UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF FLORIDA

IN RE: ZANTAC (RANITIDINE) PRODUCTS LIABILITY LITIGATION

MDL No. 2924
20-MD-2924

JUDGE ROBIN L. ROSENBERG
MAGISTRATE JUDGE BRUCE E. REINHART

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THIS DOCUMENT RELATES TO: ALL CASES

BRAND DEFENDANTS' ROADMAP BRIEF IN SUPPORT OF THEIR MOTIONS TO EXCLUDE PLAINTIFFS' GENERAL CAUSATION EXPERTS AND FOR SUMMARY JUDGMENT

I. INTRODUCTION

This brief provides the Brand Defendants'[1] ("Defendants") "roadmap" to their motions to exclude Plaintiffs' experts' opinions relating to general causation and their motion for summary judgment. Part II provides a general overview of Defendants' three motions to exclude and the core defects in Plaintiffs' experts' opinions. Part III sets forth Defendants' motion for summary judgment based on Plaintiffs' lack of admissible expert testimony on general causation.

II. DEFENDANTS' MOTIONS TO EXCLUDE

Defendants are filing three motions to exclude Plaintiffs' proposed expert testimony relating to general causation and invite this Court to review the motions in the following order:

1. Brand Defendants' Motion to Exclude Plaintiffs' General Causation Experts' Opinions Related to Epidemiology and Incorporated Memorandum of Law ("Epidemiology Motion")

2. Brand Defendants' Motion to Exclude Opinions and Testimony of Plaintiffs' Experts, Ramin Najafi, Ph.D., Charles Davis, Ph.D., and Other Experts Who Rely on Their Opinions, and Incorporated Memorandum of Law ("Testing Motion")

3. Brand Defendants' Motion to Exclude Remaining Expert Opinions Relating to General Causation and Incorporated Memorandum of Law ("Remaining Opinions Motion")

Together, Defendants' motions seek to exclude all of Plaintiffs' experts' general causation opinions as unreliable and otherwise inadmissible under Federal Rules of Evidence 104(a), 702, 703, and 403.[2] Plaintiffs' experts and the motions that address them are summarized below:

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[1] The Brand Defendants are GlaxoSmithKline LLC, Pfizer Inc., Boehringer Ingelheim Pharmaceuticals Inc., Sanofi US Services Inc., Sanofi-Aventis U.S. LLC, and Chattem Inc.

[2] Several of Plaintiffs' experts proffer opinions not directly related to general causation, including opinions regarding shipping and transportation and opinions that Defendants were or should have been aware of certain studies and Plaintiffs' experts' interpretations of those studies. In addition, the opinions of Plaintiffs' expert Dr. Errol Zeiger do not reach the question of general causation and thus cannot satisfy Plaintiffs' burden on that issue. Based on Pretrial Orders Nos. 63 (Dkt. 4660) and 77 (Dkt. 5579), Defendants reserve the right to move to exclude such opinions at the appropriate time after their motions on general causation opinions have been decided.

Plaintiffs' Expert	Primary Topic of Opinions	Motions Seeking Exclusion
Anne McTiernan, M.D., Ph.D.	Epidemiology	Epidemiology Motion Remaining Opinions Motion
Patricia Moorman, M.S.P.H., Ph.D.	Epidemiology	Epidemiology Motion Remaining Opinions Motion
Andrew Salmon, D.Phil., C.Chem.	Toxicology and Carcinogenicity	Epidemiology Motion Remaining Opinions Motion
Paul Michaels, M.D.	Cancer Biology	Epidemiology Motion Remaining Opinions Motion
Jennifer Le, Pharm.D.	Pharmacology and Toxicology	Epidemiology Motion Remaining Opinions Motion
Mira Hidajat, Ph.D.[3]	Occupational Epidemiology	Epidemiology Motion
Ramin Najafi, Ph.D.[4]	Pharmacology/Testing	Testing Motion Remaining Opinions Motion
Charles Davis, Ph.D.	Biostatistics	Testing Motion
Dipak Panigrahy, M.D.	Carcinogenicity	Remaining Opinions Motion
Michael Marletta, Ph.D.	Biology and NDMA Formation	Remaining Opinions Motion
Ronald Melnick, Ph.D.	Toxicology and NDMA formation	Remaining Opinions Motion

[3] Defendants have moved separately to strike Dr. Hidajat's report as an untimely general causation report and improper rebuttal report. *See* Defendants' Expedited Motion to Strike Expert (Dkt. 5460). This Court deferred its ruling on that motion in order to consider it in connection with Defendants' remaining motions to exclude Plaintiffs' experts' opinions. Order on Defendants' Motion to Strike Rebuttal Expert Report (Dkt. 5565).

[4] Defendants have moved separately to strike Dr. Najafi's opinions because he failed to timely produce all facts and data considered in forming his opinions and for spoliation of materials he considered. If granted, this motion would moot Defendants' motion to exclude his opinions. *See* Brand Defendants' Expedited Motion to Strike Plaintiffs' Expert Ramin (Ron) Najafi, Ph.D.

A. Epidemiology Motion

Defendants' Epidemiology Motion should be reviewed first because it provides the introduction and background sections that frame the medical, scientific, and legal issues that this Court will evaluate in addressing each of Defendants' motions. It also outlines basic principles of epidemiology and the rigorous analysis that good science, and thus Rule 702, requires to assess whether a statistical association exists between a medication and a disease and, if so, whether that relationship is causal. Next, it discusses the epidemiological data relevant to the question of whether use of ranitidine can cause the five cancers at issue in this litigation (gastric, esophageal, liver, bladder, and pancreatic). Finally, it sets forth numerous reasons why this Court should exclude the testimony of Plaintiffs' five experts, **Drs. Anne McTiernan**, **Patricia Moorman**, **Andrew Salmon**, **Paul Michaels**, and **Jennifer Le**, who opine that ranitidine is causally associated with those cancers.[5]

Plaintiffs' experts' opinions fail to satisfy the Rule 702 admissibility standards, including as set forth in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993), and its progeny. In particular, their opinions are neither generally accepted by the relevant medical, scientific, and regulatory communities—none of which has found a causal relationship between ranitidine use and cancer—nor derived from reliable methodologies. Instead, their opinions are based on results-driven approaches to the epidemiological data that contradict basic principles and methods of sound science, as highlighted in the examples below.

Dr. McTiernan is an epidemiologist who reaches her general causation opinions only by applying an inconsistent, unreliable methodology that runs counter to well-accepted tenets in the

[5] Plaintiffs also proffer a rebuttal report from Dr. Mira Hidajat, a researcher on occupational epidemiology, that is subject to Defendants' Motion to Strike. *Supra* n.3. In any case, Dr. Hidajat testified that she is not offering causation opinions and she should thus be excluded from doing so.

field and even her own approach to epidemiological data in another litigation. Dr. McTiernan unreliably discounts data from studies that specifically evaluated the question of a causal association between ranitidine use and cancer in favor of extrapolating data from dietary and occupational studies that did not evaluate ranitidine exposure at all. In fact, Dr. McTiernan did not even consider whether there was an association, much less causation, between ranitidine and cancer risk based on ranitidine data. Dr. McTiernan also assigns, without any scientific or statistical justification, greater weight to study results that arguably favored her causation opinions than to those that did not.

Dr. Moorman is a retired professor of epidemiology whose general causation methodology is similarly unreliable. Like Dr. McTiernan, she assigns greater weight to data from dietary and occupational studies that did not examine ranitidine than to most studies that investigated whether there is an association between ranitidine and cancer. She also relies on her non-replicable "qualitative judgment" about epidemiological evidence rather than the methods and standards she employs outside the courtroom. She further fails both to establish a valid association between ranitidine and cancer and to conduct a reliable Bradford Hill causation analysis.

Dr. Salmon is a toxicologist who is not qualified to render opinions about epidemiology and whose general causation opinions are, in any case, unreliable. For example, he both fails to apply a consistent methodology to his interpretation of the epidemiological data and erroneously applies the Environmental Protection Agency's precautionary regulatory approach to risk assessment to reach his opinions about causation.

Dr. Michaels is a cancer pathologist who seeks to offer opinions about the biological plausibility of ranitidine use and the development of cancer. Dr. Michaels' opinions on

epidemiology are unreliable because he does not even attempt to consider the totality of the relevant data and fails to apply any reliable methodology in interpreting the data on which he relies.

Dr. Le is a pharmacist and pharmacologist who reaches her causation opinions only by cherry picking data that favor her opinions and applying internally inconsistent standards in her analysis of the data.

B. Testing Motion

To the extent the Court grants Defendants' Epidemiology Motion, it need go no further because Plaintiffs cannot proceed without reliable and admissible expert testimony that ranitidine causes the cancers they allege. Plaintiffs have, however, offered additional reports, from experts **Drs. Ramin Najafi**, a chemist and founder of Plaintiffs' consulting laboratory Emery Pharma, and **Charles Davis**, a biostatistician, that seek to circumvent the global scientific consensus outside this litigation that there is no reliable evidence that ranitidine causes cancer by opining about the levels of NDMA purportedly in samples that Defendants produced. But the direct evidence—ranitidine epidemiology—already addresses the effects of whatever levels of NDMA were *actually* present in ranitidine. And because there is no evidence that real-world ranitidine use causes cancer of any type, this Court need not reach Dr. Najafi's speculations.

To the extent the Court addresses Drs. Najafi and Davis's opinions, it should exclude them in their entirety. Dr. Najafi employs litigation-driven testing methodologies that fail to follow even minimum standards of reliability in the field of analytical chemistry, including such basic practices as documenting his testing and results. He fails to use the relevant FDA-approved methodology and employs unpublished methods validated by no agency or independent, peer-reviewed study. Dr. Davis conducted statistical analyses of and extrapolations from certain portions of Dr. Najafi's data that Plaintiffs' counsel selected. He did not even attempt to verify

the validity of the data, and the same fatal flaws and lack of reliability that require the exclusion of Dr. Najafi's opinions also infect Dr. Davis's and likewise require their exclusion.

C. Remaining Opinions Motion

Defendants' third motion addresses Plaintiffs' remaining, tangential opinions relating to causation, none of which can satisfy Plaintiffs' burden on general causation and all of which should be excluded. Like the Testing Motion, this Court need not reach Defendants' Remaining Opinions Motion if it grants the Epidemiology Motion. The remaining opinions include those of Plaintiffs' experts **Drs. Dipak Panigrahy**, a pathologist, **Michael Marletta**, a chemist and molecular biologist, and **Ronald Melnick**, a toxicologist, as well as additional opinions of Drs. McTiernan, Moorman, Salmon, Michaels, Le, and Najafi, which are summarized below.

1. Opinions that NDMA forms from ranitidine in the human body after ingestion (endogenous formation).

Drs. Panigrahy, Michaels, Marletta, Le, and Najafi opine that NDMA forms in the human body after ingestion of ranitidine. This hypothesis, however, has been disproven by well-designed studies published in the peer-reviewed literature, including recent studies by the FDA, which Plaintiffs' experts fail to refute with any reliable scientific evidence.

2. Opinions that ranitidine use causes cancer in humans based on animal studies.

Several of Plaintiffs' experts, including Drs. Salmon, Le, and Panigrahy, seek to opine that animal studies show that ranitidine and NDMA cause cancer in humans. These opinions unreliably disregard the relevant human epidemiological evidence, rely on improper extrapolation of animal data to humans over the objections of the studies' own authors, and otherwise fail to account both for limitations in animal data generally and the limitations of the particular studies at issue specifically.

3. Opinions that there is "no threshold" at which NDMA does not present a cancer risk and that the FDA's regulatory threshold is proof of causation.

Drs. Panigrahy, Michaels, McTiernan, and Moorman opine that any amount of NDMA can cause cancer. Plaintiffs' experts' theory lacks support in, and fails to reliably refute, the relevant scientific literature. Courts have routinely rejected similar "no safe threshold" opinions in other cases where experts sought to opine that any amount of exposure to a substance could cause cancer. Dr. Panigrahy also opines that the FDA's regulatory threshold for daily intake of NDMA establishes that it causes cancer in humans. This opinion should be excluded because it is well settled in the science and the law that regulatory thresholds are not proof of causation.

III. DEFENDANTS' MOTION FOR SUMMARY JUDGMENT

Defendants also move for summary judgment under Rule 56 because Plaintiffs lack reliable and admissible expert testimony to establish general causation. Summary judgment is appropriate where "there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law," Fed. R. Civ. P. 56(a), including where plaintiffs fail to present admissible "proof concerning an essential element of [their] case." *Celotex Corp. v. Catrett*, 477 U.S. 317, 322-23 (1986).

Without admissible expert testimony on general causation, Plaintiffs cannot establish this essential element of their claims. *See McClain v. Metabolife Int'l, Inc.*, 401 F.3d 1233, 1239 (11th Cir. 2005). MDL courts have routinely granted summary judgment in other pharmaceutical product liability litigations where, as here, plaintiffs have failed to proffer admissible expert testimony on the threshold issue of causation. *See, e.g.*, *In re Mirena IUS Levonorgestrel-Related Prod. Liab. Litig. (No. II)*, 982 F.3d 113 (2d Cir. 2020); *In re Lipitor (Atorvastatin Calcium) Mktg., Sales Pracs. & Prod. Liab. Litig. (No. II)*, 892F.3d 624 (4th Cir. 2018); *In re Zoloft (Sertraline Hydrochloride) Prod. Liab. Litig.*, 858 F.3d 787 (3d Cir. 2017); *In re Viagra (Sildenafil Citrate)*

and Cialis (Tadalafil) Prod. Liab. Litig., Order Granting Summary Judgment, Dkt. 1021, No. 3:16-md-02691-RS (N.D. Cal. Apr. 8, 2020). This Court should do the same.

IV. CONCLUSION

For the foregoing reasons, and the reasons explained in further detail in each of Defendants' Motions, this Court should exclude Plaintiffs' experts' opinions related to general causation and grant Defendants' Motion for Summary Judgment.

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Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that a copy of the foregoing was filed on June 13, 2022 using the Court's CM/ECF system, which will provide automatic notification to all counsel of record.

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