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

ESTATE OF TERESA TEDESCO BY AND THROUGH GUY TEDESCO, AS PERSONAL REPRESENTATIVE,

Plaintiffs,

vs.

BOEHRINGER INGELHEIM PHARMACEUTICALS, INC.,

SANOFI US SERVICES, INC.,

CHATTEM, INC.,

PFIZER, INC.,

and

GLAXOSMITHKLINE, LLC

Defendants.
_____/

COMPLAINT & JURY DEMAND

CIVIL ACTION NO. 9:20-CV-80778

THIS DOCUMENT RELATES TO:
Estate of Teresa Tedesco, et al. v.
Boehringer Ingelheim Pharmaceuticals, Inc., et al.
Case No. 9:20-CV-80778

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INTRODUCTION

1. N-Nitrosodimethylamine ("NDMA") is a potent carcinogen. It used to be a chemical biproduct of making rocket fuel in the early 1900s but, today, its only use is to induce tumors in animals as part of laboratory experiments. Its only function is to cause cancer. It has no business being in a human body.

2. Zantac (chemically known as ranitidine), the popular antacid medication used by millions of people every day, leads to the production of staggering amounts of NDMA when it is digested by the human body. The U.S. Food and Drug Administration's ("FDA") allowable daily limit of NDMA is 96 ng (nanograms) and yet, in a single dose of Zantac, researchers are discovering over 3 million ng.

3. These recent revelations by independent researchers have caused widespread recalls of Zantac both domestically and internationally, and the FDA recently banned all Zantac products on April 1, 2020. Further, the current owner and controller of the Zantac new drug applications ("NDAs") has recalled all Zantac in the United States.

4. The high levels of NDMA observed in Zantac is a function of the ranitidine molecule: (1) the way it breaks down in the human digestive system; and (2) the way it breaks down when exposed to heat, in particular, during transport and storage.

5. Plaintiff Teresa Tedesco ("Plaintiff" or "Ms. Tedesco") took Zantac for approximately thirty-two (32) years. As a direct and proximate result thereof, Plaintiff developed breast cancer and other injuries, and died on May 12, 2018. Her cancer was caused by NDMA exposure created by the ingestion of Zantac. This lawsuit seeks damages against the Defendants for causing Ms. Tedesco to develop cancer.

PARTIES

6. Plaintiff Teresa Tedesco was at all relevant times a resident and citizen of Jeffersonville, Indiana.

7. Guy Tedesco was at all relevant times a resident and citizen of Jeffersonville, Indiana. Guy Tedesco is the son of Teresa Tedesco and is the personal representative of the Estate of Teresa Tedesco, an Indiana Estate.

8. Defendant Boehringer Ingelheim Pharmaceuticals, Inc. ("BI") is a Delaware corporation with its principal place of business located at 900 Ridgebury Road, Ridgefield, Connecticut 06877. BI is a citizen of Connecticut and Delaware, and not of any other state. BI is a subsidiary of the German company Boehringer Ingelheim Corporation. BI owned and controlled the NDA for over-the-counter ("OTC") Zantac between December 2006 and January 2017, and manufactured and distributed the drug in the United States, including Indiana, during that period.

9. Defendant Sanofi US Services Inc., ("Sanofi") is a Delaware corporation with its principal place of business located at 55 Corporate Drive, Bridgewater, New Jersey 08807, and is a wholly owned subsidiary of Sanofi S.A. Sanofi is a citizen of Delaware and New Jersey and is not a citizen of any other state. Sanofi controlled the NDA for OTC Zantac starting in January 2017 through the present and manufactured and distributed the drug in the United States, including Indiana, during that period. Sanofi voluntarily recalled all brand name OTC Zantac on October 18, 2019.

10. Defendant Chattem, Inc. ("Chattem") is a Tennessee corporation with its principal place of business located at 1715 West 38th Street Chattanooga, Tennessee 37409. Chattem is a citizen of Tennessee and not a citizen of any other state. Chattem is a wholly owned subsidiary of Sanofi S.A., a French multinational corporation. Chattem distributed OTC Zantac for Sanofi

throughout the United States, including Indiana, until Sanofi's recent voluntary recall.

11. Defendant Pfizer, Inc. ("Pfizer") is a Delaware corporation with its principal place of business located at 235 East 42nd Street, New York, New York 10017. Pfizer is a citizen of Delaware and New York and is not a citizen of any other state. In 1993, Glaxo Wellcome, plc formed a joint venture with Warner-Lambert, Inc. to develop and obtain OTC approval for Zantac. That OTC approval was obtained in 1995. In 1997, Warner-Lambert and Glaxo Wellcome ended their joint venture, with Warner-Lambert retaining control over the OTC NDA for Zantac and the Zantac trademark in the United States ("U.S.") and Glaxo Wellcome retaining control over the Zantac trademark internationally. In 2000, Warner-Lambert was acquired by Pfizer, who maintained control over the Zantac OTC NDA until December 2006.

12. Defendant GlaxoSmithKline, LLC ("GSK") is a Delaware company with its principal place of business located at 5 Crescent Drive, Philadelphia, Pennsylvania, 19112 and Five Moore Drive, Research Triangle, North Carolina, 27709. GSK is a wholly owned subsidiary of GlaxoSmithKline, PLC, which is its sole member. GlaxoSmithKline, PLC is a citizen of the United Kingdom, and is not a citizen of any state in the United States. GlaxoSmithKline, PLC is the successor-in-interest to the companies that initially developed, patented, and commercialized the molecule known as ranitidine. Ranitidine was initially developed by Allen & Hanburys Ltd., which was a subsidiary of Glaxo Labs Ltd. Allen & Hanburys Ltd. was awarded Patent No. 4,128,658 by the U.S. Patent and Trademark Office in December 1978, which covered the ranitidine molecule. In 1983, Glaxo Holdings, Ltd. was awarded approval by the U.S. FDA to sell Zantac in the United States. Glaxo Holdings, Ltd. was later absorbed into Glaxo Wellcome, PLC. And then, in 2000, GlaxoSmithKline, plc and GSK were created by the merger of Glaxo Wellcome and SmithKline Beecham. GSK, and its predecessors, controlled the prescription Zantac NDA

between 1983 and 2009.

13. At all relevant times, each Defendant acted in all aspects as the agent and alter ego of each other.

14. At all relevant times, Defendants acted in concert with one another to fraudulently convey false and misleading information concerning the safety and efficacy of Zantac and to conceal the risks of serious adverse events, including cancer associated with Zantac from the public, Plaintiffs, physicians, and other healthcare providers. These concerted efforts resulted in significant harm to those treated with Zantac, including Plaintiffs. But for the actions of Defendants, individually, jointly, and in concert with one another, Plaintiffs would not have ingested Zantac.

15. At all times alleged herein, Defendants were engaged in the business of, or were successors-in-interest to entities engaged in the business of, researching, designing, formulating, compounding, testing, manufacturing, producing, processing, assembling, inspecting, distributing, marketing, labeling, promoting, packaging, and/or advertising for sale or selling Zantac.

16. At all times alleged herein, Defendants were authorized to conduct or engage in business within each of the States and Territories of the United States and supplied Zantac within each of the States and Territories of the United States. Defendants received financial benefit and profits as a result of designing, manufacturing, marketing, advertising, selling, and distributing Zantac within each of the States and Territories of the United States.

17. The combined acts and/or omissions of each Defendant resulted in indivisible injuries to Plaintiffs. Each of the above-named Defendants is a joint tortfeasor and/or co-conspirator and is jointly and severally liable to Plaintiffs for the negligent acts and omissions

alleged herein. Each of the above-named Defendants directed, authorized, or ratified the conduct of each and every other Defendant.

JURISDICTION AND VENUE

18. This Court has subject matter jurisdiction pursuant to 28 U.S.C. § 1332. There is complete diversity of citizenship between the parties. In addition, Plaintiffs seek damages in excess of $75,000, exclusive of interest and costs.

19. This Court has personal jurisdiction over each Defendant insofar as each Defendant is authorized and licensed to conduct business in Indiana, maintains and carries on systematic and continuous contacts in this judicial district, regularly transacts business within the judicial district, and regularly avails itself of the benefits of the judicial district.

20. Additionally, the Defendants caused tortious injury by acts and omissions in this judicial district and caused tortious injury in this district by acts and omissions outside this district while regularly doing and soliciting business, engaging in a persistent course of conduct, and deriving substantial revenue from goods used or consumed and services rendered in this judicial district. The Plaintiff was, indeed, exposed to Zantac in this judicial district.

21. Venue is proper before this Court for pre-trial purposes in the Southern District of Florida, pursuant to this Court's PTO # 11 Setting Forth Procedures for Direct Filed Personal Injury Cases [Dkt. 422]. The District Court in which remand for trial is proper and where this Complaint would have been filed absent Pretrial Order No. 11 is the United States District Court for the Southern District of Indiana.

FACTUAL ALLEGATIONS

I. REGULATORY HISTORY OF RANITIDINE-CONTAINING PRODUCTS

22. The medication in question in this case is a drug that Defendants marketed and sold under the brand name "Zantac" or its generic version by either prescription or over-the-counter ("OTC"). Defendants sold ranitidine-containing products in the following forms: injection, syrup, and/or tablets and capsules.

23. Zantac (ranitidine) was originally discovered and developed by scientist John Bradshaw on behalf of GSK[1] in 1976.

24. The drug belongs to a class of medications called histamine H_2-receptor antagonists (or H_2 blockers), which decrease the amount of acid produced by cells in the lining of the stomach. Other drugs within this class include cimetidine (Tagamet), famotidine (Pepcid), and nizatidine (Tazac).

25. Cimetidine (Tagamet), discovered and developed by Smith, Kline and French[2], was the first H_2 blocker to be developed and is the prototypical histamine H_2 receptor antagonist from which the later members of the class were developed. Indeed, Zantac was specifically developed by GSK in response to the success of cimetidine.

26. Zantac was approved by the FDA, pursuant to the New Drug Application ("NDA") process in 1983 and, quickly, became one of GSK's most successful products, being the first prescription drug in history to reach $1 billion in sales.

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[1] Dr. Bradshaw was working for Glaxo Inc. at the time. Glaxo Inc. later merged with the Wellcome Foundation in 1995 to become Glaxo Wellcome plc. Then, in 2000, Glaxo Wellcome plc merged with Smithkline Beecham plc to form GlaxoSmithKline plc ("GSK") one of the defendants in this MDL. For the purposes of this PIMC, these entities will be referred to as GSK.

[2] Smith, Kline and French later merged with the Beecham Group in 1989 to form SmithKline Beecham plc. And, as discussed above, SmithKline Beecham plc was merged into GSK in 2000.

27. In 1993, GSK entered into a joint venture with Pfizer[3] to develop an over-the-counter ("OTC") version of Zantac. That joint venture led to FDA approval of an OTC version of Zantac in 1995. Zantac OTC was approved through an NDA process.

28. In 1997, GSK's patent on ranitidine expired, and generic ranitidine entered the market. Despite generic entry, however, brand name prescription and OTC Zantac continued to be sold. Although sales of brand-name Zantac declined as a result of generic and alternative products, Zantac sales remained strong over time. As recently as 2018, Zantac was one of the top 10 antacid tablet brands in the United States, with sales of Zantac 150 totaling $128.9 million—a 3.1% increase from the previous year.

29. In 1998, the joint venture between GSK and Pfizer dissolved. As part of the separation, GSK retained the rights to sell all forms of Zantac internationally and prescription Zantac in the U.S., while Pfizer retained the rights to sell OTC Zantac domestically and retained ownership over the Zantac trademark. Under this agreement, GSK retained control and responsibility over the prescription Zantac NDA and Pfizer retained control and responsibility over the OTC Zantac NDA.

30. In 2006, Pfizer sold the rights to sell and market OTC Zantac to Boehringer Ingelheim Pharmaceuticals, Inc., but continued (and still continues) to own the Zantac trademark. As part of this deal, Boehringer obtained control and responsibility over the OTC NDA.

31. In 2009, GSK ceased marketing prescription Zantac in the U.S. and abandoned the Zantac prescription NDA. Although, according to GSK's recent annual report (2019), GSK claims to have "discontinued making and selling prescription Zantac tablets in 2017 … in the U.S."[4]

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[3] The joint venture was between Glaxo Wellcome plc and Warner–Lambert, Inc. Warner-Lambert was later acquired by Pfizer, Inc. in 2000. For the purposes of this PIMC, Warner-Lambert will be referred to as Pfizer.

[4] GlaxoSmithKline, plc, *Annual Report* at 37 (2019), *available at* https://www.gsk.com/media/5894/annual-report.pdf

32. In 2017, Boehringer sold the rights of OTC Zantac to Sanofi US Services, Inc. As part of this deal, Sanofi obtained control and responsibility over the OTC NDA and currently retains that control and responsibility.

33. To date, the FDA has approved generic manufacturers for the sale of prescription ranitidine through an Abbreviated New Drug Application ("ANDA") process.

34. To date, the FDA has approved generic manufacturers for the sale of OTC ranitidine through an ANDA process.

II. RECALLS AND THE FDA'S BAN

35. On September 9, 2013, pharmacy and testing laboratory Valisure filed a Citizen Petition calling for the recall of all ranitidine products due to exceedingly high levels of NDMA found in ranitidine pills. FDA and European regulators started reviewing the safety of ranitidine with specific focus on the presence of NDMA.[5]

36. On September 24, 2019, generic maker Sandoz Inc. voluntarily recalled all of its ranitidine-containing products due to concerns of a "nitrosamine impurity, N-nitrosodimethylamine (NDMA), which was found in the recalled medicine."[6]

37. On September 26, 2019, Walgreens, Walmart, and Rite-Aid and Apotex Corp.—makers of generic OTC ranitidine—voluntarily recalled all ranitidine-containing products and removed the products from the shelves.[7] Apotex issued a statement, noting that "Apotex has learned from the U.S. Food and Drug Administration and other Global regulators that some

[5] https://www.fda.gov/drugs/drug-safety-and-availability/fda-updates-and-press-announcements-ndma-zantac-ranitidine; https://www.ema.europa.eu/en/news/ema-review-ranitidine-medicines-following-detection-ndma.
[6] https://www.fda.gov/news-events/press-announcements/fda-announces-voluntary-recall-sandoz-ranitidine-capsules-following-detection-impurity.
[7] https://www.fda.gov/drugs/drug-safety-and-availability/fda-updates-and-press-announcements-ndma-zantac-ranitidine.

ranitidine medicines including brand and generic formulations of ranitidine regardless of the manufacturer, contain a nitrosamine impurity called N-nitrosodimethylamine (NDMA)[.]"[8]

38. On September 28, 2019, CVS Health Corp. stated that it would stop selling Zantac and its own generic ranitidine products out of concern that it might contain a carcinogen.

39. On October 2, 2019, the FDA ordered testing on Zantac and specified a protocol to be used that did not involve the use of heat.[9]

40. On October 8, 2019, GSK voluntarily recalled all Zantac and ranitidine-containing products internationally.[10] As part of the recall, GSK publicly acknowledged that unacceptable levels of NDMA were discovered in Zantac and noted that "GSK is continuing with investigations into the potential source of the NDMA."[11]

41. On October 23, 2019, Dr. Reddy's Laboratories Ltd and Sanofi voluntarily recalled all of their ranitidine-containing products.[12]

42. On October 28, 2019, Perrigo Company plc, Novitium Pharma LLC, and Lannet Company Inc., voluntarily recalled all their ranitidine-containing products from the market.[13]

43. On November 1, 2019, the FDA announced the results of recent testing, finding "unacceptable levels" of NDMA in ranitidine products, and requested that drug makers begin to voluntarily recall their ranitidine products.[14]

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[8] https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/apotex-corp-issues-voluntary-nationwide-recall-ranitidine-tablets-75mg-and-150mg-all-pack-sizes-and.

[9] https://www.fda.gov/drugs/drug-safety-and-availability/fda-updates-and-press-announcements-ndma-zantac-ranitidine

[10] https://www.gov.uk/government/news/zantac-mhra-drug-alert-issued-as-glaxosmithkline-recalls-all-unexpired-stock

[11] Justin George Varghese, *GSK recalls popular heartburn drug Zantac globally after cancer scare*, Reuters (Oct. 8, 2019), available at https://www.reuters.com/article/us-gsk-heartburn-zantac/gsk-recalls-popular-heartburn-drug-zantac-globally-after-cancer-scare-idUSKBN1WN1SL.

[12] https://www.fda.gov/drugs/drug-safety-and-availability/fda-updates-and-press-announcements-ndma-zantac-ranitidine.

[13] *Id.*

[14] https://www.fda.gov/drugs/drug-safety-and-availability/laboratory-tests-ranitidine.

44. Between November 1, 2019 and February 27, 2020, the following ranitidine makers recalled their products from the market, citing NDMA concerns: Aurobindo Pharma USA, Amneal Pharmaceuticals, LLC, American Health Packaging, Golden State Medical Supply, Precision Dose Inc., Glenmark Pharmaceutical Inc., Appco Pharma LLC, and Northwind Pharmaceuticals.[15]

45. On January 2, 2020, research laboratory, Emery Pharma, submitted a Citizen Petition to the FDA, showing that NDMA accumulates in ranitidine at unsafe rates when exposed to heat levels that would occur during transport and storage.

46. On April 1, 2020, the FDA issued a public statement requesting the immediate removal of all ranitidine products from the market due to the risk to public health.[16] "The agency has determined that the impurity in some ranitidine products increases over time and when stored at higher than room temperatures and may result in consumer exposure to unacceptable levels of this impurity." Based upon its own testing and evaluation, the FDA concluded that "NDMA levels increase in ranitidine even under normal storage conditions and NDMA has been found to increase significantly in samples stored at higher temperatures, including temperatures the product may be exposed to during distribution and handling by consumers."

47. The FDA's reaction to the NDMA crisis involving ranitidine has come under attack. Over 43 different countries and jurisdictions took action to restrict or ban ranitidine products before the FDA took any action.[17]

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[15] https://www.fda.gov/drugs/drug-safety-and-availability/fda-updates-and-press-announcements-ndma-zantac-ranitidine.

[16] Press Release, *FDA Requests Removal of All Ranitidine Products (Zantac) from the Market*, U.S. Food and Drug Administration (April 1, 2020), *available at* https://www.fda.gov/news-events/press-announcements/fda-requests-removal-all-ranitidine-products-zantac-market

[17] Margaret Newkirk and Susan Berfield, *FDA recalls are always voluntary and sometimes haphazard—and the agency doesn't want more authority to protect consumers*, Bloomberg Businessweek (Dec. 3, 2019), *available at* https://www.bloomberg.com/graphics/2019-voluntary-drug-recalls-zantac/.

III. DANGERS OF NDMA

48. According to the U.S. Environmental Protection Agency ("EPA"), "NDMA is a semivolatile chemical that forms in both industrial and natural processes."[18] It is one of the simplest members of a class of N-nitrosamines, a family of potent carcinogens. The dangers that NDMA poses to human health have long been recognized. A news article published in 1979 noted that "NDMA has caused cancer in nearly every laboratory animal tested so far."[19] NDMA is no longer produced or commercially used in the United States, except for research, such as a tumor initiator in animal bioassays. In other words, its only use today is to cause cancer in laboratory animals.

49. Both the EPA and the International Agency for Research on Cancer ("IARC") have classified NDMA as a probable human carcinogen.[20]

50. The American Conference of Governmental Industrial Hygienists classifies NDMA as a confirmed animal carcinogen.[21]

51. The U.S. Department of Health and Human Services ("DHHS") states that NDMA is reasonably anticipated to be a human carcinogen.[22] This classification is based upon DHHS's findings that NDMA caused tumors in numerous species of experimental animals, at several

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[18] https://www.epa.gov/sites/production/files/2017-10/documents/ndma_fact_sheet_update_9-15-17_508.pdf

[19] Jane Brody, *Bottoms Up: Alcohol in moderation can extend life*, The Globe and Mail (CANADA) (Oct. 11, 1979); *see* Rudy Platiel, *Anger grows as officials unable to trace poison in reserve's water*, The Globe and Mail (CANADA) (Jan. 6, 1990) (reporting that residents of Six Nations Indian Reserve "have been advised not to drink, cook or wash in the water because testing has found high levels of N-nitrosodimethylamine (NDMA), an industrial byproduct chemical that has been linked to cancer"); Kyrtopoulos et al, *DNA adducts in humans after exposure to methylating agents*, 405 MUT. RES. 135 (1998) (noting that "chronic exposure of rats to very low doses of NDMA gives rise predominantly to liver tumors, including tumors of the liver cells (hepatocellular carcinomas), bile ducts, blood vessels and Kupffer cells").

[20] https://www.who.int/water_sanitation_health/dwq/chemicals/ndmasummary_2ndadd.pdf; https://www.epa.gov/sites/production/files/2017-10/documents/ndma_fact_sheet_update_9-15-17_508.pdf

[21] https://www.epa.gov/sites/production/files/2017-10/documents/ndma_fact_sheet_update_9-15-17_508.pdf.

[22] *Id.* at 3.

different tissue sites, and by several routes of exposure, with tumors occurring primarily in the liver, respiratory tract, kidney, and blood vessels.[23]

52. The FDA considers NDMA a chemical that "could cause cancer" in humans.[24]

53. The World Health Organization ("WHO") states that there is "conclusive evidence that NDMA is a potent carcinogen" and that there is "clear evidence of carcinogenicity."[25]

54. As early as 1980, consumer products containing unsafe levels of NDMA and other nitrosamines have been recalled by manufacturers, either voluntarily or at the direction of the FDA.

55. Most recently, beginning in the summer of 2018, there have been recalls of several generic drugs used to treat high blood pressure and heart failure—Valsartan, Losartan, and Irbesartan—because the medications contained nitrosamine impurities that do not meet the FDA's safety standards.

56. The no-observed-adverse-effect level ("NOAEL") is the level of exposure at which there is no biologically or significant increase in the frequency or severity of any adverse effects of the chemical. Due to NDMA's ability to affect DNA at a microscopic level, there is no NOAEL for NDMA. This means any amount of NDMA exposure increases risk.

57. That said, the FDA has set an acceptable daily intake ("ADI") level for NDMA at 96 nanograms. This means, according to the FDA, consumption of 96 nanograms of NDMA a day would increase the risk of developing cancer by 0.001% over the course of a lifetime. That risk increases as the level of NDMA exposure increases. However, any level above 96 nanograms is

[23] https://www.epa.gov/sites/production/files/2017-10/documents/ndma_fact_sheet_update_9-15-17_508.pdf.
[24] https://www.fda.gov/news-events/press-announcements/statement-alerting-patients-and-health-care-professionals-ndma-found-samples-ranitidine
[25] World Health Organization, *Guidelines for Drinking Water Quality, N-Nitrosodimethylamine (NDMA)* (3rd ed. 2008), *available at* https://www.who.int/water_sanitation_health/dwq/ chemicals/ndmasummary_2ndadd.pdf.

considered unacceptable.[26] For example, tobacco smoke also contains NDMA. One filtered cigarette contains between 5 to 43 nanograms of NDMA.

58. In mouse studies examining the carcinogenicity of NDMA through oral administration, animals exposed to NDMA developed cancer in the kidney, bladder, liver, and lung. In comparable rat studies, similar cancers were observed in the liver, kidney, pancreas, and lung. In comparable hamster studies, similar cancers were observed in the liver, pancreas, and stomach. In comparable Guinea-pig studies, similar cancers were observed in the liver and lung. In comparable rabbit studies, similar cancers were observed in the liver and lung.

59. In other long-term animal studies in mice and rats utilizing different routes of exposures—inhalation, subcutaneous injection, and intraperitoneal (abdomen injection)—cancer was observed in the lung, liver, kidney, nasal cavity, and stomach.

60. Alarmingly, Zantac is in the FDA's category B for birth defects, meaning it is considered safe to take during pregnancy. However, in animal experiments, for those animals exposed to NDMA during pregnancy, the offspring had elevated rates of cancer in the liver and kidneys.

61. NDMA is, itself, a very small molecule. This allows it to freely pass through all areas of the body, including the blood-brain and placental barrier. This is particularly concerning as ranitidine has been marketed for pregnant women and young children for years.

62. In addition, NDMA breaks down into various derivative molecules that, themselves, are associated with causing cancer. In animal studies, derivatives of NDMA induced cancer in the stomach and intestine (including colon).

[26] https://www.fda.gov/drugs/drug-safety-and-availability/fda-updates-and-press-announcements-angiotensin-ii-receptor-blocker-arb-recalls-valsartan-losartan.

63. Research shows that lower levels of NDMA, *i.e.*, 40 ng, are fully metabolized in the liver, but high doses enter the body's general circulation.

64. Numerous *in vitro* studies confirm that NDMA is a mutagen—causing mutations in human and animal cells.

65. Overall, the animal data demonstrates that NDMA is carcinogenic in all animal species tested: mice, rats, Syrian golden, Chinese and European hamsters, guinea-pigs, rabbits, ducks, mastomys, fish, newts, and frogs.

66. Pursuant to the EPA cancer guidelines, "tumors observed in animals are generally assumed to indicate that an agent may produce tumors in humans."[27]

67. In addition to the overwhelming animal data linking NDMA to cancer, there are numerous human epidemiological studies exploring the effects of dietary exposure to various cancers. And, while these studies (several discussed below) consistently show increased risks of various cancers, the exposure levels considered in these studies are a very small fraction—as little as 1 millionth—the exposures noted in a single Zantac capsule, *i.e.*, 0.191 ng/day (dietary) v. 304,500 ng/day (Zantac).

68. In a 1995 epidemiological case-control study looking at NDMA dietary exposure with 220 cases, researchers observed a statistically significant 700% increased risk of gastric cancer in persons exposed to more than 0.51 ng/day.[28]

69. In a 1995 epidemiological case-control study looking at NDMA dietary exposure with 746 cases, researchers observed statistically significant elevated rates of gastric cancer in persons exposed to more than 0.191 ng/day.[29]

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[27] *See* https://www3.epa.gov/airtoxics/cancer_guidelines_final_3-25-05.pdf.

[28] Pobel, *et al*., *Nitrosamine, nitrate and nitrite in relation to gastric cancer: a case-control study in Marseille, France*, 11 EUROP. J. EPIDEMIOL. 67–73 (1995).

[29] La Vecchia, *et al*., *Nitrosamine intake and gastric cancer risk*, 4 EUROP. J. CANCER. PREV. 469–474 (1995).

70. In another 1995 epidemiological case-control study looking at, in part, the effects of dietary consumption on cancer, researchers observed a statistically significant elevated risk of developing aerodigestive cancer after being exposed to NDMA at .179 ng/day.[30]

71. In a 1999 epidemiological cohort study looking at NDMA dietary exposure with 189 cases and a follow up of 24 years, researchers noted that "*N*-nitroso compounds are potent carcinogens" and that dietary exposure to NDMA more than doubled the risk of developing colorectal cancer.[31]

72. In a 2000 epidemiological cohort study looking at occupational exposure of workers in the rubber industry, researchers observed significant increased risks for NDMA exposure for esophagus, oral cavity, pharynx, prostate, and brain cancer.[32]

73. In a 2011 epidemiological cohort study looking at NDMA dietary exposure with 3,268 cases and a follow up of 11.4 years, researchers concluded that "[d]ietary NDMA intake was significantly associated with increased cancer risk in men and women" for all cancers, and that "NDMA was associated with increased risk of gastrointestinal cancers" including rectal cancers.[33]

74. In a 2014 epidemiological case-control study looking at NDMA dietary exposure with 2,481 cases, researchers found a statistically significant elevated association between NDMA exposure and colorectal cancer.[34]

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[30] Rogers, *et al*., *Consumption of nitrate, nitrite, and nitrosodimethylamine and the risk of upper aerodigestive tract cance*r, 5 CANCER EPIDEMIOL. BIOMARKERS PREV. 29–36 (1995).

[31] Knekt, *et al*., *Risk of Colorectal and Other Gastro-Intestinal Cancers after Exposure to Nitrate, Nitrite and N-nitroso Compounds: A Follow-Up Study*, 80 INT. J. CANCER 852–856 (1999)

[32] Straif, *et al., Exposure to high concentrations of nitrosamines and cancer mortality among a cohort of rubber workers*, 57 OCCUP ENVIRON MED 180–187 (2000).

[33] Loh, *et al*., *N-nitroso compounds and cancer incidence: the European Prospective Investigation into Cancer and Nutrition (EPIC)–Norfolk Study*, 93 AM J CLIN NUTR. 1053–61 (2011).

[34] Zhu, *et al*., *Dietary N-nitroso compounds and risk of colorectal cancer: a case-control study in Newfoundland and Labrador and Ontario, Canada*, 111 BR J NUTR. 6, 1109–1117 (2014).

75. In addition to studies demonstrating that NDMA directly causes cancer, research shows that exposure the NDMA (1) can exacerbate existing but dormant cancers (*i.e.*, not malignant), (2) promote otherwise "initiated cancer cells" to develop into cancerous tumors; and (3) reduce the ability of the body to combat cancer. Thus, in addition to NDMA being a direct cause of cancer itself, NDMA can also be a continuing factor to a cancer injury caused by some other source.

76. NDMA is also known to be genotoxic—meaning, it can cause DNA damage in human cells. Indeed, multiple studies demonstrate that NDMA is genotoxic both *in vivo* and *in vitro.* However, recent studies have shown that the ability of NDMA to cause mutations in cells is affected by the presence of enzymes typically found in living humans, suggesting that "humans may be especially sensitive to the carcinogenicity of NDMA."[35]

IV. HOW RANITIDINE TRANSFORMS INTO NDMA WITHIN THE BODY

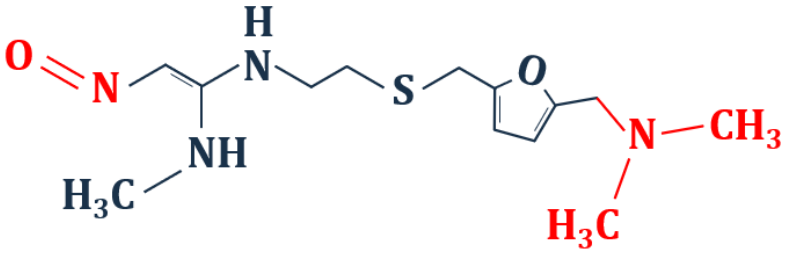
77. The NDMA contained in ranitidine-containing products is not caused by any direct contamination. Rather, the ranitidine molecule, itself, contains the constituent molecules to form NDMA. *See* Figure 1.

78. Specifically, the O=N (Nitroso) on one side of the ranitidine molecule can combine with the H_3C-N-CH_3 (DMA) on the other side to form NDMA. The NDMA forms out of the ranitidine molecule itself.

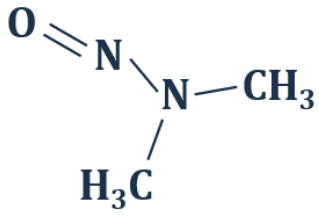
[35] World Health Organization, *Guidelines for Drinking Water Quality, N-Nitrosodimethylamine (NDMA)* (3rd ed. 2008), *available at* https://www.who.int/water_sanitation_health/dwq/ chemicals/ndmasummary_2ndadd.pdf.

Figure 1 – Diagram of Ranitidine & NDMA Molecules

Ranitidine Molecule



NDMA Molecule



79. The formation of NDMA by the reaction of DMA and a nitroso source (such as a nitrite) is well characterized in the scientific literature and has been identified as a concern for contamination of the American water supply.[36] Indeed, in 2003, alarming levels of NDMA in drinking water processed by wastewater treatment plants was specifically linked to the presence of ranitidine.[37]

80. Ranitidine leads to NDMA exposure by: (1) formation of NDMA in the human stomach; (2) formation of NDMA due to an enzymatic reaction throughout the human body; and (3) formation of NDMA due to heat and time.

A. Formation of NDMA in the Environment of the Human Stomach

81. When the ranitidine molecule is exposed to the acidic environment of the stomach, particularly when accompanied by nitrites (a chemical commonly found in heartburn-inducing foods), the Nitroso molecule (0=N) and the DMA molecule (H_3C-N-CH_3) break off and reform as NDMA.

[36] Ogawa, *et al.*, *Purification and properties of a new enzyme, NG, NG-dimethylarginine dimethylaminohydrolase, from rat kidney*, 264 J. BIO. CHEM. 17, 10205-10209 (1989).
[37] Mitch, *et al.*, *N-Nitrosodimethylamine (NDMA) as a Drinking Water Contaminant: A Review*, 20 ENV. ENG. SCI. 5, 389-404 (2003).

82. In 1981, Dr. Silvio de Flora, an Italian researcher from the University of Genoa, published the results of experiments he conducted on ranitidine in the well-known journal, the Lancet. When ranitidine was exposed to human gastric fluid in combination with nitrites, his experiment showed "toxic and mutagenic effects[.]"[38] Dr. de Flora hypothesized that these mutagenic effects could have been caused by the "formation of more than one nitroso derivative [which includes NDMA] under our experimental conditions." *Id.* Dr. de Flora cautioned that, in the context of ranitidine ingestion, "it would seem prudent to … suggest[] a diet low in nitrates and nitrites, by asking patients not to take these at times close to (or with) meals[.]"[39] *Id.*

83. GSK knew of Dr. de Flora's publication because, two weeks later, GSK responded in the Lancet, claiming that the levels of nitrite needed to induce the production of nitroso derivatives (*i.e.*, NDMA) were not likely to be experienced by people in the real world.[40]

84. In its submission to the FDA, GSK explained that the level of nitrite present would be unrealistic and, thus, these results had no "practical clinical significance"[41]:

> Although N-nitroso-nitrolic acid was a potent mutagen, it is not likely to be formed in the stomach of a patient ingesting ranitidine, as an unrealistically large amount of nitrite needs to be present to form and maintain the nitrosamine. For this reason, and also because ranitidine was not carcinogenic in life-span studies in rodents, the in vitro nitrosation of ranitidine to a mutagenic nitrosamine does not seem to have practical clinical significance.

[38] De Flora, *Cimetidine, Ranitidine and Their Mutagenic Nitroso Derivatives*, THE LANCET 993-994 (Oct. 31, 1981).

[39] This admonition came two years before the FDA's approved Zantac in 1983. Notwithstanding, in 1998 GSK applied for and obtained an indication for OTC Zantac "[f]or the prevention of meal-induced heartburn at a dose of 75 mg taken 30 to 60 minutes prior to a meal." *See* https://www.accessdata.fda.gov/drugsatfda_docs/nda/98/20520s1_Zantac.pdf. So, GSK specifically invited patients to take Zantac shortly before eating heartburn-inducing food.

[40] R. T., Brittain, et al, *Safety of Ranitidine*, THE LANCET (Nov. 14, 1981).

[41] Excerpted from the Summary Basis of Approval submitted to the FDA to obtain approval of Zantac in the early 1980s. This document was obtained through a Freedom of Information Act request to the FDA.

85. Around this same time—before Zantac was approved by the FDA—GSK conducted another study to examine, among other things, how long-term use of ranitidine could effect the levels of nitrite in the human stomach.[42] Remarkably, in the study that was presented to the FDA, GSK admitted that ranitidine use caused the proliferation of bacteria in the human stomach that are known to convert nitrates to nitrites, which leads to elevated levels of nitrite in the stomach environment. GSK acknowledged this could increase the risk of developing NDMA and, in turn, cancer, but then dismissed this risk because people were only expected to use ranitidine-containing products for a short-term period:

> The importance of this finding is not clear. High levels of nitrite could react with certain organic compounds to form nitrosamines, which are known carcinogens. To date, however, neither ranitidine nor cimetidine have been carcinogenic in rodents, so the level of human risk cannot be estimated from animal studies. Ranitidine is recommended only for short-term use and carcinogenic risk, if any, should thus be minimized.

86. GSK knew—and indeed specifically admitted—that ranitidine could react with nitrite in the human stomach to form NDMA and, at the same time, that long-term use of ranitidine could lead to elevated levels of nitrite in the human stomach.

87. In response to Dr. de Flora's findings, in 1982, GSK conducted a clinical study specifically investigating gastric contents in human patients.[43] The study, in part, specifically measured the levels of N-Nitroso compounds in human gastric fluid. GSK indicated that there were no elevated levels, and even published the results of this study five years later, in 1987. The study, however, was rigged. It did not use gold-standard mass spectrometry to test for NDMA, but instead, used a process that could not measure N-nitrosamines efficiently. And worse, in the

[42] The results of this study are discussed in the Summary Basis of Approval, obtained from the FDA.

[43] Thomas, *et al*., *Effects of one year's treatment with ranitidine and of truncal vagotomy on gastric contents*, 6 *GUT*. Vol. 28, 726-738 (1987).

testing it did do, GSK refused to test gastric samples that contained ranitidine in them out of concern that samples with ranitidine would contain "high concentrations of N-nitroso compounds being recorded." *Id.* So, GSK did not test for NDMA in any gastric fluid that contained ranitidine.

88. In 1983, the same year Zantac obtained approval from the FDA, seven researchers from the University of Genoa published a study discussing ranitidine and its genotoxic effects (ability to harm DNA).[44] The researchers concluded "it appears that reaction of ranitidine with excess sodium nitrite under acid conditions gives rise to a nitroso-derivative (or derivatives) [like NDMA] capable of inducing DNA damage in mammalian cells." *Id.*

89. Then, again in 1983, Dr. de Flora, along with four other researchers, published their complete findings.[45] The results "confirm our preliminary findings on the formation of genotoxic derivatives from nitrite and ranitidine[.]" *Id.* Again, the authors noted that, "the widespread clinical use [of ranitidine] and the possibility of a long-term maintenance therapy suggest the prudent adoption of some simple measures, such as a diet low in nitrates and nitrites or the prescription of these anti-ulcer drugs at a suitable interval from meals." *Id.* This admonition carries weight considering GSK's studies indicate that long-term ranitidine consumption, itself, leads to elevated levels of nitrites in the human gut.

90. The high instability of the ranitidine molecule was elucidated in scientific studies investigating ranitidine as a source of NDMA in drinking water and specific mechanisms for the breakdown of ranitidine were proposed.[46] These studies underscore the instability of the NDMA

[44] Maura, *et al*., *DNA Damage Induced by Nitrosated Ranitidine in Cultured Mammalian Cells*, 18 TOX. LTTRS. 97-102 (1983).
[45] De Flora, *et al*., *Genotoxicity of nitrosated ranitidine*, 4 CARCINOGENESIS 3, 255-260 (1983).
[46] Le Roux, *et al*., *NDMA Formation by Chloramination of Ranitidine: Kinetics and Mechanism*, 46 *Environ. Sci. Technol.* 20, 11095-11103 (2012).

group on the ranitidine molecule and its ability to form NDMA in the environment of water treatment plants which supply many American cities with water.

91. In 2016, researchers at Stanford University conducted an experiment on healthy volunteers (Stanford Study).[47] They measured the NDMA in urine of healthy individuals over the course of 24 hours, administered one dose of ranitidine, and then measured the NDMA in the urine of the same individuals for another 24 hours. On average, the level of NDMA increased by 400 times, to approximately 47,000 nanograms. The only change during that 24-hour period was the consumption of ranitidine. This study directly demonstrated that unsafe levels of NDMA are formed in the human body as a result of ranitidine ingestion. The scientists further explained that humans do not typically excrete NDMA in their urine, so that the observed 47,000 nanograms likely only captured 1/100 of the actual NDMA levels in the human body.

92. These studies did not appreciate the full extent of NDMA formation risk from ranitidine; specifically, the added danger of this drug having not only a labile DMA group but also a readily available nitroso source in its nitrite group on the opposite terminus of the molecule. Recent testing of NDMA levels in ranitidine batches are so high that the nitroso for NDMA likely comes from no other source than the ranitidine molecule itself.

93. Valisure, LLC is an online pharmacy that also runs an analytical laboratory that is ISO 17025 accredited by the International Organization for Standardization ("ISO") – an accreditation recognizing the laboratories technical competence for regulatory. Valisure's mission is to help ensure the safety, quality, and consistency of medications and supplements in the market. In response to rising concerns about counterfeit medications, generics, and overseas

[47] Zeng, *et al*., *Oral intake of ranitidine increases urinary excretion of N-nitrosodimethylamine*, 37 CARCINOGENESIS 625-634 (2016).

manufacturing, Valisure developed proprietary analytical technologies that it uses in addition to FDA standard assays to test every batch of every medication it dispenses.

94. As part of its testing of Zantac, and other ranitidine products, in every lot tested, Valisure discovered high levels of NDMA. Valisure's ISO 17025 accredited laboratory used FDA recommended GC/MS headspace analysis method FY19-005-DPA8 for the determination of NDMA levels. As per the FDA protocol, this method was validated to a lower limit of detection of 25 ng.[48] The results of Valisure's testing show levels of NDMA well above 2 million ng per 150 mg Zantac tablet, shown below in Table 1.

Table 1 – Ranitidine Samples Tested by Valisure Laboratory Using GC/MS Protocol

150 mg Tablets or equivalent	**Lot #**	**NDMA per tablet (ng)**
Reference Powder*	125619	2,472,531
Zantac, Brand OTC	18M498M	2,511,469
Zantac (mint), Brand OTC	18H546	2,834,798
Wal-Zan, Walgreens	79L800819A	2,444,046
Wal-Zan (mint), Walgreens	8ME2640	2,635,006
Ranitidine, CVS	9BE2773	2,520,311
Zantac (mint), CVS	9AE2864	3,267,968
Ranitidine, Equate	9BE2772	2,479,872
Ranitidine (mint), Equate	8ME2642	2,805,259
Ranitidine, Strides	77024060A	2,951,649

95. Valisure's testing shows, on average, 2,692,291 ng of NDMA in a 150 mg Zantac tablet. Considering the FDA's permissible limit is 96 ng, this would put the level of NDMA at

[48] US Food and Drug Administration. (updated 01/25/2019). Combined N-Nitrosodimethlyamine (NDMA) and N-Nitrosodiethylamine (NDEA) Impurity Assay, *FY19-005-DPA-S.*

28,000 times the legal limit. In terms of smoking, a person would need to smoke at least 6,200 cigarettes to achieve the same levels of NDMA found in one 150 mg dose of Zantac.

96. Valisure, however, was concerned that the extremely high levels of NDMA observed in its testing were a product of the modest oven heating parameter of 130 °C in the FDA recommended GC/MS protocol. So, Valisure developed a low temperature GC/MS method that could still detect NDMA but would only subject samples to 37 °C, the average temperature of the human body. This method was validated to a lower limit of detection of 100 ng.

97. Valisure tested ranitidine tablets by themselves and in conditions simulating the human stomach. Industry standard "Simulated Gastric Fluid" ("SGF" 50 mM potassium chloride, 85 mM hydrochloric acid adjusted to pH 1.2 with 1.25 g pepsin per liter) and "Simulated Intestinal Fluid" ("SIF" 50 mM potassium chloride, 50 mM potassium phosphate monobasic adjusted to pH 6.8 with hydrochloric acid and sodium hydroxide) were used alone and in combination with various concentrations of nitrite, which is commonly ingested in foods like processed meats and is elevated in the stomach by antacid drugs. The inclusion of nitrite in gastric fluid testing is commonplace and helps simulate the environment of a human stomach.

98. Indeed, Zantac was specifically advertised to be used when consuming foods containing high levels of nitrates, like tacos, pizza, *etc*.[49]

99. The results of Valisure's tests on ranitidine tablets in biologically relevant conditions demonstrate significant NDMA formation under simulated gastric conditions with nitrite present (*see* Table 2).

[49] *See, e.g.*, https://www.ispot.tv/ad/dY7n/zantac-family-taco-night; https://youtu.be/jzS2kuB5_wg; https://youtu.be/Z3QMwkSUlEg; https://youtu.be/qvh9gyWqQns.

Table 2 – Valisure Biologically Relevant Tests for NDMA Formation

Ranitidine Tablet Studies	**NDMA (ng/mL)**	**NDMA per tablet (ng)**
Tablet without Solvent	Not Detected	Not Detected
Tablet	Not Detected	Not Detected
Simulated Gastric Fluid ("SGF")	Not Detected	Not Detected
Simulated Intestinal Fluid	Not Detected	Not Detected
SGF with 10 mM Sodium Nitrite	Not Detected	Not Detected
SGF with 25 mM Sodium Nitrite	236	23,600
SGF with 50 mM Sodium Nitrite	3,045	304,500

100. Under biologically relevant conditions, when nitrites are present, high levels of NDMA are found in one dose of 150 mg Zantac, ranging between 245 and 3,100 times above the FDA-allowable limit. In terms of smoking, one would need to smoke over 500 cigarettes to achieve the same levels of NDMA found in one dose of 150 mg Zantac at the 25 nanogram level (over 7,000 for the 50 nanogram level).

101. When the scientific data is assessed overall, the literature demonstrates that the ingestion of ranitidine in the presence of human-relevant levels of nitrite in the stomach—a substance that is commonly found in foods that induce heartburn and that is known to be elevated in people taking ranitidine for longer than a month—the ranitidine molecule breaks down into levels of NDMA that would dramatically increase a person's risk of developing cancer.

B. Formation of NDMA in the Other Organs of Human Body

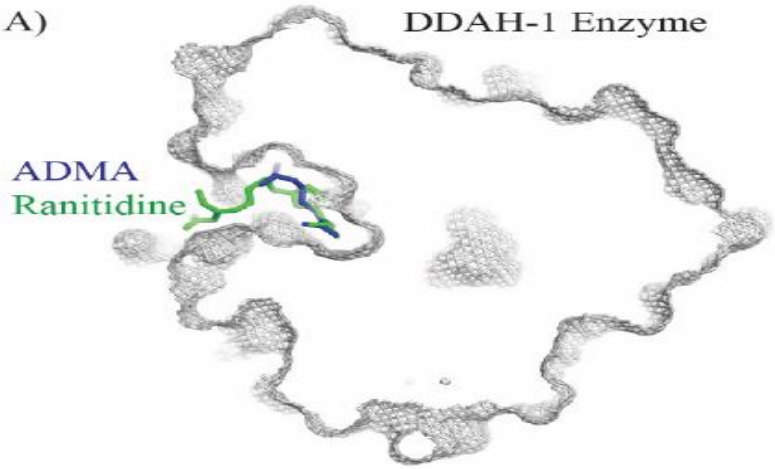
102. In addition to the gastric fluid mechanisms investigated in the scientific literature, Valisure identified a possible enzymatic mechanism for the liberation of ranitidine's DMA group via the human enzyme dimethylarginine dimethylaminohydrolase ("DDAH"), which can occur in other tissues and organs separate from the stomach.

103. Liberated DMA can lead to the formation of NDMA when exposed to nitrite present on the ranitidine molecule, nitrite freely circulating in the body, or other potential pathways,

particularly in weak acidic conditions such as that in the kidney or bladder. The original scientific paper detailing the discovery of the DDAH enzyme in 1989 specifically comments on the propensity of DMA to form NDMA: "This report also provides a useful knowledge for an understanding of the endogenous source of dimethylamine as a precursor of a potent carcinogen, dimethylnitrosamine [NDMA]."[50]

104. In Figure 2, below, computational modelling demonstrates that ranitidine (shown in green) can readily bind to the DDAH-1 enzyme (shown as a cross-section in grey) in a manner similar to the natural substrate of DDAH-1 known as asymmetric dimethylarginine ("ADMA," shown in blue).

Figure 2 – Computational Modelling of Ranitidine Binding to DDAH-1 Enzyme



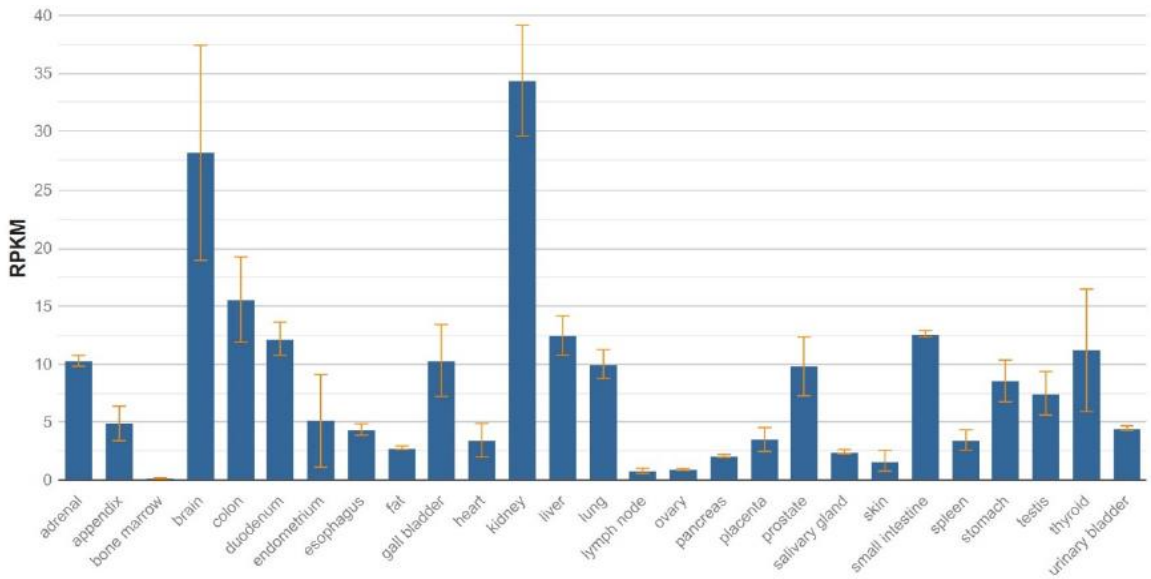
	Predicted Affinity (kcal/mol)
ADMA	-5.9 ± 0.2
Ranitidine	-6.1 ± 0.1

105. These results indicate that the enzyme DDAH-1 increases formation of NDMA in the human body when ranitidine is present; therefore, the expression of the DDAH-1 gene is useful for identifying organs most susceptible to this action.

[50] Ogawa, *et al.*, *Purification and properties of a new enzyme, NG, NG-dimethylarginine dimethylaminohydrolase, from rat kidney*, 264 *J. BIO. CHEM.* 17, 10205-10209 (1989).

106. Figure 3 below, derived from the National Center for Biotechnology Information, illustrates the expression of the DDAH-1 gene in various tissues in the human body.

Figure 3 – Expression levels of DDAH-1 enzyme by Organ



107. DDAH-1 is most strongly expressed in the kidneys but also broadly distributed throughout the body, such as in the liver, prostate, stomach, bladder, brain, colon, and prostate. This offers both a general mechanism for NDMA formation in the human body from ranitidine and specifically raises concern for the effects of NDMA on numerous organs, including the bladder.

108. The possible enzymatic reaction of ranitidine to DDAH-1, or other enzymes, suggests that high levels of NDMA can form throughout the human body. Indeed, ranitidine metabolizes and circulates throughout the human body, crossing the placental and blood-brain barrier, within 1-2 hours. When the ranitidine interacts with the DDAH-1 enzyme in various organs throughout the body, it breaks down into NDMA. This observation is validated by the Stanford study.

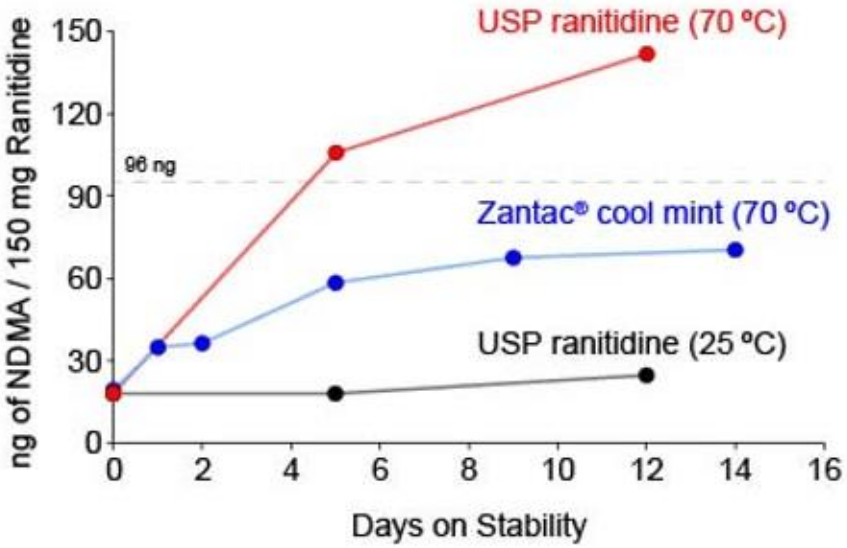
C. Formation of NDMA by Exposure to Heat and/or Time

109. The risk of creating NDMA by exposing ranitidine to heat has been well-known and documented. Early studies, including the one conducted by GSK in the early 1980s, demonstrated that NDMA formed when ranitidine was exposed to heat. This point was underscored in the Valisure petition, which specifically developed a detection protocol that did not use heat.

110. In response to Valisure, on October 2, 2019, the FDA recommended that researchers use the LC-HRMS protocol for detecting NDMA in ranitidine because the "testing method does not use elevated temperatures" and has been proven capable of detecting NDMA.

111. On January 2, 2020, Emery Pharma, an FDA-certified pharmaceutical testing laboratory, conducted a series of tests on ranitidine using the FDA-recommended LC-HRMS protocol. The researchers exposed ranitidine to 70 ˚C for varying periods of time. The results showed that increasing levels of NDMA formed based on exposure to heat. The following diagram reveals how NDMA accumulates over time when exposed to 70 ˚C:

Figure 4 – Rate of Development of NDMA when Exposed to Heat



112. The researchers cautioned:

> NDMA accumulates in ranitidine-containing drug products on exposure to elevated temperatures, which would be routinely reached during shipment and during storage. More importantly, these conditions occur post-lot release by the manufacturer. Hence, while NDMA levels in ranitidine may be acceptable at the source, they may not be so when the drug is purchased and subsequently at the time of consumption by the consumer.

113. The results of this data demonstrate that in normal transport and storage, and especially when exposed to heat, the ranitidine molecule systematically breaks down into NDMA, accumulating over time in the finished product. Considering ranitidine-containing products have an approved shelf life of 36 months, the possibility of the drug accumulating dangerously high levels of NDMA prior to consumption is very real—a point underscored by the FDA's swift removal of the product from the market.

D. Evidence Also Directly Links Ranitidine Exposure to Cancer

114. In addition to numerous epidemiology studies examining how NDMA causes cancer in humans, researchers have also specifically looked at ranitidine and found an association with cancer.

115. One epidemiology study, published in 2004, showed that men taking either ranitidine or cimetidine (Tagamet) had increased risks of bladder cancer.[51]

116. A study published in 2018, demonstrated an increased risk of liver cancer associated with use of ranitidine in comparison with other histamine type 2 receptor antagonists (H2RAs) in the class. The purpose of the study was to determine whether there was an increased risk of liver cancer associated with proton pump inhibitors, a different class of medications indicated for the treatment of GERD. This finding is particularly notable as the authors adjusted

[51] D. Michaud, et al, *Peptic Ulcer Disease and the Risk of Bladder Cancer in a Prospective Study of Male Health Professionals*, 13 CANCER EPI. BIOMARK. & PREV. 250–254, 252 (Feb. 2004).

for variables and, more significantly, did not study or consider long term use of H2RAs or the possibility of a dose dependent increase in risk.[52]

117. In 2018, a study found an increased risk in hepatocellular carcinoma associated with use of H2RAs.[53] The authors were evaluating the risk of cancer in association with proton pump inhibitors and looked at H2RAs as a confounder. The study only considered use of H2RAs within one year of cancer diagnosis and still found an increased odds ratio associated with use of H2RAs and hepatocellular carcinoma, a type of liver cancer.

118. A number of other studies have been published over the years showing an increased risk of various cancers associated with use of ranitidine and/or H2RAs.[54] However it is especially noteworthy that Memorial Sloan Kettering, in conjunction with various researchers, plan to publish a study specifically looking at ranitidine users and cancer risks in the Journal of the American Medical Association ("JAMA"). The article was accepted and is set for publication.

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[52] Kim Tu Tran,, et al., *Proton pump inhibitor and histamine-2 receptor antagonist use and risk of liver cancer in two population-based studies*, 48 ALIMENTARY PHARMA & THERAP 1, 55-64 (2018).

[53] Shao, Y-HJ, et al., *Association between proton pump inhibitors and the risk of hepatocellular carcinoma*, 48 ALIMENTARY PHARMA & THERAP 4, 460-468 (2018).

[54] Robert W. Mathes, et al., *Relationship between histamine2-receptor antagonist medications and risk of invasive breast cancer*, 17 CANCER EPID. & PREV BIOMARKERS 1, 67-72 (2008); *see also* Ahn, Jeong Soo, et al., *Acid suppressive drugs and gastric cancer: a meta-analysis of observational studies*, 19 WORLD J. GASTROENTEROLOGY 16, 2560 (2013); Lai, Shih-Wei, et al., *Use of proton pump inhibitors correlates with increased risk of pancreatic cancer: a case-control study in Taiwan*, 46 KUWAIT MED J. 1, 44-48 (2014); Poulsen et al., *Proton Pump Inhibitors and risk of gastric cancer – a population based cohort study*, 100 BRITISH J CANCER 1503-1507 (2009); E Wennerström, *Acid-suppressing therapies and subsite-specific risk of stomach cancer*, 116 BRITISH J CANCER 9, 1234-1238 (2017).

V. DEFENDANTS KNEW OR SHOULD HAVE KNOWN OF THE NDMA RISK

119. During the time that Defendants manufactured and sold Zantac in the United States, the weight of scientific evidence showed that Zantac exposed users to unsafe levels of NDMA. Defendants failed to disclose this risk to consumers on the drug's label—or through any other means—and Defendants failed to report these risks to the FDA.

120. Going back as far as 1981, two years before Zantac entered the market, research showed elevated rates of NDMA, when properly tested. This was known or should have been known by the Defendants or any other maker or distributor of ranitidine-containing products.

121. Defendants concealed the Zantac–NDMA link from consumers in part by not reporting it to the FDA, which relies on drug manufacturers (or others, such as those who submit citizen petitions) to bring new information about an approved drug like Zantac to the agency's attention.

122. Manufacturers of an approved drug are required by regulation to submit an annual report to the FDA containing, among other things, new information regarding the drug's safety pursuant to 21 C.F.R. § 314.81(b)(2):

> The report is required to contain . . . [a] brief summary of significant new information from the previous year that might affect the safety, effectiveness, or labeling of the drug product. The report is also required to contain a brief description of actions the applicant has taken or intends to take as a result of this new information, for example, submit a labeling supplement, add a warning to the labeling, or initiate a new study.

123. 21 C.F.R. § 314.81(b)(2)(v) provides:

> The manufacturer's annual report also must contain copies of unpublished reports and summaries of published reports of new toxicological findings in animal studies and in vitro studies (*e.g.*, mutagenicity) conducted by, or otherwise obtained by, the [manufacturer] concerning the ingredients in the drug product."

124. Defendants ignored these regulations and, disregarding the scientific evidence available to them, did not report to the FDA significant new information affecting the safety or labeling of Zantac.

125. Knowledge regarding the risk of NDMA in ranitidine was sufficiently available in the publicly available scientific literature that any maker or distributor, consistent with their heightened obligations to ensure the safety of their products, should have known about the potential NDMA risks associated with ranitidine consumption.

126. Defendants never conducted or provided the relevant studies to the FDA, nor did they present to the FDA with a proposed disclosure noting the link between ranitidine and NDMA. Accordingly, because the Defendants never properly disclosed the risk to the FDA, they never proposed any labeling or storage / transportation guidelines that would have addressed this risk. Thus, the FDA was never able to reject any proposed warning or proposal for transport / storage.

127. Nothing prevented any Defendant from, on it own, taking actions to prevent accumulation of NDMA in ranitidine pills by ensuring cooled storage and transport. Such actions would not have required FDA approval, nor would they have violated any regulatory decisions or laws.

128. In a 1981 study published by GSK, the originator of the ranitidine molecule, the metabolites of ranitidine in urine were studied using liquid chromatography.[55] Many metabolites were listed, though there is no indication that NDMA was looked for. Plaintiff believes this was intentional—a gambit by the manufacturer to avoid detecting a carcinogen in their product. All Defendants knew or should have known about this study and, therefore, were obligated to investigate this issue properly. None did.

[55] Carey, *et al*., *Determination of ranitidine and its metabolites in human urine by reversed-phase ion-pair high-performance liquid chromatography*, 255 J. CHROMATOGRAPHY B: BIOMEDICAL SCI. & APPL. 1, 161-168 (1981).

129. Indeed, in that same year, Dr. de Flora published a note in the Lancet discussing the results of his experiments showing that ranitidine was turning into mutagenic N-nitroso compounds, of which NDMA is one, in human gastric fluid when accompanied by nitrites – a substance commonly found in food and in the body. GSK was aware of this as GSK specifically responded to the note and attempted to discredit it. Defendants knew or should have known about this scientific exchange as it was in a popular scientific journal, the Lancet. Therefore, the Defendants were obligated to investigate this issue properly, and none did.

130. By 1987, after numerous studies raised concerns over ranitidine and cancerous nitroso compounds (discussed previously), GSK published a clinical study specifically investigating gastric contents in human patients and N-nitroso compounds.[56] This study specifically indicated that there were no elevated levels of N-nitroso compounds (of which NDMA is one). However, the study was rigged to fail. It used an analytical system called a "nitrogen oxide assay" for the determination of N-nitrosamines, which was developed for analyzing food and is a detection method that indirectly and non-specifically measures N-nitrosamines. Furthermore, in addition to this approach being less accurate, GSK also removed all gastric samples that contained ranitidine out of concern that samples with ranitidine would contain "high concentrations of N-nitroso compounds being recorded." So, without the chemical being present in any sample, any degradation into NDMA could not, by design, be observed. Again, this spurious test was intentional and designed to mask any potential cancer risk. The inadequacy of this test was knowable in light of its scientific publication in 1987. All Defendants either knew or should have known about the inadequacy of this study and should have investigated the issue

[56] Thomas, *et al.*, *Effects of one year's treatment with ranitidine and of truncal vagotomy on gastric contents*, 6 *GUT.* Vol. 28, 726-738 (1987).

properly and/or took action to protect consumers from the NDMA risks in their products. None did.

131. In fact, upon information and belief, none of the Defendants ever used a mass spectrometry assay to test for the presence of nitrosamines in any of the studies and trials they did in connection with their trials associated with the ranitidine NDA. That is because when using mass spectrometry, it requires heating of up to 130 degrees Celsius, which can result in excessive amounts of nitrosamines being formed. Had the Defendants used a mass spectrometry assay, it would have revealed in the finding of large amounts of NDMA, and the FDA would never have approved Zantac as being safe.

132. Based on the public scientific information available starting in 1983 (or earlier), the Defendants knew or should have known that NDMA could form in ranitidine by exposure to heat and/or over time in storage. No Defendants, upon information and belief, took action to reduce this risk through altering supply-chain conduct or warning consumers. Additionally, no Defendants took any action to further investigate this issue notwithstanding the signal that existed in the scientific literature.

133. There are multiple alternatives to Zantac that do not pose the same risk, such as Cimetidine (Tagamet), Famotidine (Pepcid), Omeprazole (Prilosec), Esomeprazole (Nexium), and Lansoprazole (Prevacid).

VI. PLAINTIFF-SPECIFIC ALLEGATIONS

134. Plaintiff began using Zantac in approximately 1983 and continued to use it through approximately 2018. Plaintiff used Zantac manufactured, designed, packaged, marketed, sold, and/or distributed by Defendants.

135. Plaintiff was diagnosed with breast cancer in approximately 2006 while taking

Zantac, and resulting in her death on May 12, 2018.

136. As a result of his diagnosis and subsequent treatment, Plaintiff suffered bodily injury resulting in pain and suffering, disability, disfigurement, great mental anguish, loss of capacity of the enjoyment of life, shortened life expectancy, expenses for hospitalization, medical and nursing treatment, loss of earnings, destruction of the power to labor and earn money, funeral expenses, and death.

137. Based on prevailing scientific evidence, exposure to Zantac (and the attendant NDMA) can cause bladder cancer in humans.

138. Plaintiff's breast cancer was caused by ingestion of Zantac.

139. At all relevant times, Defendants had knowledge that there was a significant increased risk of cancer associated with Zantac, and death related to those events, and despite this knowledge Defendants continued to manufacture, market, distribute, store, sell, and profit from sales of Zantac.

140. Despite such knowledge, Defendants knowingly, purposely, and deliberately failed to adequately warn Plaintiff, patients, consumers, medical providers, and the public of the increased risk of serious injury associated with using Zantac including, and death related to those events.

141. Had any Defendant warned Plaintiff that Zantac could lead to exposure to NDMA or, in turn, cancer, Plaintiff would not have taken Zantac.

142. Upon information and belief, Plaintiff's prescribing physicians would not have prescribed Zantac to Plaintiff, would have changed the way in which they treated Plaintiff's relevant conditions, changed the way they warned Plaintiff about the signs and symptoms of serious adverse effects of Zantac, and discussed with Plaintiff the true risks of cancer, had

Defendants provided said physicians with an appropriate and adequate warning regarding the risks associated with the use of Zantac.

143. Upon information and belief, Plaintiff's physicians were unaware of the increased risk of multiple types of cancer associated with the use of Zantac, and, if they had been informed, would have used and prescribed alternative therapies to Plaintiff.

144. Plaintiff would not have taken ranitidine-containing products had Plaintiff known of or been fully and adequately informed by Defendants of the true increased risks and serious dangers of taking the drugs..

145. As a direct and proximate result of Defendants' conduct, Plaintiff suffered serious and/or permanent injuries, which resulted in damages to Plaintiff in sums in excess of the jurisdictional limits of the Court.

146. Defendants' conduct was committed with knowing, reckless, conscious, wanton, willful, and deliberate disregard for the value of human life and the rights and safety of consumers, including Plaintiff, thereby entitling Plaintiff to punitive and exemplary damages so as to punish and deter similar conduct in the future.

EQUITABLE TOLLING / ESTOPPEL

147. Plaintiff asserts all applicable statutory and common law rights and theories related to the tolling or extension of any applicable statute of limitations, including equitable tolling, delayed discovery, discovery rule and/or fraudulent concealment.

148. The discovery rule applies to toll the running of the statute of limitations until Plaintiff knew, or through the exercise of reasonable care and diligence should have known, of facts that Plaintiff had been injured, the cause of the injury, and the tortious nature of the wrongdoing that caused the injury.

149. The nature of Plaintiff's injuries, damages, or their causal relationship to Defendants' conduct was not discovered, and through reasonable care and due diligence could not have been discovered until a date within the applicable statute of limitations for filing Plaintiff's claims.

150. The running of the statute of limitations is tolled due to equitable tolling. Defendants are estopped from relying on any statutes of limitation or repose by virtue of their acts of fraudulent concealment, through affirmative misrepresentations and omissions to Plaintiff and defects associated with Zantac including the severity, duration, and frequency of risks and complications. Defendants affirmatively withheld and/or misrepresented facts concerning the safety of Zantac. As a result of Defendants' misrepresentations and concealment, Plaintiff and Plaintiff's physicians were unaware, and could not have known or have learned through reasonable diligence that Plaintiff had been exposed to the risks alleged herein and that those risks were the direct and proximate result of the wrongful acts and/or omissions of the Defendants.

151. Given the Defendants' affirmative actions of concealment by failing to disclose this known but non-public information about the defects – information over which the Defendants had exclusive control – and because Plaintiff could not reasonably have known that Defendants' Zantac products were and are defective, Defendants are estopped from relying on any statutes of limitations or repose that might otherwise be applicable to the claims asserted herein.

VII. EXEMPLARY / PUNITIVE DAMAGES ALLEGATIONS

152. Defendants' conduct as alleged herein was done with reckless disregard for human life, oppression, and malice. Defendants were fully aware of the safety risks of Zantac, particularly the carcinogenic potential of Zantac as it transforms into NDMA within the chemical environment of the human body and/or during transport and/or storage. Nonetheless, Defendants deliberately crafted their label, marketing, and promotion to mislead consumers.

153. This was not done by accident or through some justifiable negligence. Rather, Defendants knew that it could turn a profit by convincing consumers that Zantac was harmless to humans, and that full disclosure of the true risks of Zantac would limit the amount of money Defendants would make selling Zantac. Defendants' object was accomplished not only through their misleading label, but through a comprehensive scheme of selective misleading research and testing, false advertising, and deceptive omissions as more fully alleged throughout this pleading. Plaintiff was denied the right to make an informed decision about whether to purchase and use Zantac, knowing the full risks attendant to that use. Such conduct was done with conscious disregard of Plaintiff's rights.

154. Accordingly, Plaintiff requests punitive damages against Defendants for the harms caused to Plaintiff.

CAUSES OF ACTION

COUNT I: STRICT PRODUCTS LIABILITY MANUFACTURING DEFECT

155. Plaintiff incorporates by reference each allegation set forth in preceding paragraphs as if fully stated herein.

156. At all times herein mentioned, Defendants designed, distributed, manufactured, sold, tested, and marketed the drugs ingested by Plaintiff to patients and physicians.

157. At all relevant times, the medication ingested by Plaintiff wa expected to and did reach Plaintiff without a substantial change in its condition as manufactured, distributed, and sold by Defendants.

158. At all relevant times, the medications ingested by Plaintiff were used in a manner that was foreseeable and intended by Defendants.

159. The ranitidine-containing products ingested by Plaintiff were not reasonably safe for their intended use and were defective with respect to their manufacture, as described herein, in that Defendants deviated materially from their design and manufacturing specifications and/or such design and/or manufacture posed an unreasonable risk of harm to Plaintiff.

160. The Defendants' ranitidine-containing products are inherently dangerous and defective, unfit and unsafe for its intended and reasonably foreseeable uses, and do not meet or perform to the expectations of patients and their health care providers.

161. The ranitidine-containing products create risks to the health and safety of the patients that are far more significant and devastating than the risks posed by other products and procedures available to treat the corresponding medical conditions, and which far outweigh the utility of the ranitidine-containing products.

162. Defendants have intentionally and recklessly manufactured the ranitidine-containing products with wanton and willful disregard for the rights and health of the Plaintiff, and with malice, placing their economic interests above the health and safety of the Plaintiff.

163. As a direct and proximate result of the Defendants' defective manufacture of the ranitidine-containing products, Plaintiff has been injured, sustained severe and permanent pain, suffering, disability, impairment, loss of enjoyment of life, economic loss and damages including, but not limited to medical expenses, lost income, and other damages.

164. WHEREFORE, Plaintiff respectfully requests this Court to enter judgment in Plaintiff's favor for compensatory and punitive damages, together with interest, costs herein incurred, attorneys' fees and all such other and further relief as this Court deems just and proper.

COUNT II: STRICT LIABILITY – DESIGN DEFECT

165. Plaintiff incorporates by reference each allegation set forth in preceding paragraphs as if fully stated herein.

166. Plaintiff brings this strict liability claim against Defendants for defective design.

167. At all relevant times, Defendants engaged in the business of testing, developing, designing, manufacturing, marketing, selling, distributing, and promoting Zantac products, which are defective and unreasonably dangerous to consumers, including Plaintiff, thereby placing Zantac products into the stream of commerce. These actions were under the ultimate control and supervision of Defendants. At all relevant times, Defendants designed, researched, developed, manufactured, produced, tested, assembled, labeled, advertised, promoted, marketed, sold, and distributed the Zantac products used by Plaintiff, as described herein.

168. At all relevant times, Defendants' Zantac products were manufactured, designed, and labeled in an unsafe, defective, and inherently dangerous manner that was dangerous for use

by or exposure to the public, including Plaintiff.

169. At all relevant times, Defendants' Zantac products reached the intended consumers, handlers, and users or other persons coming into contact with these products within this judicial district and throughout the United States, including Plaintiff, without substantial change in their condition as designed, manufactured, sold, distributed, labeled, and marketed by Defendants. At all relevant times, Defendants registered, researched, manufactured, distributed, marketed, and sold Zantac products within this judicial district and aimed at a consumer market within this judicial district. Defendants were at all relevant times involved in the retail and promotion of Zantac products marketed and sold in this judicial district.

170. Defendants' Zantac products, as researched, tested, developed, designed, licensed, manufactured, packaged, labeled, distributed, sold, and marketed by Defendants were defective in design and formulation in that, when they left the control of Defendants' manufacturers and/or suppliers, they were unreasonably dangerous and dangerous to an extent beyond that which an ordinary consumer would contemplate.

171. Defendants' Zantac products, as researched, tested, developed, designed, licensed, manufactured, packaged, labeled, distributed, sold, and marketed by Defendants were defective in design and formulation in that, when they left the hands of Defendants' manufacturers and/or suppliers, the foreseeable risks exceeded the alleged benefits associated with their design and formulation.

172. At all relevant times, Defendants knew or had reason to know that Zantac products were defective and were inherently dangerous and unsafe when used in the manner instructed and provided by Defendants.

173. Therefore, at all relevant times, Defendants' Zantac products, as researched, tested,

developed, designed, registered, licensed, manufactured, packaged, labeled, distributed, sold, and marketed by Defendants were defective in design and formulation, in one or more of the following ways:

a. When placed in the stream of commerce, Defendants' Zantac products were defective in design and formulation, and, consequently, dangerous to an extent beyond that which an ordinary consumer would contemplate;

b. When placed in the stream of commerce, Defendants' Zantac products were unreasonably dangerous in that they were hazardous and posed a grave risk of cancer and other serious illnesses when used in a reasonably anticipated manner;

c. When placed in the stream of commerce, Defendants' Zantac products contained unreasonably dangerous design defects and were not reasonably safe when used in a reasonably anticipated or intended manner;

d. Defendants did not sufficiently test, investigate, or study their Zantac products and, specifically, the ability for Zantac to transform into the carcinogenic compound NDMA within the human body;

e. Exposure to Zantac products presents a risk of harmful side effects that outweigh any potential utility stemming from the use of the drug;

f. Defendants knew or should have known at the time of marketing Zantac products that exposure to Zantac could result in cancer and other severe illnesses and injuries;

g. Defendants did not conduct adequate post-marketing surveillance of their Zantac products; and

h. Defendants could have employed safer alternative designs and formulations.

174. Plaintiff used and was exposed to Defendants' Zantac products without knowledge of Zantac's dangerous characteristics.

175. At all times relevant to this litigation, Plaintiff used and/or was exposed to the use of Defendants' Zantac products in an intended or reasonably foreseeable manner without knowledge of Zantac's dangerous characteristics.

176. Plaintiff could not reasonably have discovered the defects and risks associated with Zantac products before or at the time of exposure due to the Defendants' suppression or obfuscation of scientific information linking Zantac to cancer.

177. The harm caused by Defendants' Zantac products far outweighed their benefit, rendering Defendants' product dangerous to an extent beyond that which an ordinary consumer would contemplate. Defendants' Zantac products were and are more dangerous than alternative products, and Defendants could have designed Zantac products to make them less dangerous. Indeed, at the time Defendants designed Zantac products, the state of the industry's scientific knowledge was such that a less risky design or formulation was attainable.

178. At the time Zantac products left Defendants' control, there was a practical, technically feasible, and safer alternative design that would have prevented the harm without substantially impairing the reasonably anticipated or intended function of Defendants' Zantac products. For example, the Defendants could have added ascorbic acid (Vitamin C) to each dose of Zantac, which is known to scavenge nitrites and reduce the ability of the body to recombine ranitidine into NDMA.[57]

179. Defendants' defective design of Zantac products was willful, wanton, malicious,

[57] *See, e.g.*, Vermeer, *et al*., *Effect of ascorbic acid and green tea on endogenous formation of N nitrosodimethylamine and N-nitrosopiperidine in humans*. 428 MUTAT. RES., FUNDAM. MOL. MECH. MUTAGEN. 353–361 (1999); Garland, *et al*., *Urinary excretion of nitrosodimethylamine and nitrosoproline in humans: Interindividual and intraindividual differences and the effect of administered ascorbic acid and α-tocopherol*, 46 CANCER RESEARCH 5392–5400 (1986).

and conducted with reckless disregard for the health and safety of users of the Zantac products, including Plaintiff.

180. Therefore, as a result of the unreasonably dangerous condition of their Zantac products, Defendants are strictly liable to Plaintiff.

181. The defects in Defendants' Zantac products were substantial and contributing factors in causing Plaintiff's injuries, and, but for Defendants' misconduct and omissions, Plaintiff would not have sustained injuries.

182. Defendants' conduct, as described above, was reckless. Defendants risked the lives of consumers and users of their products, including Plaintiff, with knowledge of the safety problems associated with Zantac products, and suppressed this knowledge from the general public. Defendants made conscious decisions not to redesign, warn or inform the unsuspecting public. Defendants' reckless conduct warrants an award of punitive damages.

183. As a direct and proximate result of Defendants placing their defective Zantac products into the stream of commerce, and the resulting injuries, Plaintiff sustained pecuniary loss including general damages in a sum which exceeds the jurisdictional minimum of this Court.

184. As a proximate result of Defendants placing their defective Zantac products into the stream of commerce, as alleged herein, there was a measurable and significant interval of time during which Plaintiff has suffered great mental anguish and other personal injury and damages, resulting in his death.

185. As a proximate result of the Defendants placing their defective Zantac products into the stream of commerce, as alleged herein, Plaintiff sustained loss of income and/or loss of earning capacity.

186. WHEREFORE, Plaintiff respectfully requests this Court to enter judgment in

Plaintiff's favor for compensatory and punitive damages, together with interest, costs herein incurred, attorneys' fees and all such other and further relief as this Court deems just and proper.

COUNT III: STRICT LIABILITY – FAILURE TO WARN

187. Plaintiff incorporates by reference each allegation set forth in preceding paragraphs as if fully stated herein.

188. Plaintiff brings this strict liability claim against Defendants for failure to warn.

189. At all relevant times, Defendants engaged in the business of testing, developing, designing, manufacturing, marketing, selling, distributing, and promoting Zantac products which are defective and unreasonably dangerous to consumers, including Plaintiff, because they do not contain adequate warnings or instructions concerning the dangerous characteristics of Zantac and NDMA. These actions were under the ultimate control and supervision of Defendants. At all relevant times, Defendants registered, researched, manufactured, distributed, marketed, and sold Zantac and other ranitidine formulations within this judicial district and aimed at a consumer market. Defendants were at all relevant times involved in the retail and promotion of Zantac products marketed and sold in in this judicial district.

190. Defendants researched, developed, designed, tested, manufactured, inspected, labeled, distributed, marketed, promoted, sold, and otherwise released into the stream of commerce their Zantac products, and in the course of same, directly advertised or marketed the products to consumers and end users, including Plaintiff, and therefore had a duty to warn of the risks associated with the use of Zantac products.

191. At all relevant times, Defendants had a duty to properly test, develop, design, manufacture, inspect, package, label, market, promote, sell, distribute, maintain, supply, provide proper warnings, and take such steps as necessary to ensure their Zantac products did not cause

users and consumers to suffer from unreasonable and dangerous risks. Defendants had a continuing duty to warn Plaintiff of dangers associated with Zantac. Defendants, as a manufacturer, seller, or distributor of pharmaceutical medication, are held to the knowledge of an expert in the field.

192. At the time of manufacture, Defendants could have provided the warnings or instructions regarding the full and complete risks of Zantac products because they knew or should have known of the unreasonable risks of harm associated with the use of and/or exposure to such products.

193. At all relevant times, Defendants failed and deliberately refused to investigate, study, test, or promote the safety or to minimize the dangers to users and consumers of their product and to those who would foreseeably use or be harmed by Defendants' Zantac products, including Plaintiff.

194. Even though Defendants knew or should have known that Zantac posed a grave risk of harm, they failed to exercise reasonable care to warn of the dangerous risks associated with use and exposure. The dangerous propensities of their products and the carcinogenic characteristics of NDMA as produced within the human body as a result of ingesting Zantac, as described above, were known to Defendants, or scientifically knowable to Defendants through appropriate research and testing by known methods, at the time they distributed, supplied or sold the product, and were not known to end users and consumers, such as Plaintiff.

195. Defendants knew or should have known that their products created significant risks of serious bodily harm to consumers, as alleged herein, and Defendants failed to adequately warn consumers, *i.e.*, the reasonably foreseeable users, of the risks of exposure to their products. Defendants have wrongfully concealed information concerning the dangerous nature of Zantac and the potential for ingested Zantac to transform into the carcinogenic NDMA compound, and

further, have made false and/or misleading statements concerning the safety of Zantac products.

196. At all relevant times, Defendants' Zantac products reached the intended consumers, handlers, and users or other persons coming into contact with these products within this judicial district and throughout the United States, including Plaintiff, without substantial change in their condition as designed, manufactured, sold, distributed, labeled, and marketed by Defendants.

197. Plaintiff was exposed to Defendants' Zantac products without knowledge of their dangerous characteristics.

198. At all relevant times, Plaintiff used and/or was exposed to the use of Defendants' Zantac products while using them for their intended or reasonably foreseeable purposes, without knowledge of their dangerous characteristics.

199. Plaintiff could not have reasonably discovered the defects and risks associated with Zantac products prior to or at the time of Plaintiff consuming Zantac. Plaintiff relied upon the skill, superior knowledge, and judgment of Defendants to know about and disclose serious health risks associated with using Defendants' products.

200. Defendants knew or should have known that the minimal warnings disseminated with their Zantac products were inadequate, failed to communicate adequate information on the dangers and safe use/exposure, and failed to communicate warnings and instructions that were appropriate and adequate to render the products safe for their ordinary, intended and reasonably foreseeable uses.

201. The information that Defendants did provide or communicate failed to contain relevant warnings, hazards, and precautions that would have enabled consumers such as Plaintiff to utilize the products safely and with adequate protection. Instead, Defendants disseminated information that was inaccurate, false, and misleading, and which failed to communicate

accurately or adequately the comparative severity, duration, and extent of the risk of injuries with use of and/or exposure to Zantac; continued to aggressively promote the efficacy of their products, even after they knew or should have known of the unreasonable risks from use or exposure; and concealed, downplayed, or otherwise suppressed, through aggressive marketing and promotion, any information or research about the risks and dangers of ingesting Zantac.

202. This alleged failure to warn is not limited to the information contained on Zantac's labeling. The Defendants were able, in accord with federal law, to comply with relevant state law by disclosing the known risks associated with Zantac through other non-labeling mediums, *i.e.*, promotion, advertisements, public service announcements, and/or public information sources. But the Defendants did not disclose these known risks through any medium.

203. Defendants are liable to Plaintiff for injuries caused by their negligent or willful failure, as described above, to provide adequate warnings or other clinically relevant information and data regarding the appropriate use of their products and the risks associated with the use of Zantac.

204. Had Defendants provided adequate warnings and instructions and properly disclosed and disseminated the risks associated with their Zantac products, Plaintiff could have avoided the risk of developing injuries and could have obtained or used alternative medication.

205. As a direct and proximate result of Defendants placing defective Zantac products into the stream of commerce, Plaintiff was injured and has sustained pecuniary loss resulting and general damages in a sum exceeding the jurisdictional minimum of this Court.

206. As a proximate result of Defendants placing defective Zantac products into the stream of commerce, as alleged herein, there was a measurable and significant interval of time during which Plaintiff suffered great mental anguish and other personal injury and damages

resulting in his death.

207. As a proximate result of Defendants placing defective Zantac products into the stream of commerce, as alleged herein, Plaintiff sustained loss of income and/or loss of earning capacity.

208. WHEREFORE, Plaintiff respectfully requests this Court to enter judgment in Plaintiff's favor for compensatory and punitive damages, together with interest, costs herein incurred, attorneys' fees and all such other and further relief as this Court deems just and proper.

COUNT IV: NEGLIGENCE

209. Plaintiff incorporates by reference each allegation set forth in preceding paragraphs as if fully stated herein.

210. Defendants, directly or indirectly, caused Zantac products to be sold, distributed, packaged, labeled, marketed, promoted, and/or used by Plaintiff. At all relevant times, Defendants registered, researched, manufactured, distributed, marketed, and sold Zantac within this judicial district and aimed at a consumer market within this district.

211. At all relevant times, Defendants had a duty to exercise reasonable care in the design, research, manufacture, marketing, advertisement, supply, promotion, packaging, sale, and distribution of Zantac products, including the duty to take all reasonable steps necessary to manufacture, promote, and/or sell a product that was not unreasonably dangerous to consumers and users of the product.

212. At all relevant times, Defendants had a duty to exercise reasonable care in the marketing, advertisement, and sale of the Zantac products. Defendants' duty of care owed to consumers and the general public included providing accurate, true, and correct information concerning the risks of using Zantac and appropriate, complete, and accurate warnings concerning

the potential adverse effects of Zantac and, in particular, its ability to transform into the carcinogenic compound NDMA.

213. At all relevant times, Defendants knew or, in the exercise of reasonable care, should have known of the hazards and dangers of Zantac and, specifically, the carcinogenic properties of NDMA when Zantac is ingested and/or transported and stored.

214. Accordingly, at all relevant times, Defendants knew or, in the exercise of reasonable care, should have known that use of Zantac products could cause or be associated with Plaintiff's injuries, and thus, create a dangerous and unreasonable risk of injury to the users of these products, including Plaintiff.

215. Defendants also knew or, in the exercise of reasonable care, should have known that users and consumers of Zantac were unaware of the risks and the magnitude of the risks associated with use of Zantac.

216. As such, Defendants breached their duty of reasonable care and failed to exercise ordinary care in the design, research, development, manufacture, testing, marketing, supply, promotion, advertisement, packaging, sale, and distribution of Zantac products, in that Defendants manufactured and produced defective Zantac which carries the potential to transform into the carcinogenic compound NDMA; knew or had reason to know of the defects inherent in their products; knew or had reason to know that a user's or consumer's use of the products created a significant risk of harm and unreasonably dangerous side effects; and failed to prevent or adequately warn of these risks and injuries. Indeed, Defendants deliberately refused to test Zantac products because they knew that the chemical posed serious health risks to humans.

217. Defendants were negligent in their promotion of Zantac, outside of the labeling context, by failing to disclose material risk information as part of their promotion and marketing

of Zantac, including the internet, television, print advertisements, *etc*. Nothing prevented Defendants from being honest in their promotional activities, and, in fact, Defendants had a duty to disclose the truth about the risks associated with Zantac in their promotional efforts, outside of the context of labeling.

218. Despite their ability and means to investigate, study, and test the products and to provide adequate warnings, Defendants failed to do so. Indeed, Defendants wrongfully concealed information and further made false and/or misleading statements concerning the safety and use of Zantac.

219. Defendants' negligence included:

a. Manufacturing, producing, promoting, formulating, creating, developing, designing, selling, and/or distributing Zantac products without thorough and adequate pre- and post-market testing;

b. Manufacturing, producing, promoting, formulating, creating, developing, designing, selling, and/or distributing Zantac while negligently and/or intentionally concealing and failing to disclose the results of trials, tests, and studies of Zantac and the carcinogenic potential of NDMA as created in the human body as a result of ingesting Zantac, and, consequently, the risk of serious harm associated with human use of Zantac;

c. Failing to undertake sufficient studies and conduct necessary tests to determine whether or not Zantac products were safe for their intended consumer use;

d. Failing to use reasonable and prudent care in the design, research, manufacture, and development of Zantac products so as to avoid the risk of serious harm associated with the prevalent use of Zantac products;

e. Failing to design and manufacture Zantac products so as to ensure they were at least as safe and effective as other medications on the market intended to treat the same symptoms;

f. Failing to provide adequate instructions, guidelines, and safety precautions to those persons Defendants could reasonably foresee would use Zantac products;

g. Failing to disclose to Plaintiff, users/consumers, and the general public that use of Zantac presented severe risks of cancer and other grave illnesses;

h. Failing to warn Plaintiff, consumers, and the general public that the product's risk of harm was unreasonable and that there were safer and effective alternative medications available to Plaintiff and other consumers;

i. Systematically suppressing or downplaying contrary evidence about the risks, incidence, and prevalence of the side effects of Zantac products;

j. Representing that their Zantac products were safe for their intended use when, in fact, Defendants knew or should have known the products were not safe for their intended purpose;

k. Declining to make or propose any changes to Zantac products' labeling or other promotional materials that would alert consumers and the general public of the risks of Zantac;

l. Advertising, marketing, and recommending the use of the Zantac products, while concealing and failing to disclose or warn of the dangers known (by Defendants) to be associated with or caused by the use of or exposure to Zantac;

m. Continuing to disseminate information to their consumers, which indicate or imply that Defendants' Zantac products are not unsafe for regular consumer use; and

n. Continuing the manufacture and sale of their products with the knowledge that the products were unreasonably unsafe and dangerous.

220. Defendants knew and/or should have known that it was foreseeable consumers such as Plaintiff would suffer injuries as a result of Defendants' failure to exercise ordinary care in the manufacturing, marketing, labeling, distribution, and sale of Zantac.

221. Plaintiff did not know the nature and extent of the injuries that could result from the intended use of and/or exposure to Zantac.

222. Defendants' negligence was the proximate cause of Plaintiff's injuries, *i.e.*, absent Defendants' negligence, Plaintiff would not have developed cancer.

223. Defendants' conduct, as described above, was reckless. Defendants regularly risked the lives of consumers and users of their products, including Plaintiff, with full knowledge of the dangers of their products. Defendants have made conscious decisions not to redesign, re-label, warn, or inform the unsuspecting public, including Plaintiff. Defendants' reckless conduct therefore warrants an award of punitive damages.

224. As a direct and proximate result of Defendants placing defective Zantac products into the stream of commerce, Plaintiff was injured and has sustained pecuniary loss and general damages in a sum exceeding the jurisdictional minimum of this Court.

225. As a proximate result of Defendants placing defective Zantac products into the stream of commerce, as alleged herein, there was a measurable and significant interval of time during which Plaintiff suffered great mental anguish and other personal injury and damages.

226. As a proximate result of Defendants placing defective Zantac products into the stream of commerce, as alleged herein, Plaintiff sustained a loss of income, and loss of earning capacity.

227. WHEREFORE, Plaintiff respectfully requests this Court to enter judgment in Plaintiff's favor for compensatory and punitive damages, together with interest, costs herein incurred, attorneys' fees and all such other and further relief as this Court deems just and proper.

COUNT V: BREACH OF EXPRESS WARRANTIES

228. Plaintiff incorporates by reference each allegation set forth in preceding paragraphs as if fully stated herein.

229. At all relevant times, Defendants engaged in the business of testing, developing, designing, manufacturing, marketing, selling, distributing, and promoting Zantac products, which are defective and unreasonably dangerous to consumers, including Plaintiff, thereby placing Zantac products into the stream of commerce. These actions were under the ultimate control and supervision of Defendants.

230. Defendants had a duty to exercise reasonable care in the research, development, design, testing, packaging, manufacture, inspection, labeling, distributing, marketing, promotion, sale, and release of Zantac products, including a duty to:

a. ensure that their products did not cause the user unreasonably dangerous side effects;

b. warn of dangerous and potentially fatal side effects; and

c. disclose adverse material facts, such as the true risks associated with the use of and exposure to Zantac, when making representations to consumers and the general public, including Plaintiff.

231. As alleged throughout this pleading, the ability of Defendants to properly disclose those risks associated with Zantac is not limited to representations made on the labeling.

232. At all relevant times, Defendants expressly represented and warranted to the

purchasers of their products, by and through statements made by Defendants in labels, publications, package inserts, and other written materials intended for consumers and the general public, that Zantac products were safe to human health and the environment, effective, fit, and proper for their intended use. Defendants advertised, labeled, marketed, and promoted Zantac products, representing the quality to consumers and the public in such a way as to induce their purchase or use, thereby making an express warranty that Zantac products would conform to the representations.

233. These express representations include incomplete warnings and instructions that purport, but fail, to include the complete array of risks associated with use of and/or exposure to Zantac. Defendants knew and/or should have known that the risks expressly included in Zantac warnings and labels did not and do not accurately or adequately set forth the risks of developing the serious injuries complained of herein. Nevertheless, Defendants expressly represented that Zantac products were safe and effective, that they were safe and effective for use by individuals such as the Plaintiff, and/or that they were safe and effective as consumer medication.

234. The representations about Zantac, as set forth herein, contained or constituted affirmations of fact or promises made by the seller to the buyer, which related to the goods and became part of the basis of the bargain, creating an express warranty that the goods would conform to the representations.

235. Defendants placed Zantac products into the stream of commerce for sale and recommended their use to consumers and the public without adequately warning of the true risks of developing the injuries associated with the use of Zantac.

236. Defendants breached these warranties because, among other things, Zantac products were defective, dangerous, and unfit for use, did not contain labels representing the true

and adequate nature of the risks associated with their use, and were not merchantable or safe for their intended, ordinary, and foreseeable use and purpose. Specifically, Defendants breached the warranties in the following ways:

a. Defendants represented through their labeling, advertising, and marketing materials that Zantac products were safe, and intentionally withheld and concealed information about the risks of serious injury associated with use of Zantac and by expressly limiting the risks associated with use within their warnings and labels; and

b. Defendants represented that Zantac products were safe for use and intentionally concealed information that demonstrated that Zantac, by transforming into NDMA upon human ingestion, had carcinogenic properties, and that Zantac products, therefore, were not safer than alternatives available on the market.

237. Plaintiff detrimentally relied on the express warranties and representations of Defendants concerning the safety and/or risk profile of Zantac in deciding to purchase the product. Plaintiff reasonably relied upon Defendants to disclose known defects, risks, dangers, and side effects of Zantac. Plaintiff would not have purchased or used Zantac had Defendants properly disclosed the risks associated with the product, either through advertising, labeling, or any other form of disclosure.

238. Defendants had sole access to material facts concerning the nature of the risks associated with their Zantac products, as expressly stated within their warnings and labels, and knew that consumers and users such as Plaintiff could not have reasonably discovered that the risks expressly included in Zantac warnings and labels were inadequate and inaccurate.

239. Plaintiff had no knowledge of the falsity or incompleteness of Defendants'

statements and representations concerning Zantac.

240. Plaintiff used and/or was exposed to Zantac as researched, developed, designed, tested, manufactured, inspected, labeled, distributed, packaged, marketed, promoted, sold, or otherwise released into the stream of commerce by Defendants.

241. Had the warnings, labels, advertisements, or promotional material for Zantac products accurately and adequately set forth the true risks associated with the use of such products, including Plaintiff's injuries, rather than expressly excluding such information and warranting that the products were safe for their intended use, Plaintiff could have avoided the injuries complained of herein.

242. As a direct and proximate result of Defendants' breach of express warranty, Plaintiff has sustained pecuniary loss and general damages in a sum exceeding the jurisdictional minimum of this Court.

243. As a proximate result of Defendants' breach of express warranty, as alleged herein, there was a measurable and significant interval of time during which Plaintiff suffered great mental anguish and other personal injury and damages.

244. As a proximate result of Defendants' breach of express warranty, as alleged herein, Plaintiff sustained a loss of income and/or loss of earning capacity.

245. WHEREFORE, Plaintiff respectfully requests this Court to enter judgment in Plaintiff's favor for compensatory and punitive damages, together with interest, costs herein incurred, attorneys' fees, and all such other and further relief as this Court deems just and proper.

COUNT VI: BREACH OF IMPLIED WARRANTIES

246. Plaintiff incorporates by reference every allegation set forth in preceding paragraphs as if fully stated herein.

247. At all relevant times, Defendants engaged in the business of testing, developing, designing, manufacturing, marketing, selling, distributing, and promoting Zantac products, which were and are defective and unreasonably dangerous to consumers, including Plaintiff, thereby placing Zantac products into the stream of commerce.

248. Before the time Plaintiff used Zantac products, Defendants impliedly warranted to their consumers, including Plaintiff, that Zantac products were of merchantable quality and safe and fit for the use for which they were intended; specifically, as consumer medication.

249. But Defendants failed to disclose that Zantac has dangerous propensities when used as intended and that use of Zantac products carries an increased risk of developing severe injuries, including Plaintiff's injuries.

250. Plaintiff was an intended beneficiary of the implied warranties made by Defendants to purchasers of their Zantac products.

251. The Zantac products were expected to reach and did in fact reach consumers and users, including Plaintiff, without substantial change in the condition in which they were manufactured and sold by Defendants.

252. At all relevant times, Defendants were aware that consumers and users of their products, including Plaintiff, would use Zantac products as marketed by Defendants, which is to say that Plaintiff was a foreseeable user of Zantac.

253. Defendants intended that Zantac products be used in the manner in which Plaintiff, in fact, used them and which Defendants impliedly warranted to be of merchantable quality, safe, and fit for this use, even though Zantac was not adequately tested or researched.

254. In reliance upon Defendants' implied warranty, Plaintiff used Zantac as instructed and labeled and in the foreseeable manner intended, recommended, promoted, and marketed by

Defendants.

255. Plaintiff could not have reasonably discovered or known of the risks of serious injury associated with Zantac.

256. Defendants breached their implied warranty to Plaintiff in that Zantac products were not of merchantable quality, safe, or fit for their intended use, or adequately tested. Zantac has dangerous propensities when used as intended and can cause serious injuries, including those injuries complained of herein.

257. The harm caused by Defendants' Zantac products far outweighed their benefit, rendering the products more dangerous than an ordinary consumer or user would expect and more dangerous than alternative products.

258. As a direct and proximate result of Defendants' breach of implied warranty, Plaintiff has sustained pecuniary loss and general damages in a sum exceeding the jurisdictional minimum of this Court.

259. As a proximate result of the Defendants' breach of implied warranty, as alleged herein, there was a measurable and significant interval of time during which Plaintiff suffered great mental anguish and other personal injury and damages.

260. As a proximate result of Defendants' breach of implied warranty, as alleged herein, Plaintiff sustained a loss of income and/or loss of earning capacity.

261. WHEREFORE, Plaintiff respectfully requests this Court to enter judgment in Plaintiff's favor for compensatory and punitive damages, together with interest, costs herein incurred, attorneys' fees and all such other and further relief as this Court deems just and proper.

COUNT VII: WRONGFUL DEATH

262. Plaintiff incorporates by reference every allegation set forth in preceding paragraphs as if fully stated herein.

263. Plaintiff brings this claim on behalf of the Estate and for the benefit of the Plaintiff Decedent's lawful beneficiaries.

264. As a direct and proximate result of the actions and/or omissions of the Defendant set forth above, Plaintiff suffered bodily injury resulting in pain and suffering, disability, disfigurement, mental anguish, loss of capacity of the enjoyment of life, shortened life expectancy, expenses for hospitalization, medical and nursing treatment, loss of earnings, destruction of the power to labor and earn money, funeral expenses, and death.

265. As a direct and proximate cause of the actions and/or omissions of the Defendant, Plaintiff incurred hospital, nursing, and medical expenses, and estate administration expenses as a result of Decedent's death. Plaintiff brings this claim on behalf of Decedent's lawful beneficiaries for these damages and for all pecuniary losses under applicable state and statutory and/or common laws.

266. Defendant's conduct was committed with knowing, reckless, conscious, wanton, willful, and deliberate disregard for the value of human life and the rights and safety of consumers, including Plaintiff, thereby entitling Plaintiff to punitive and exemplary damages so as to punish and deter similar conduct in the future.

267. WHEREFORE, Plaintiff respectfully request that this Court enter judgment in Plaintiff's favor for compensatory and punitive damages, together with interest, costs herein incurred, attorneys' fees and all relief as this Court deems just and proper. Additionally, Plaintiff demands a jury trial on all issues contained herein.

JURY TRIAL DEMAND

268. Plaintiffs demand a trial by jury on all the triable issues within this pleading.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs demand judgment against the Defendants on each of the above-referenced claims and causes of action and as follows:

1. Awarding compensatory damages in excess of the jurisdictional amount, including, but not limited to pain, suffering, emotional distress, loss of enjoyment of life, and other non-economic damages in an amount to be determined at trial of this action;

2. Awarding compensatory damages to Plaintiffs for past and future damages, including, but not limited to, Plaintiff's pain and suffering and for severe and permanent personal injuries sustained by the Plaintiff including health care costs and economic loss;

3. Awarding economic damages in the form of medical expenses, out of pocket expenses, lost earnings and other economic damages in an amount to be determine at trial of this action;

4. Punitive damages;

5. Pre-judgment interest;

6. Post-judgment interest;

7. Awarding Plaintiffs' reasonable attorneys' fees;

8. Awarding Plaintiffs the costs of these proceedings; and

9. Such other and further relief as this Court deems just and proper.

Dated: May 12, 2020

Respectfully submitted,

/s/ Jennifer A. Moore

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