by *Daubert* and progeny, are reserved to the jury."); *id.* at *25 ("Delaware law does not impose a bright line threshold dose requirement, as discussed above. Moreover, none of these challenges rises above the credibility-oriented questions that *Daubert* and progeny for years have reserved to the jury."); *id.* at *27 ("These challenges, along with claims of cherry-picking and flawed reliance on certain NDMA studies, fall victim to the wisdom of *Daubert*: they belong to the jury."); *id.* at *29 ("At this stage, it cannot be said that the scope of his review and the science used to formulate his opinions do not support admissibility. Defendants may have succeeded at times in making this a close call. But close calls go to the jury.").

[99] *Id.* at *28 ("Likewise, the arguments that Dr. Miller made a 'faulty assumption' and improperly 'flipped the burden' of proof, or turned 'limitations in the 'negative' studies into strengths in the studies he preferred,' go to weight, not admissibility."); *id.* at *35 ("As the several cases repeatedly cited above make clear, such criticism goes to weight, not admissibility."); *id.* at *37 (discussing Defendants' challenges to Emery's Simulated Gastric Fluid Test as going to "weight, not admissibility").

This Court has made clear that, under DRE 702, an expert's opinion must be "'the product of reliable principles and methods' reliably applied to the facts of each case."[100] For instance, in *Bowen v. E.I. DuPont de Nemours & Co., Inc.*, the plaintiffs' expert applied an established model (the "Potts-Guy model") for estimating the amount of a substance that human skin will absorb, and the plaintiffs argued that the expert's opinion was admissible because that model was a "widely accepted methodology."[101] This Court noted that the issue was "not whether the Potts-Guy model is ever a reliable tool," but rather, whether it was applied reliably in the present case by the expert being challenged.[102] We held that the expert's decision to "rely exclusively upon the Potts-Guy model and to ignore or discard 'more favorable' methodologies" "directly undermine[d] the reliability of his methodology."[103] Analogously, in this case, Defendants repeatedly challenged Plaintiffs' experts for "cherry-picking" favorable data regarding NDMA while ignoring studies focusing directly on ranitidine.[104] Rather than addressing

[100] *Bowen*, 906 A.2d at 797 (quoting D.R.E. 702).

[101] *Id.*

[102] *Id.*

[103] *Id.*

[104] *See* Order at *17 (discussing Dr. Sawyer's opinion, which relied on the Hidajat occupational, rubber worker, study); *id.* at *28 (discussing Dr. Miller's opinion, which relied on dietary and occupational studies); *id.* at *26–27 (discussing Dr. Margulis' opinion, which relied on studies in animals and non-living organisms in addition to his principal reliance on NDMA dietary and worker studies).

Defendants' arguments and determining whether the challenged experts reliably applied appropriate methodologies, the court dismissed these objections and labeled them as questions for the jury.

The Superior Court appeared to view its role as not extending to evaluating the strength of an expert's science. But the proponent of expert evidence is charged with establishing its sufficiency and reliability, and a trial court must determine whether that burden is met.[105] Although that may present a substantial challenge, as few judges are steeped in scientific knowledge, the trial judge may receive and evaluate testimony and ask questions of the experts and the parties' lawyers until the court feels comfortable drawing conclusions on sufficiency and reliability. An expert who cannot explain to the court's satisfaction why her method is reliably applied should not be permitted to opine for a jury.

The Superior Court did not require Plaintiffs' experts to meet that burden. More particularly, the court did not require the challenged experts to explain their rejection of epidemiological, peer-reviewed studies. For example, Defendants challenged Dr. Neugut's analysis and reliance on non-statistically significant results to support his opinion, even though in his professional work he requires that findings

[105] *See Zayas v. State*, 273 A.3d 776, 788 (Del. 2022) (reversing admission of opinion based on "an incomplete factual predicate"); *Scaife v. AstraZeneca LP*, 2009 WL 1610575, at *18 (Del. Super. June 9, 2009) (excluding an expert opinion because "the expert cannot accept some but reject other data from the medical literature without explaining the bases for her acceptance or rejection").

be statistically significant to find an association between an exposure and an outcome. In denying the motion, the Superior Court surmised that all of Defendants' challenges were reserved for the jury.[106] Similarly, Dr. Rustgi declined to provide an explanation of how he weighed the diverse set of studies he considered.[107] Rather than assessing whether Dr. Rustgi's opinion was based on a reliable methodology and application, the court held that

> This Court will not inject itself into a dispute over which party has the better science. Defendants' quarrel with Dr. Rustgi's reading of the Wang study is also unavailing, as the balance of Defendants' challenges to admissibility sound in areas reserved in the first instance to the expert witness's discretion and, ultimately, the jury's wisdom (i.e., cherry picking evidence, improper rejection of relevant data, vagueness in describing methodology, inconsistent testimony, etc.)[.] These issues present a classic battle of the experts. Resolution of those disputes lies with the jury.[108]

In a similar way, Dr. Miller reached his conclusions by prioritizing studies that compared cancer rates in ranitidine users to the general population, despite acknowledging that studies comparing ranitidine users to users of other heartburn medications better controlled for confounders and therefore delivered stronger, more reliable results. Notwithstanding this objection and others, the Superior Court found

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[106] A9046–48 (Deposition of Alfred Neugut); Order at *20.

[107] A10044 (Deposition of Dr. Rustgi, where he states: "I think they're all important. I can't say that I emphasize one over the other.").

[108] Order at *21 (footnotes omitted).

that "Defendants may have succeeded at times in making this a close call. But close calls go to the jury."[109] This is not the correct standard under Delaware law.

As another example, Dr. Trock admitted that the exact probability that NDMA is responsible for the outcomes observed in the occupational studies is "really speculation" that he "can't put a number on."[110] The Superior Court dismissed this issue with the occupational studies and others raised by Defendants by repeating its view that "Defendants can take up these challenges before the jury."[111] By failing to require Plaintiffs' experts to explain their reliance on these studies and their rejection of epidemiological, peer-reviewed studies of the product, the Superior Court did not fulfill its role as gatekeeper.

In sum, we conclude that the trial court misinterpreted DRE 702 and the Plaintiffs' burden in three ways. First, the trial court stated that DRE 702 should be applied with a "liberal thrust" favoring admission, contrary to the preponderance-of-the-evidence standard and *Daubert*. Second, the court misconstrued Delaware's admissibility standard as being different from, and impliedly more permissive than, the analogous federal standard. Third, the court dismissed any argument regarding

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[109] *Id.* at *28.

[110] A011012–13.

[111] Order at *30. Defendants raised other concerns with Dr. Trock's opinion, including the reliability of his analysis and his failure to address epidemiological evidence that was inconsistent with his opinion. *See id.* at *29.

the experts' application of methodology as going to weight rather than admissibility, relinquishing the court's role as a gatekeeper. These collective errors resulted in the court finding that Plaintiffs' experts' opinions were admissible even though their sufficiency and reliability was not established by a preponderance of the evidence.

B. The trial court erred in defining the general causation question as focusing on the allegedly toxic agent rather than the product at issue in the case.

In addition to its error in framing the legal standard governing admissibility of expert opinions, the trial court also erred in defining the general causation question presented by Plaintiffs' claims. General causation in toxic tort cases addresses whether a substance is capable of causing a particular injury or condition in the general population, while specific causation addresses whether a substance caused a particular plaintiff's injury.[112] On appeal, Appellants argue that the Superior Court erred in focusing the general causation analysis on NDMA, rather than ranitidine.[113] NDMA is a ubiquitous substance found in many common materials and even in air and water.[114] Appellants assert that Plaintiffs bear the

[112] *See, e.g. Richards v. Copes-Vulcan*, 213 A.3d 1196, 1197–98 (Del. 2019) (addressing Ohio law); *Sheehan v. Oblates of St. Francis de Sales*, 15 A.3d 1247, 1254–55 (Del. 2011) (explaining that, in a sexual abuse case, general causation related to the type of injuries that survivors of childhood sexual abuse suffer, while specific causation related to the actual cause of the plaintiff's injuries); *Tumlinson v. Advanced Micro Devices, Inc.*, 2013 WL 7084888, at *1 (Del. Super. Oct 15, 2013), *aff'd* 81 A.3d 1264 (Del. 2013).

[113] Appellants' Opening Br. at 28.

[114] MDL Order at 1106.

burden of showing that use of the Defendants' *product* may cause the alleged cancers and not that NDMA alone causes cancer.[115] Further, Appellants argue that "[t]he Court gave no tenable justification for [its] holding, which takes an approach contrary to that of every independent scientist who has investigated whether there is a relationship between ranitidine and cancer."[116]

In framing the general causation question in this case, the Superior Court held that "the discrete issue before the Court at this stage is whether NDMA can cause cancer . . . [but] [b]oth sides disagree as to how to frame the general causation question."[117] In resolving this question, the Superior Court acknowledged that "[t]his fundamental dispute of whether the science should focus on ranitidine versus NDMA lies at the heart of every challenge mounted in the Motions."[118] The Superior Court stated that although Defendants' desire to have the inquiry focus on ranitidine, not NDMA, is "understandable," "the Court cannot turn a blind eye to the focus on NDMA."[119] The court then listed facts from the record that could be viewed as

[115] Appellants' Opening Br. at 28.

[116] *Id.*

[117] Order at *8.

[118] *Id.* at *10.

[119] *Id.* at *9.

exhibiting Defendants' knowledge and recognition—by voluntarily participating in the recall—that ranitidine may contain NDMA.[120]

The experts' reliance on, and the Superior Court's acceptance of, studies regarding NDMA, without connecting the NDMA exposure in those studies to the exposure caused by ranitidine—the product at issue—was inconsistent with DRE 702 and Delaware law. A general causation expert's opinion must focus on the product at issue and must show that exposures examined in non-product studies on which the expert relied are reliably linked to the exposures caused by the product at issue.[121]

The Superior Court viewed the issue as similar to one resolved in a series of opinions in *In re Asbestos Litigation*, in which the Superior Court and this Court considered whether the plaintiffs' experts could rely on data regarding the disease-producing effects of chrysotile to establish that the defendants' brake pads, which contained chrysotile, were capable of causing mesothelioma.[122] We agree that the decisions in *In re Asbestos Litigation* directly address the general causation question that Defendants raised in the *Daubert* motions in this case. But we disagree with the

[120] *Id.*

[121] *See In re Asbestos Litig.*, 911 A.2d 1176, 1202 (Del. Super. 2006); *Grenier II*, 981 A.2d at 531.

[122] Order at *10.

trial court that those precedents support the admissibility of the opinions proffered by Plaintiffs' general causation experts.

In *In re Asbestos Litigation*, the Superior Court declined to adopt the syllogism "that the Court need not evaluate the *Daubert* evidence that has been presented because we already know that friction products contain chrysotile, chrysotile causes disease and, therefore, friction products cause disease."[123] The court rejected the plaintiffs' position that "Chrysler's admission that its products contain a known carcinogen ends the inquiry," and instead explained that

> [P]laintiffs must establish that their experts can reliably conclude that exposure to friction products increases the risk of contracting an asbestos-related disease. This does not, however, preclude the plaintiffs from attempting to carry this burden by presenting competent evidence that friction products, in certain circumstances, release respirable chrysotile fibers [that can cause disease].[124]

The court found that to satisfy the reliability component of DRE 702 and *Daubert*, the plaintiffs bore the burden of establishing a link between the product and the carcinogen or disease-causing agent in order to establish the general causation link between the product and the disease.

The *Asbestos* court explained that the plaintiffs' general causation experts could rely on studies of the disease-causing agent, as opposed to the product, but

[123] *In re Asbestos Litig.*, 911 A.2d at 1201.

[124] *Id.* at 1202.

only if they reliably linked those studies to the product at issue.[125] That is, to rely on evidence or data concerning other asbestos-containing products, the plaintiffs' experts had to show that the exposures from other products were "indistinguishable" or identical to exposures from the defendants' products.

In *General Motors Corp. v. Grenier* ("*Grenier I*")[126] this Court agreed with that standard. But the *Grenier I* court found that the Superior Court made certain factual findings at the *Daubert* hearing that were not supported by the record and therefore remanded the case for reconsideration of whether the challenged experts' opinions created a "bridge, grounded in reliable science, between the scientific data regarding the association between unrefined chrysotile and asbestos-related diseases and the association between friction products and asbestos-related diseases."[127] The trial court then clarified its decision, and this Court affirmed, holding that the experts had "provide[d] the necessary scientific basis" to conclude that "the two forms of chrysotile [] [were] equally carcinogenic" by submitting research that compared "the morphology, size and shape of respirable chrysotile fibers," which are the "primary factors that explain the carcinogenicity of asbestos."[128]

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[125] *Id.*

[126] 981 A.2d 524 (Del. 2009) ("*Grenier I*").

[127] *Id.* at 530.

[128] *Grenier II*, 981 A.2d at 536–37.

These cases encapsulate the general causation question that Plaintiffs were facing with respect to ranitidine. It was not enough for Plaintiffs' experts to opine that NDMA—a pervasive substance found in air and water—causes cancer, ranitidine contains or degrades into NDMA, and therefore ranitidine causes cancer. As the decisions in *In re Asbestos Litigation* make clear, a general causation expert's conclusion must reliably bridge the gap by scientifically linking the disease-causing agent to the product at issue. The Superior Court's holding regarding the general causation question was inconsistent with this precedent.[129]

Although it is true that "NDMA's dangers, the science, the studies, and the opinions therein must be given due consideration,"[130] ultimately an expert offering an opinion regarding general causation for a product must opine as to the product itself. The general causation standard explained in *In re Asbestos Litigation* requires a trial judge to closely examine what a proffered expert is—and is not—saying. An expert may rely on studies of the allegedly toxic or carcinogenic agent within the product, but they also must reliably link the toxic agent (here, NDMA) and the product at issue in order to opine that the product is capable of causing the harm alleged. Appellants aptly point out that "Plaintiffs' general-causation experts did

[129] *See In re Asbestos Litig.*, 911 A.2d at 1202.

[130] Order at *10.

not undertake the sort of painstaking, peer-reviewed analysis that this Court found sufficient in *Grenier II*."[131]

The MDL court explained the problem with the MDL experts' reliance on NDMA studies that were based on dietary and occupational data:

> [R]eliance on studies of NDMA-rich foods and NDMA-rich air, [] focused on the consumption of processed meats and the inhalation of fumes in rubber factories. Processed meats contain other carcinogens besides NDMA, and people struggle to accurately remember what they have eaten the prior day, let alone what they have eaten throughout the entire course of their lifetime. And the inhalation of rubber factory fumes (which also contain many carcinogens in addition to NDMA) is too far removed from the ingestion of ranitidine to be reliably applied.[132]

Similar infirmities arise in the challenged reports in this case: Plaintiffs' experts do not reliably opine as to general causation with respect to ranitidine. Plaintiffs' experts rely on data regarding NDMA exposure in food and rubber fumes to draw conclusions about alleged harms caused by NDMA exposures from ranitidine. Plaintiffs' experts do not account for the fact that food and rubber fumes contain other chemicals, including other established carcinogens. None of Plaintiffs' experts accounted for those other exposures or concluded that the levels of NDMA in ranitidine were comparable to the levels of NDMA that the subjects in the dietary

[131] Appellants' Opening Br. at 34.

[132] MDL Order at 1094.

and occupational studies ingested or inhaled. In other words, Plaintiffs' experts did not reliably link the NDMA studies to the product at issue.

Dr. Sawyer was the only expert Plaintiffs offered to opine as to the conversion between "the inhalation doses of NDMA . . . into an equivalent oral dose."[133] But Dr. Sawyer's opinion faced numerous challenges that the court failed to resolve. The court admitted that "his science may be a bridge too far," but dismissed these challenges as questions for the jury.[134]

Properly applied, Rule 702 and Delaware precedent required the trial judge, not the jury, to resolve the challenges to Dr. Sawyer's report. Dr. Sawyer relied on a single occupational study of rubber factory workers in the United Kingdom from the 1960s, the "Hidajat study." The Superior Court quoted the MDL court multiple times to describe the Hidajat study, but ignored that court's conclusion that "an expert opinion that relies upon the dietary or occupational studies [] to conclude that ranitidine can cause cancer utilizes an unreliable methodology for [] [many] reasons."[135]

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[133] Order at *17.

[134] *Id.* ("Dr. Sawyer's opinion is limited, plainly so. He is not testifying on causation, but instead on his conversion of inhalation dose to oral dose. Defendants reject his science. Perhaps, as presented during oral arguments, his science may be a bridge too far. But at this juncture, the criticisms go to weight and do not preclude admission.").

[135] MDL Order at 1214–15.

The Superior Court gave no explanation for its conclusion that Dr. Sawyer's methodology and wholesale dependence on the Hidajat study was reliable, and did not distinguish the MDL court's opposite conclusion. Instead, the court noted that Dr. Sawyer's opinion was limited to "conversion of inhalation dose to oral dose."[136] But, although limited, Dr, Sawyer's opinion was essential to Plaintiff's general causation burden because Plaintiffs' other experts did not opine as to whether the levels of NDMA in these studies were comparable to levels of NDMA in ranitidine. Without Dr. Sawyer's opinion, which was not based on a reliable methodology, Plaintiffs lost the link between the general NDMA studies and ranitidine.

The problems with Plaintiffs' experts' analysis and conclusions are not limited to Dr. Sawyer. Dr. Miller, whom Plaintiffs relied on to provide opinions regarding NDMA exposure and pancreatic cancer, acknowledged that he did not "attempt[] to correlate the doses observed" in the non-ranitidine studies "to the doses in ranitidine."[137] Dr. Hatzaras, who was testifying as to "whether NDMA exposure from ranitidine can cause esophageal, stomach and colorectal cancer," conducted a literature review[138] that relied on dietary and occupational NDMA studies, including

[136] Order at *17.

[137] A7814–16 (Deposition of Dr. Miller).

[138] Of the nine peer-reviewed studies that Dr. Hatzaras examined that considered whether there is an association between ranitidine use and colorectal cancer, none reported a statistically significant increased risk of colorectal cancer and two reported statistically significant decreased risks. A188. Dr. Hatzaras reviewed seven peer-reviewed studies to examine an association between ranitidine and esophageal cancer; only one of these studies actually examined ranitidine use and

the Hidajat rubber worker study.[139] Another of Plaintiffs' experts, Dr. Margulis, admitted that "none of those rubber worker studies reported an increased risk of kidney cancer,"[140] but he nevertheless relied on the occupational studies in reaching his opinion on "whether it is likely that the NDMA in ranitidine can cause cancer."[141]

The Superior Court did not address these gaps nor discuss why it was appropriate for the experts to opine that ranitidine causes cancer when the research on which these experts relied did not examine NDMA exposure from ranitidine or establish that the exposure to NDMA in the occupational and dietary studies could be scientifically linked to the exposure to NDMA caused by ingesting ranitidine. Further, none of the experts explained their reliance on non-ranitidine studies rather than the ranitidine studies, which showed no increased cancer risk.

* * *

Because the Superior Court erred in defining Rule 702 and the general causation question, we reverse. Plaintiffs did not carry their burden to establish the

gastric/esophageal cancer and none of these study authors concluded that ranitidine was causally associated with an increased risk of esophageal cancer. A189. Similarly, for gastric cancer, eleven peer-reviewed studies examined whether there is an association between ranitidine use and gastric cancer, and none of these study authors concluded there was a casual association between ranitidine and gastric cancer. A190–91. Despite these findings by his peers, Dr. Hatzaras interpreted "all non-statistically significant risk estimates above 1.0 as an increased risk" and did not apply his disregard of statistical significance consistently. A194.

[139] Order at *21–22.

[140] A7499–500 (Deposition of Dr. Margulis).

[141] Order at *26.

admissibility of their general causation experts' opinions by a preponderance of the evidence. Having reached that conclusion, we do not need to address Defendants' argument that the Superior Court erred in holding that Plaintiffs' experts did not need to identify a threshold dose required to cause the cancers at issue, and we offer no conclusion regarding the Superior Court's holdings on that issue.

IV. CONCLUSION

For the foregoing reasons, we **REVERSE** the Superior Court's decision denying Defendants' motions to exclude Plaintiffs' expert opinions and remand this case to the Superior Court for further proceedings consistent with this decision. Jurisdiction is not retained.