EFiled: Jun 02 2025 12:22PM EDT
Transaction ID 76377732
Case No. N25C-06-011 ZAN

IN THE SUPERIOR COURT OF THE STATE OF DELAWARE

In re: Zantac (Ranitidine) Litigation	)	
	)	
George Kimmerling,	)	
	)	
Plaintiff,	)	C.A. No. _____
v.	)	
	)	
Boehringer Ingelheim Pharmaceuticals, Inc.; Boehringer Ingelheim USA Corporation; and Patheon Manufacturing Services, LLC,	)	DEMAND FOR JURY TRIAL
	)	
Defendants.	)	

COMPLAINT

Plaintiff, George Kimmerling, files this complaint and demand for Jury Trial and alleges as follows.

TABLE OF CONTENTS

Page

INTRODUCTION

1. This is a personal injury action for damages relating to Defendants' design, manufacture, sale, marketing, advertising, promotion, testing, labeling, packaging, handling, distribution, and storage of ranitidine-containing drugs, which includes the brand name, Zantac, and its various generic forms ("Ranitidine-Containing Drugs," "Ranitidine-Containing Products," or "RCPs" unless specifically identified).

2. Plaintiff brings this action for personal injuries suffered as a result of ingesting the defective and unreasonably dangerous Ranitidine-Containing Drugs and developing various cancers and their sequelae as a result of this ingestion.

PARTIES

I. PLAINTIFF

3. Plaintiff resides in New Jersey and is a citizen of New Jersey and no other state.

4. Plaintiff consumed brand and generic, prescription and over-the-counter, Ranitidine-Containing Drugs starting in approximately January 1990 until approximately January 2019.

5. As a direct and proximate result of consuming N-Nitrosodimethylamine ("NDMA")-contaminated Ranitidine-Containing Drugs, Plaintiff was diagnosed with prostate cancer, kidney cancer, and bladder cancer.

6. Based on prevailing scientific evidence, exposure to Ranitidine-Containing Drugs (and the attendant NDMA) can cause prostate cancer, kidney cancer, and bladder cancer in humans.

7. Had any Defendant warned Plaintiff that Ranitidine-Containing Drugs could lead to exposure to NDMA or, in turn, cancer, Plaintiff would not have taken Ranitidine-Containing Drugs.

8. Plaintiff is informed and believes and based thereon alleges that as a direct and proximate result of Plaintiff's use of and/or exposure to Ranitidine-Containing Drugs supplied and distributed by Defendants herein, Plaintiff suffered significant harm, conscious pain and suffering, physical injury and bodily impairment including, but not limited to cancer, other permanent physical deficits, permanent bodily impairment and other sequelae. Plaintiff's injuries required hospitalizations, in-patient surgeries, medication treatments, and other therapies to address the adverse physical effects and damage caused by Plaintiff's use of and/or exposure to Ranitidine-Containing Drugs.

9. As a direct and proximate result of the wrongful conduct, acts, omissions, fraudulent concealments, fraudulent misrepresentations, and fraudulent business practices by Defendants, Plaintiff used and/or was exposed to Ranitidine-Containing Drugs and were diagnosed with serious health injuries including cancer.

10. As a result of using and/or being exposed to Defendants' Ranitidine-Containing Drugs, Plaintiff has been permanently and severely injured, having suffered serious consequences from Ranitidine-Containing Drugs.

11. As a result of using and/or being exposed to Defendants' inadequate warnings for Ranitidine-Containing Drugs, Plaintiff has been permanently and severely injured, having suffered serious consequences from Ranitidine-Containing Drugs.

12. As a further direct and proximate result of defects in Ranitidine-Containing Drugs, warnings, and the wrongful conduct, acts, omissions, and fraudulent misrepresentations of Defendants, Plaintiff suffered severe mental and physical pain and have and will sustain permanent injuries and emotional distress, along with economic loss due to medical expenses and living-related expenses as a result of lifestyle changes.

13. As a further direct and proximate result of defects in Ranitidine-Containing Drugs, warnings, and the wrongful conduct, acts, omissions, and fraudulent misrepresentations of Defendants, Plaintiff required extensive emergency medical treatment, health care, attention and services, thereby incurring medical, incidental, and service expenses pertaining to emergency medical treatments and procedures undertaken in efforts to maintain and/or save Plaintiff.

14. Plaintiff is an individual who suffered damages as a result of injuries resulting from Plaintiff's use and/or exposure to Ranitidine-Containing Drugs and is authorized to bring an action for the causes of actions alleged herein including, but not limited to, injuries and damages sustained by Plaintiff, resulting from Plaintiff's use and/or exposure to Ranitidine-Containing Drugs. Said injuries and damages sustained by Plaintiff were factually and proximately caused and/or substantially contributed to by the wrongful conduct of Defendants.

15. The product warnings for Ranitidine-Containing Drugs in effect during the time period Plaintiff used and/or were exposed to Ranitidine-Containing Drugs were vague, incomplete or otherwise inadequate, both substantively and graphically, to alert consumers to the severe health risks associated with Ranitidine-Containing Drugs use and/or exposure.

16. The Defendants, and each of them, inclusive, did not provide adequate warnings to consumers including Plaintiff and the general public about the increased risk of serious adverse events that are described herein.

17. Had Plaintiff been adequately warned of the potential life-threatening side effects of the Ranitidine-Containing Drugs, Plaintiff would not have purchased, used, or been exposed to Ranitidine-Containing Drugs.

By reason of the foregoing, Plaintiff developed serious and dangerous side effects including cancer and other cancers, related sequelae, physical pain and suffering,

mental anguish, a loss of enjoyment of life. By reason of the foregoing, Plaintiff suffered economic losses and special damages including, but not limited to, loss of earning and medical expenses. Plaintiff's general and special damages are in excess of the jurisdictional limits of the Court.

18. Plaintiff has reviewed their potential legal claims and causes of action against the Defendants and have intentionally chosen only to pursue claims based on state law. Any reference to any federal agency, regulation or rule is stated solely as background information and does not raise a federal question. Plaintiff has chosen to only pursue claims based on state law and are not making any claims which raise federal questions. Accordingly, Plaintiff contends that Delaware State jurisdiction and venue is proper.

II. BRAND NAME DRUG MAKERS

19. GlaxoSmithKline, LLC ("GSK"), is a Delaware limited liability 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 citizen of Delaware, Pennsylvania, and North Carolina. GSK is a wholly owned subsidiary of GlaxoSmithKline, plc, which is its sole member. At all relevant times, GSK has conducted business and derived substantial revenue from its designing, manufacturing, advertising, distributing, selling, and marketing of RCPs within the State of Delaware and each state in the

United States.

20. GSK, and its predecessors, have controlled the prescription brand name Zantac NDAs since 1983. NDA # 018703, for 150 and 300 mg prescription Zantac tablets, was approved in June 1983. This original NDA served as a basis for approval of every brand name and generic NDA submitted for RCPs in the United States as it established, for the FDA, the safety of ranitidine drug substance, including whether the molecule was liable to form into nitrosamines, including NDMA. After its original approval, GSK submitted numerous supplemental NDAs, seeking reapproval of the Zantac labeling, manufacturing, storage, and various indications for use—each supplemental presenting an opportunity for GSK to submit an amended label. NDA # 019593, for injectable Zantac, was approved in December 1986. NDA # 019675, for syrup Zantac, was approved in December 1988. NDA # 020095, for 150 and 300 mg prescription Zantac capsules, was approved in March 1994. NDA # 020251, for effervescent Zantac, was approved in March 1994.

21. 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. In 1993, Glaxo Wellcome, plc formed a joint venture with Warner-Lambert, Inc. to develop and obtain OTC approval for Zantac. In December 1995, NDA 20-520 Zantac OTC 75 mg tablets

was approved. In 1998, NDA 20-745 OTC Zantac 75 mg effervescent tablets were approved. Also, in 1998, 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 and Glaxo Wellcome retaining control over the Zantac trademark internationally. In 2000, Pfizer acquired Warner-Lambert and maintained control over the Zantac OTC NDA until December 2006. At all relevant times, Pfizer has conducted business and derived substantial revenue from its manufacturing, advertising, distributing, selling, and marketing of Zantac within the State of Delaware and each state in the United States.

22. Defendant, Boehringer Ingelheim Pharmaceuticals, Inc., is a Delaware corporation with its principal place of business located at 900 Ridgebury Road, Ridgefield, Connecticut 06877. Boehringer Ingelheim Pharmaceuticals, Inc. is a citizen of Connecticut, Delaware, and Nevada. Boehringer Ingelheim Pharmaceuticals, Inc. is a subsidiary of the German company Boehringer Ingelheim Corporation. Boehringer Ingelheim Pharmaceuticals, Inc. 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 during that period and afterwards. At all relevant times, Boehringer Ingelheim Pharmaceuticals, Inc. has conducted business and derived substantial revenue from its manufacturing, advertising, distributing, selling, and marketing of Zantac within

the State of Delaware and each state in the United States.

23. Defendant, Boehringer Ingelheim USA Corporation, is a Delaware corporation with its principal place of business located at 900 Ridgebury Rd., Ridgebury, Connecticut 06877. Boehringer Ingelheim USA Corporation is a citizen of Delaware, Connecticut, and Nevada. At all relevant times, Boehringer Ingelheim USA Corporation has conducted business and derived substantial revenue from its manufacturing, advertising, distributing, selling, and marketing of Zantac within the State of Delaware and each state in the United States.

24. Collectively, Defendants, Boehringer Ingelheim Pharmaceuticals, Inc. and Defendant Boehringer Ingelheim USA Corporation, shall be referred to as "Boehringer."

25. Sanofi US Services Inc. 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. Sanofi controlled the NDA for OTC Zantac starting in January 2017 through the present and manufactured and distributed the drug in the United States during that period. Sanofi voluntarily recalled all brand name OTC Zantac on October 18, 2019. At all relevant times, Sanofi has conducted business and derived substantial revenue from its manufacturing, advertising, distributing, selling, and marketing of Zantac within the State of Delaware and each state in the

United States.

26. Sanofi-Aventis U.S. LLC was and is a Delaware limited liability company with its principal place of business located at 55 Corporate Drive, Bridgewater, New Jersey 08807. Sanofi-Aventis U.S. LLC is a citizen of Delaware and New Jersey. Sanofi-Aventis US LLC is a wholly owned subsidiary of Sanofi S.A. At all relevant times, Sanofi-Aventis U.S. LLC has conducted business and derived substantial revenue from its manufacturing, advertising, distributing, selling, and marketing of Zantac within the State of Delaware and each state in the United States.

27. Collectively, Sanofi US Services Inc. and Sanofi-Aventis U.S. LLC, shall be referred to as "Sanofi." Throughout the time that Sanofi controlled the OTC Zantac NDAs, Boehringer Ingelheim Promeco, S.A. de C.V. and Patheon Manufacturing Services LLC manufactured the finished drug product.

III. MANUFACTURING DEFENDANT

28. Defendant, Patheon Manufacturing Services LLC, is a Delaware limited liability company with its principal place of business located at 5900 Martin Luther King Jr. Hwy, Greenville, North Carolina 27834. Defendant Patheon was and is a citizen of Delaware, New York, California, Massachusetts, Wisconsin, and Pennsylvania. DPI Newco, LLC is the sole member of Patheon. Thermo Fisher (CN) Luxembourg Holding S.a.r.l. is the sole member of DPI

Newco, LLC. Thermo CIDTEC, Inc. and TFS Life Holding, LLC are the two members of Thermo Fisher (CN) Luxembourg Holding S.a.r.l. Thermo CIDTEC, Inc. is incorporated in New York and also maintains its principal place of business in New York. TFS Life Holding, LLC has five members: (1) Thermo Fisher Scientific Life Technologies Investment UK I Limited, which is an English company; (2) Thermo Fisher Scientific Sweden Holdings, LLC; (3) Thermo Fisher Scientific Investments (Sweden) S.a.r.l.; (4) Thermo Fisher Scientific Life Investments U.S. Financing II, LLC; and (5) TFS Group Holding II, LLC. Thermo Fisher Scientific Sweden Holdings, LLC has two members, Thermo Fisher Scientific Investments (Sweden) S.a.r.l. and TFS Group Holding II, LLC. Thermo Fisher Scientific Investments (Sweden) S.a.r.l. has two members, CHK Holdings, Inc., a Delaware corporation with its principal place of business in Massachusetts, and FSWH International Holdings, LLC. Fisher Scientific Worldwide Holdings, I C.V. is the sole member of FSWH International Holdings, LLC. Fisher Scientific Worldwide Holdings I C.V. has two members, Fisher Scientific Worldwide, Inc., a Delaware corporation with its principal place of business in Massachusetts, and FSIR Holdings (U.S.), Inc. also a Delaware corporation with its principal place of business in Massachusetts. TFS Group Holding II, LLC has two members, Thermo Fisher Scientific Life Investments C.V. and TFS Group Holding I, LLC. Thermo Fisher Scientific Life Investments C.V. has two members, Thermo Fisher

Scientific Life Investments GP. LLC and Thermo Fisher Scientific Life Holdings II C.V., Thermo Fisher Scientific Life Holdings III C.V. is the sole member of Thermo Fisher Scientific Life Investments GP LLC. Thermo Fisher Scientific Life Holdings III C.V. has five members: (1) Thermo Fisher Scientific AL-1, LLC; (2) TFLP, LLC; (3) Thermo Fisher Scientific, Inc., a Delaware corporation with its principal place of business in Massachusetts; (4) Thermo BioAnalysis, LLC; and (5) Erie Scientific, LLC. TFLP, LLC is the sole member of Thermo Fisher Scientific AL-1, LLC. TFPL has five members: (1) Thermo Electron Corporation, a Delaware corporation with its principal place of business in Massachusetts; (2) Erie Scientific, LLC, whose sole member is Apogent Technologies, Inc., a Wisconsin corporation with its principal place of business in Massachusetts; (3) Apogent Technologies, Inc.; (4) Fisher Scientific Worldwide, Inc., a Delaware corporation with its principal place of business in Massachusetts; and (5) Fisher WWD Holding, LLC, whose sole member is Fisher Scientific Worldwide, Inc., a Delaware corporation with its principal place of business in Massachusetts. Thermo BioAnalysis, LLC has three members: (1) Thermo Fisher Scientific, Inc.; (2) Life Sciences International Limited, an English company; and (3) Life Sciences International, LLC, whose sole member is Helmet Securities Limited, an English company. TFS Group Holding I, LLC has twelve members: (1) Thermo Fisher Scientific, Inc.; (2) Thermo Luxembourg Holding, LLC (Thermo Luxembourg

Holding S.a.r.l.), whose sole member is Thermo Fisher Scientific Germany BV & Co. KG, which is owned by Thermo Fisher Scientific, Inc. and Thermo Fisher Scientific Germany B.V., a Dutch company; (3) Molecular Bioproducts, Inc., a California corporation with its principal place of business also in California; (4) Thermo Fisher Scientific Investments (Sweden) S.a.r.l., which has two members, CHK Holdings, Inc., a Delaware corporation with its principal place of business in Massachusetts, and FSWH International Holdings, LLC, whose sole member is Fisher Scientific Worldwide Holdings I, C.V., whose members are Fisher Scientific Worldwide, Inc., a Delaware corporation with its principal place of business in Massachusetts, and FSIR Holdings (U.S.), Inc., a Delaware corporation with its principal place of business in Massachusetts; (5) Fisher Scientific Worldwide Holdings I C.V.; (6) Thermo Fisher Scientific Life Investments U.S. Financing I, LLC, whose members are FSIR Holdings (U.S.), Inc. and FSWH International Holdings, LLC; (7) Fisher Scientific Worldwide, Inc.; (8) Fisher Clinical Services, Inc., a Pennsylvania corporation with its principal place of business also in Pennsylvania; (9) Liberty Lane Investment, LLC, whose sole member is FSIR Holdings (U.S.), Inc; (10) Fisher Scientific International, LLC, whose sole member is Thermo Fisher Scientific, Inc; (11) Thermo Fisher Scientific Life Investments U.S. Financing II, LLC, whose members are Perbio Science Sweden Holdings AB, a Swedish Company, and Thermo Fisher Scientific Life

Investments II S.a.r.l., which is owned by Perbio Science AB, a Swedish company; and (12) Erie LP Holding, LLC, whose sole member is Erie UK Holding Company, a Delaware corporation with its principal place of business in Massachusetts.

29. Patheon was, at times, engaged in the manufacture, distribution, labeling, packaging, handling, storage, transport and/or selling of OTC Zantac on behalf of Defendants Pfizer, Boehringer, and Sanofi from 1995 until it was withdrawn from the market. At all relevant times, Patheon has conducted business and derived substantial revenue from its manufacturing, advertising, distributing, selling, and marketing of Zantac within the State of Delaware and every state in the United States.

JURISDICTION AND VENUE

30. This Court has jurisdiction over the subject matter of this action and the parties under the DEL. CONSTIT. art. IV, § 7.

31. This Court possesses general personal jurisdiction over each Defendant because they are each incorporated or established in Delaware, maintain and carry on systematic and continuous contacts in Delaware, regularly transact business within Delaware, and are citizens of Delaware.

32. Every Defendant has sufficient minimum contacts with Delaware such that maintenance of the suit does not offend traditional notions of fair play and substantial justice.

33. This Court has personal jurisdiction over Defendants pursuant to, and consistent with, Delaware's long-arm statute, 10 DEL. C. § 3104, and the requirements of due process.

34. Venue properly lies in Delaware because the Defendants are citizens of Delaware.

35. This lawsuit is not subject to removal based on the existence of a federal question. Plaintiff asserts common law and/or statutory claims under state law. These claims do not arise under the Constitution, laws, or treaties of the United States. 28 U.S.C. § 1447(c).

36. Additionally, even if removal is effectuated in contravention of 28 U.S.C. § 1441(b)(2), there is no subject matter jurisdiction within federal court because there is not complete diversity.

37. Additionally, at least one Defendants is a forum Defendant, making any removal illegal under the removal statute.

38. Plaintiff seeks relief that is within the jurisdictional limits of the Court.

REGULATORY HISTORY OF RANITIDINE

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

40. 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.

41. In 1977, Smith, Kline, and French ("SKF") launched cimetidine (Tagamet)—the first histamine 2 receptor blocker ("H2RA")—and it was a tremendous success.

42. Eager to get into the lucrative H2RA market, Glaxo (the predecessor to GSK) rushed Zantac's approval through the U.S. Food and Drug Administration ("FDA")—starting with investigation approval in December 1979, and final submission of the New Drug Application ("NDA") by February 1982.

43. Zantac was an important product for GSK (then Glaxo). As one GSK executive put it in 1983:

> [T]he sheer size of this opportunity and the potential rewards from it dwarf anything we've done so far. It's not just that Zantac is bigger than all our other products put together...it's bigger than the whole company. You've all heard the numbers. My mind finds it difficult to absorb all those zeroes...especially when I'm salivating so hard.
>
> (LAUGHTER)

[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.

44. Zantac was approved by the FDA, pursuant to the NDA process in 1983 (NDA 18-703) and, quickly, became one of GSK's most successful products, being the first prescription drug in history to reach $1 billion in sales, which in the pharmaceutical industry is referred to as a "Blockbuster."

45. In 1993, GSK entered into a joint venture with Pfizer[2] to develop an OTC version of Zantac. That joint venture led to FDA approval of a 75 mg OTC version of Zantac in December 1995. Zantac 75 OTC was approved through an NDA process (NDA 20-520).

46. In 1997, GSK's patent on ranitidine expired, and generic ranitidine-containing drugs entered the market. Despite generic entry, however, brand name prescription and OTC Zantac continued to be sold. Although sales of brand-name Zantac declined some as a result of generic and alternative products, ranitidine-containing drug sales remained strong over time, including purchases made by the United States and Plaintiff States. 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.

47. In December 1998, the joint venture between GSK and Pfizer dissolved. As part of the separation, GSK retained the rights to sell all forms of

[2] 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 Complaint, Warner-Lambert will be referred to as Pfizer.

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.

48. As part of this agreement, Pfizer agreed to pay GSK royalties on OTC annual sales in excess of $130 million. Thus, GSK continued to have a financial interest in the sale of OTC Zantac. Additionally, GSK continued to manufacture the ranitidine drug substance, also known as active pharmaceutical ingredient ("API"), for all Pfizer OTC Zantac products.

49. In October 2003, Pfizer submitted NDA 21-698 for approval to market OTC Zantac 150 mg. The FDA approved NDA 21-698 OTC Zantac 150 mg on August 31, 2004.

50. In 2004, in addition to GSK, Pfizer began also using ranitidine API manufactured by Uquifa, located in Barcelona, Spain.

51. In 2006, Pfizer through a divestiture agreement of its consumer healthcare products to Johnson & Johnson, ultimately transferred all assets pertaining to its Zantac OTC line of products, including the rights to sell and market all formulations of OTC Zantac in the United States and Canada, as well as all intellectual property, research and development, and customer and supply

contracts to Boehringer Ingelheim Pharmaceuticals, Inc. As part of this deal, Boehringer obtained control and responsibility over all of the Zantac OTC NDAs.

52. The royalty agreement for GSK was transferred to Boehringer, which continued to make royalty payments to GSK for OTC sales.

53. Boehringer also continued to make purchases of API from GSK for it is OTC products, which lasted until 2010.

54. In November 2017, GSK ceased marketing prescription Zantac in the U.S. However, GSK still retains control over the prescription Zantac NDAs.

55. In 2016, 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.

56. To date, the FDA has approved numerous generic manufacturers for the sale of prescription and OTC Ranitidine-Containing Drugs through an Abbreviated New Drug Application ("ANDA") process. That process relies on the data presented in the original NDAs submitted by the Brand Drug Makers to the FDA, including the original approval of Zantac in 1983. But-for the various approvals of Zantac NDAs, no OTC ranitidine or generic prescription ranitidine products would have been available for purchase in the United States.

GENERAL ALLEGATIONS

I. NDMA Is a Dangerous Carcinogen

57. NDMA is a yellow oily substance that is part of the N-nitrosamine chemical family.

58. Before 1976, NDMA was primarily used in the production of rocket fuel, rubber, and copolymers. However, in 1976 NDMA was banned, and now it is only used in research, specifically, to induce genetic damage in laboratory experiments as a positive control.

59. NDMA is considered the most well-studied of the N-nitrosamine family.

60. It is generally accepted that NDMA is a carcinogen. In 1978, the International Agency for Research on Cancer ("IARC") reviewed NDMA and classified it a Class 2A "probable human carcinogen." IARC based its conclusion on the overwhelming evidence of animal and cell data (including human cell data). While there was no human epidemiology for NDMA at that time, IARC stated that NDMA "should be regarded for practical purposes as if it were carcinogenic to humans." IARC has not re-reviewed NDMA since. IARC does not re-review its classifications unless the carcinogen has been nominated and a committee recommends review. This is a function of IARC focusing on unknown carcinogens; not ones that everyone already agrees are carcinogenic (like NDMA). As NDMA has been known as a carcinogen for fifty years, and with every regulatory agency treating it as such, IARC has not re-reviewed NDMA or

amended its position that NDMA should be treated as a human carcinogen.

61. Both the FDA and the Environmental Protection Agency ("EPA") consider NDMA to be a "probable human carcinogen" in accordance with IARC.

62. The Department of Health and Human Service's Report on Carcinogens ("ROC") states that NDMA is "reasonably anticipated to be a human carcinogen[.]"

63. In 1989, the U.S. Department of Health and Human Services' Agency for Toxic Substances and Disease Registry ("ATSDR") assessed the carcinogenicity of NDMA and concluded: "it is reasonable to anticipate that NDMA will be carcinogenic in humans. It is important to recognize that this evidence also indicates that oral exposures of acute and intermediate duration are sufficient to induce cancer." The ATSDR further explained that "it is reasonable to expect that exposure to NDMA by eating, drinking, or breathing could cause cancer in humans."

64. Recently, in 2023, the ATSDR revised its toxicological profile on NDMA, systematically reviewing data on NDMA. Although the ATSDR no longer makes classifications, it noted "NDMA's carcinogenicity is widely recognized."

65. In 2002, the World Health Organization ("WHO"), of which IARC is part, issued a chemical assessment document for NDMA, and stated:

> Based upon laboratory studies in which tumours have been induced in all species examined at relatively low doses, NDMA is clearly carcinogenic. There is overwhelming evidence that NDMA is mutagenic and clastogenic. …. Qualitatively, the metabolism of NDMA appears to be similar in humans and animals; as a result, it is considered highly likely that NDMA is carcinogenic to humans, potentially at relatively low levels of exposure.

66. In 2002, Canadian regulators concluded that "owing to the considerable evidence of carcinogenicity of NDMA in laboratory species, evidence of direct interaction with DNA consistent with tumour formation, as well as the apparent lack of qualitative species-specific differences in the metabolism of this substance, NDMA is highly likely to be carcinogenic to humans."

67. In 2020, when the FDA ordered the immediate withdrawal of all ranitidine from the market due to finding NDMA, the FDA stated that "NDMA is a probable human carcinogen (a substance that could cause cancer)." The FDA specifically explained that "sustained higher levels of exposure may increase the risk of cancer in humans."

68. The dangers of NDMA are recognized by the Defendants. On September 25, 2019, GSK's occupational toxicologists prepared a Hazard Assessment Report on NDMA. This document was created "to protect the scientists and anybody handling" NDMA in the laboratory. GSK's scientists reviewed the literature on NDMA and repeatedly indicated that NDMA is a human carcinogen:

> There appear to be no qualitative differences in metabolism of NDMA between humans and laboratory animals, and there is no reason to believe that humans would respond qualitatively differently.
>
> N-Nitrosodimethylamine (NDMA) is reasonably anticipated to be a human carcinogen based on sufficient evidence of carcinogenicity from studies in experimental animals.
> …
>
> There is overwhelming evidence that NDMA is mutagenic and clastogenic. … Positive results have been observed in human as well as rodent cells.
> …
>
> Qualitatively, the metabolism of NDMA appears to be similar in humans and animals; as a result, it is considered highly likely that NDMA is carcinogenic to humans, potentially at relatively low levels of exposure.
> …
>
> NDMA is a genotoxic carcinogen, and exposure should be reduced to the extent possible.

69. Because NDMA has been studied for so long, it is also understood how NDMA, mechanistically, causes cancer in cells. Unmetabolized NDMA is, itself, harmless. However, in the body, NDMA is quickly metabolized by an enzyme called cytochrome p450. As the NDMA molecule breaks down, it creates formaldehyde and a "methyldiazonium ion." Both of these metabolites are genotoxic, especially the methyldiazonium ion, which is known to cause DNA adducts, i.e., bind to genetic material and cause mutations.

70. When NDMA is ingested by humans, nearly all of it is metabolized and converted into its genotoxic metabolites. Although human experimentation with NDMA is considered unethical, one experiment was done in the 1980s to confirm the rapid and near-complete metabolization of NDMA. In the

Spiegelhalder study, researchers noted: "[i]t is well accepted that exposure to nitrosamines must be considered to be a cancer risk. To calculate this risk, it is necessary to estimate total exposure." To explore human metabolism of NDMA, volunteers ingested beer, orange juice, and orange juice with 6% alcohol that were spiked with known quantities of NDMA. When urine was collected, the subjects who consumed the NDMA-spiked orange juice without alcohol, had no detectable NDMA in the urine, indicating that all the NDMA had been metabolized. Conversely, 0.5 – 2.5% of the NDMA was recovered in the urine of volunteers that consumed alcohol. This makes sense as alcohol (ethanol) is known to competitively inhibit the cytochrome p450 enzyme that is also used to metabolize NDMA.

71. The absorption and metabolism of NDMA is well-studied, and its mechanism of causing DNA damage is well characterized. NDMA is mutagenic and/or genotoxic (depending on the assay used) in virtually all systems tested. Indeed, NDMA is so effective and consistent in causing genetic damage, NDMA is routinely used as a positive control in genotoxicity studies.

72. In *every* study, in *every* species, and in *every* sex, NDMA caused tumors to develop.

73. Numerous human epidemiological studies have been conducted involving both occupational and dietary exposure to NDMA. And the greater

weight of the evidence is clear: NDMA exposure causes cancer in humans:

- De Stefani, et al., Dietary Nitrosodimethylamine and the Risk of Lung Cancer: A Case-Control Study from Uruguay, 5 CANCER EPI. BIOMARKERS & PREVENTION 679, 679–682 (1996).

- Goodman, et al., High-Fat Foods and the Risk of Lung Cancer, 3 EPI. 4, 288-299 (1992).

- Hidajat, et al., Lifetime exposure to rubber dusts, fumes and N-nitrosamines and cancer mortality in a cohort of British rubber workers with 49 years follow-up, 76 OCCUP. ENV. MED. BRIT. MED. J., 250, 250–258 (2019).

- Jakszyn, et al., Endogenous versus exogenous exposure to N-nitroso compounds and gastric cancer risk in the European Prospective Investigation into Cancer and Nutrition (EPIC-EURGAST) study, 27 CARCINOGENESIS 7, 1497–1501 (2006).

- Jakszyn, et al., Red Meat, Dietary Nitrosamines, and Heme Iron and Risk of Bladder Cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC), 20 CANCER EPI. BIOMARKER & PREVENTION 3, 555–559 (2011).

- Jakszyn, et al., Nitrosamines and Heme Iron and Risk of Prostate Cancer in the European Prospective Investigation into Cancer and Nutrition, 21 CANCER EPI. BIOMARKER & PREVENTION 3, 547–551 (2012).

- Keszei, et al., Dietary N-nitroso compounds, endogenous nitrosation, and the risk of esophageal and gastric cancer subtypes in the Netherlands Cohort Study, 97 AMER. J. CLIN. NUTRITION 135, 135–46 (2013).

- Knekt, et al., Risk of Colorectal Cancer and Gastro-Intestinal Cancers After Exposure to Nitrate, Nitrite, and N-Nitroso Compounds: A Follow Up Study, 80 INT. J. CANCER 852, 852–856 (1999).

- Larsson, et al., Processed meat consumption, dietary nitrosamines and stomach cancer risk in a cohort of Swedish women, 119 INT. J. CANCER 915, 915–919 (2006).

- La Vecchia, et al., Nitrosamine intake and gastric cancer risk, 4 EUR. J. CANCER PREV. 461, 461–474 (1995).

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

- Palli, et al., Dietary patterns, nutrient intake and gastric cancer in a high-risk area of Italy, 12 CANCER CAUSES AND CONTROL 163, 163–172 (2001).

- Pobel, et al., Nitrosamine, nitrate and nitrite in relation to gastric cancer: A case-control study in Marseille, France, 11 EUR. J. EPI. 67, 67–73 (1995).

- Rogers, et al., Consumption of Nitrate, Nitrite, and Nitrosodimethylamine and the Risk of Upper Aerodigestive Tract Cancer, 4 CANCER EPI. BIOMARKER & PREVENTION 29, 29–36 (1995).

- Ronco, et al., Meat Consumption, Animal Products, and the Risk of Bladder Cancer: A Case-Control Study in Uruguayan Men, 15 ASIAN PAC. J. OF CANCER PREVENTION 5805, 5805–5809 (2014).

- Seyyedsalehi, et al., Association of Dietary Nitrate, Nitrite, and N-Nitroso Compounds Intake and Gastrointestinal Cancers: A Systematic Review and Meta-Analysis, 11 TOXICS 190, 1-13 (2023).

- Song, et al., Dietary Nitrates, Nitrites, and Nitrosamines Intake and the Risk of Gastric Cancer: A Meta-Analysis, 7 Nutrients 9872, 9872–9895 (2015).

- Zheng, et al., Dietary N-Nitroso Compounds and Risk of Hepatocellular Carcinoma: A USA-Based Study, 74 HEPATOLOGY 6, 3161–3173 (2021).

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

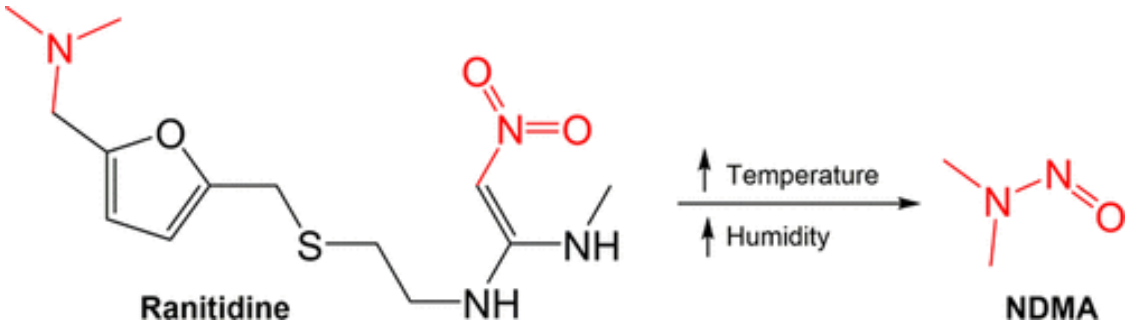
74. The World Health Organization has recommended that long-term total daily ingested NDMA amounts from all sources in an average male adult should be less than 200 ng, because a 70-year estimated risk of cancer increase.

75. It is estimated that the average adult consumes 100 to 110 nanograms ("ngs") of NDMA daily in the water and food supply. This means that ingesting more than 100 ng of NDMA daily from prescription drugs (either from contaminated product ingestion or conversion in the stomach) would bring the daily ingested amount of NDMA to above 200 ng and significantly increase the risk of cancer.

76. FDA guidelines limit NDMA exposure from daily medications or more than 96 ngs.

II. Ranitidine Is an Unstable Molecule and Will Naturally Degrade into NDMA, Accelerated by Heat and Humidity, Exposing Users to NDMA Upon Ingestion

77. Ranitidine, is an amine-based pharmaceutical, that has been shown to decompose to N-nitrosodimethylamine (NDMA):



78. The ranitidine molecule contains the necessary tertiary amine group and a nitrosation source (both highlighted in red in Figure above) to form NDMA. Using suitably isotopically labeled ranitidine hydrochloride, GSK researchers have confirmed the formation of NDMA solely from an intermolecular reaction of ranitidine hydrochloride without involvement of impurities. They also identified factors that influence the rate of degradation to include heat and humidity.

79. Testing done by GSK on both ranitidine drug substance batches manufactured by different suppliers, including GSK, and various finished ranitidine products, show high levels of NDMA. For the ranitidine drug substance, they observed NDMA levels of up to greater than 40 mcg/g (40 ppm). To put this in context, each 150 mg ranitidine pill contains 168 mg of ranitidine hydrochloride drug substance, and each 300 mg pill contains 336 mg of ranitidine hydrochloride drug substance. If the underlying drug substance contained 40 ppm of NDMA (as observed in GSK testing), a 150 mg ranitidine pill would contain 6,720 ngs of NDMA. And a 300 mg pill would contain 13,440 ngs of NDMA. This is 140 times the FDA limit of NDMA. For finished drug product, GSK observed up to

7.6 mcg/g (7.6 ppm) in film coated tablets, which equals 2.28 mcg of NDMA in a 300 mg pill, or 2,280 ngs. That would be 23 times the FDA limit. GSK tested 221 tablets. Of these, 209 (94.6%) contained NDMA levels in excess of the acceptable daily limit.

80. The FDA published testing results for pills that had been submitted by drug sponsors for testing. FDA tested 29 tablets and observed NDMA up to 2.85 ppm, or 855 ngs in a 300 mg pill. Overall, 12 of 29 (41%) of the tested pills were above the acceptable daily limit.

81. The Therapeutic Goods Administration (TGA) of the Australian government tested 135 batch samples of ranitidine. The TGA found NDMA levels up to 14 ppm, or 4,200 ngs in a 300 mg dose. Of the batches, 109 of 135 (89%) were in excess of the acceptable daily limit.

82. The South Korean Ministry of Food and Drug Safety tested 269 ranitidine products in 2019. They observed seven products with NDMA level as high as 53.50 ppm. With a maximal daily dose of ranitidine in Korea of 600 mg, at 53.5 ppm, that means daily use of ranitidine products could expose patients to 32,100 ngs of NDMA in a single day—334 times the FDA's acceptable daily limit.

83. The European Medicines Agency ("EMA") issued an Assessment Report in September 2020. The EMA did not, itself, test any finished product, but indicated that various drug makers had submitted testing results. According to the

EMA, "[a]lmost for all drug products tested so far, NDMA has been identified in levels above the current limit of 0.16 ppm[.]" The EMA confirmed that this degradation was accelerated by heat and humidity.

84. Emery Pharma, a research and development laboratory in Oakland, California, conducted the most robust testing of finished ranitidine product. A total of 761 pills provided by Defendants were tested. There were only 4 batches with NDMA levels that were lower than the FDA's NDMA acceptable daily intake of 96 ngs. For unexpired tablets produced by drug makers, including GSK, the mean NDMA level for a 150 mg dose was 1,576.3 ngs. For expired tablets produced by drug makers, including GSK, and tested by Emery, the mean NDMA level for a 150 mg dose was 2,374.3 ngs. For all tablets, the mean NDMA level for a 150 mg dose was 1954.2 ngs. The range of average NDMA levels found in the tablets was from 49.3 ngs/150 mg to 28,052.8 ngs/150 mg. This range is consistent with testing done by GSK on ranitidine drug substance and finished product.

85. Abe Y, et al., (2020) stored commercially available ranitidine reagent powders and formulations under various conditions. When ranitidine tablets from two different brands were stored under accelerated condition (40^0C with 75% relative humidity) for up to 8 weeks the amount of NDMA in them substantially increased from 0.19 to 116 ppm (57 ng to 34,800 ng in 300 mg dose) and from

2.89 to 18 ppm (867 ng to 5,400 ng in 300 mg dose), respectively.

III. Ranitidine Breaks Down into NDMA in the Stomach, Exposing Users to Endogenously Generated NDMA

86. There is also substantial evidence that ranitidine use leads to endogenous formation of NDMA. Animal, human, and in vitro studies have demonstrated that ranitidine interacts with sodium nitrate in gastric fluid, leading to the formation of up to hundreds of thousands of ngs of NDMA. Although such endogenous formation is difficult to quantify, its occurrence in humans is well established by a robust record of scientific evidence spanning four decades.

87. Numerous scientific studies have been conducted to assess the association of ranitidine with cancer. Those studies, however, have not been able to specifically quantify the amount of NDMA exposure and, thus, have limitations. Nonetheless, numerous reliable human epidemiological studies have shown a clear association between use of ranitidine and the development of bladder, breast, colorectal, esophageal, liver, lung, pancreatic, prostate, and stomach/gastric cancer.

IV. For Nearly Four Decades Defendants Concealed the Link Between Ranitidine and NDMA, Until Valisure Blew the Whistle and the FDA Pulled Ranitidine Off the Market

88. From the very outset of ranitidine development, GSK was aware that ranitidine was an unstable molecule that could degrade and form into NDMA. GSK concealed that fact, which was not revealed to the world until Relator Valisure published its testing data in September 2019 (after first disclosing this

information to the United States). Within months of Valisure's public disclosure, the FDA investigated the issue and ordered all ranitidine products off the market. The following paragraphs detail how GSK committed this fraud, caused millions of Americans to be exposed to a genotoxic carcinogen without their consent, leading to the United States and the Plaintiff States to pay billions of ranitidine products that, absent the fraud, would never have been on the market.

A. In the 1970s, the Scientific Community Grew Increasingly Concerned with the Ability of Pharmaceutical Compounds to Nitrosate and Form into NDMA, Leading to Recalls of Drugs

89. Methapyrilene is an antihistamine that was developed in the 1950s that was effective at causing drowsiness—it was used to treat insomnia. In the 1970s, it was discovered that the drug caused liver tumors in rats. Researchers realized that the drug, due to its amine chemical structure, was capable of interacting with a nitrosating agent, like sodium nitrite (commonly found in the human stomach), to form NDMA. The FDA pulled the drug off the market in 1978 following these discoveries. And this prompted researchers to begin studying now secondary and tertiary amine drug products could form nitrosamines.

90. In 1980, IARC published a monograph where it raised serious concerns about the ability of nitrosatable drugs to from nitrosamines, including NDMA: "The formation of N-nitroso compounds is theoretically possible with all compounds that contain amino groups. Secondary amines react directly; tertiary

and, in some cases, primary amines may react by more complicated mechanisms." IARC explained that because the "formation of N-nitroso compounds from nitrosatable amine precursors and nitrosating agents, such as nitrite or nitrous gases, is not usually taken into account in carcinogenicity tests of the parent compound, additional investigations are necessary to evaluate this possible hazard." IARC explained that "If valid comparisons are to be made, the reactions must be carried out under standard conditions for set times, and the identity and yield of N-nitroso compounds established by mass spectrometry or other appropriate methods. The WHO Expert Group recommended a 'Nitrosation Assay Procedure' (NAP test)" which would help elucidate the ability of drug compounds to react and form nitrosamines.

91. The NAP test has since become the standard method for assessing a molecules affinity to nitrosate and form NDMA.

B. In the 1980s, before Ranitidine Was Approved, FDA Raised Concerns about Ability of Ranitidine to Nitrosate and Form Nitrosamines

92. Shortly after the FDA gave investigational approval, concerns arose about the possibility of ranitidine being carcinogenic due to nitrosation.

93. On May 2, 1980, GSK scientists met with the FDA. During the meeting the "FDA voiced their concern about the nitrosation potential of ranitidine." And even after GSK provided background information about the work

it had done in this regard, it "did not allay the FDA's concern." Instead, FDA "urged that a comprehensive description be sent to the FDA describing the exact details and conditions under which the experiments were carried out and this would be a factual report without editorialization." GSK agreed to provide that data.

94. A few months later, concerns about nitrosation and ranitidine also increased among investors. On November 1, 1980, a stockbroker issued a "Special Report" titled "Ranitidine – Cause for Concern?" The Special Report began by discussing how ranitidine would take on "considerable importance in determining Glaxo's future revenue, especially in the key US market." The Special Report noted that cimetidine and ranitidine were chemically similar, and that "cimetidine is capable of being nitrosated by nitrites under the acidic conditions of the stomach and nitroso compounds (especially N-nitroso compounds) are known to be carcinogenic[.]" It also noted that long-term use "leads to change in the types of bacteria which colonize the gut" specifically, an increase in "certain bacteria which reduce nitrate … to nitrite, thus leading to an increased likelihood of nitrosation." The Special Report notes that ranitidine "is very easily nitrosated but forms C-nitroso compound which is not suspected of carcinogenic potential. However, under forcing conditions a second nitroso group can be inserted into the ranitidine" that "could be potentially harmful[.]" The Special Report finishes with a "cause

for concern" about whether concerns about the carcinogenicity of ranitidine "could affect sales of ranitidine once it is marketed."

95. In response to this Special Report, GSK's public relations executives stated "it would be unwise to at this stage to over-react to this particular circular … we will take every opportunity to put the company's view to media and analysts. Group PR … will be watching the situation very closely with a view to proposing rapid defensive action should the position deteriorate." Glaxo's Drs. R. T. Brittain and D. Jack (important later) were specifically copied on the memo.

96. Thus, in the span of a few months, both the FDA and the investment market had taken notice of a potential issue with ranitidine to nitrosate and form a nitrosamine. And GSK committed to providing all data about its findings to the FDA.

C. In Early 1980s, Scientists Raise Concern about the Ability of Cimetidine to Nitrosate into Nitrosamines

97. The similarities between cimetidine and ranitidine are not by accident. Cimetidine works by physically blocking the H_2 receptors found in gastric parietal cells, which then prevents its activation. This, in turn, prevents the production of stomach acid. Because the drug works structurally, Glaxo was able to develop ranitidine by mimicking cimetidine's structure. Glaxo refined the cimetidine model by replacing the imidazole ring of cimetidine with a furan ring with a nitrogen-containing substituent. This is why, chemically, cimetidine and ranitidine

are very similar.

98. Both molecules have a dimethylamine ("DMA") component in them. This means, when given an external source of nitro is given, it can react to form a nitrosamine. However, ranitidine, unlike cimetidine, has a nitro group in the molecule itself. This is why ranitidine, as opposed to cimetidine, will form NDMA on standing, through an intermolecular interaction, without any addition of an external nitro source. Although, cimetidine, when combined with a nitro source, like nitrite in the stomach, does react, like ranitidine, to form NDMA in the human stomach.

99. Before the approval of ranitidine, research on cimetidine had already revealed the danger of N-nitrosamine formation. In 1981, a study by a team of British researchers published in *The Lancet* found that people who took cimetidine had significantly higher levels of nitrosamines in their gastric juice.[3] The researchers believed this was a function of the ability of long-term use of cimetidine to impact the PH levels in the stomach which, in turn, allows the growth of specific bacteria that convert nitrates into nitrites. This greater amount of stomach nitrite levels could then interact with cimetidine, leading to the formation of carcinogenic nitrosamines.

D. In 1981, GSK's Experiments Reveal that Ranitidine forms NDMA

[3] Reed et al., *Effect of Cimetidine on Gastric Juice N-Nitrosamine Concentration*, 318 LANCET 8246, 553–556 (1981).

100. In the first half of 1981, GSK specifically acknowledged the risk of nitrosation and cancer. Dr. L.E. Martin sent a report, covering six months prior to June 1981, to Dr. Brittain (copying various GSK scientists including Drs. M. Harris and D. Poynter). Dr. Martin was the "Head" of GSK's "Biochemical Pharmacology Department" with over 30 researchers reporting to him (including, among others, Dr. R. Tanner). In this report, Dr. Martin noted that "[c]oncern is still expressed by some physicians as to whether treatment with H2 receptor antagonists for long periods may increase the incidence of stomach cancer. It has been suggested that this increase in stomach cancer may be caused by N-nitroso compounds." This "concern" mirrors the issues being raised concerning ranitidine's close chemical relative, cimetidine. The report stated "Smith, Kline & French" which made cimetidine "and ourselves are having to give considerable through to evaluating the role of nitrite in the diet…. A study is in progress in which the *in vitro* nitrosation of ranitidine and cimetidine are being compared in human gastric juice." The results were reported in the next six-month report.

101. Specifically, Dr. Martin reported to Dr. Brittain (also copying Drs. M. Harris and Poynter) about a study titled "Formation of N-Nitrosodimethylamine [NDMA] from Ranitidine." Dr. Martin notes that "SKF reported to [GSK] that they had observed the formation of N-nitrosodimethylamine [NDMA] from ranitidine." He explained, drawing on well-established principles of organic

chemistry, that "[r]anitidine is a tertiary amine and therefore when incubated under strongly acid conditions with high concentrations of sodium nitrite could react with the formation of N-nitrosodimethylamine." So, "a study was undertaken on the formation of N-nitrosodimethylamine [NDMA] under the WHO (NAP) conditions." GSK, using gas chromatography / mass spectrometry, performed the NAP test, using 10 mmol of ranitidine and 40mmol of nitrite and "found that about 2% of the ranitidine present [] was converted into N-nitrosodimethylamine." The experiment yielded 144 µgs of NDMA, or 144,000 ngs, from only 31.5 mg of ranitidine. When done with lower levels of nitrite, they did not see NDMA. This summary of the experiment was not shared with the FDA, even though FDA had already urged, and GSK agreed, to provide "a comprehensive description … describing the exact details and conditions under which the experiments were carried out" as it relates to the nitrosation of ranitidine into nitrosamines.

102. To put this result in context, this percent yield of NDMA formation was 25 times greater than methapyrilene (which had a yield of 0.08% under the NAP test), which had three years prior, been pulled off the market out of concern of NDMA formation.

E. Independent Researchers Raise Concern about Nitrosation of Ranitidine and GSK Misleads Them

103. Independent researchers raised alarm about the potential nitrosation of ranitidine. In September 1981, Italian researchers Dr. De Flora and Dr. Brambilla,

reached out to GSK about experiments they were conducting regarding the nitrosation of ranitidine. It is unknown if GSK immediately responded to them.

104. Then, on October 31, 1981, Dr. De Flora, published an abstract in *the Lancet*, titled "Cimetidine, Ranitidine, and their Mutagenic Nitroso Derivatives."[4] Dr. De Flora reported on experiments with ranitidine, that showed "preincubation with nitrite in human gastric juice from untreated individuals (60min at 37°C) or simply acidification of nitrite-ranitidine mixtures results in toxic and mutagenic effects in bacteria." Dr. De Flora explains that "ranitidine reacts with nitrite at lower doses than cimetidine[.]" This, chemically, makes sense because ranitidine contains its own nitro group within the molecule. He goes on to state that these experiments were only *in vitro* but that "the predictive value of these *in vitro* tests is recognized, and it would seem prudent to avoid nitrosation as far as possible by, for example, suggesting a diet low in nitrates and nitrites, by asking patients not to take these at times close to (or with) meals, or by giving inhibitors of nitrosation such as ascorbic acid." Dr. De Flora explained that nitrosated ranitidine was mutagenic because it was converting into a nitrosamine, but had not yet identified what that specific nitrosamine was, i.e., NDMA.

105. Dr. Brittain, who not only had been put on notice of the potential

[4] De Flora, et al., *Cimetidine, ranitidine, and their mutagenic nitroso derivatives*, 2 LANCET 8253, 993–994 (1981).

impact to sales of ranitidine if it were shown that it could nitrosate into a nitrosamine like NDMA just a year prior, but was aware of GSK's nitrosation studies with ranitidine and the link to NDMA, published a response two weeks later (Drs. Martin, Harris, and Poynter were co-authors).[5] This study allowed GSK to deflect any concerns about nitrosation and NDMA and derail the FDA and independent researchers from making the connection.

106. In the response to Dr. De Flora, GSK indicated that its "detailed investigations can, we believe, place in perspective [Dr. De Flora's] findings in terms of the safety of ranitidine in man." GSK stated that "we were obviously concerned as to whether or not a mutagenic N-nitroso derivative of ranitidine could be formed in the stomach." And they explained that "if the concentration of sodium nitrite was increased to 40mmol/1 a further reaction occurred whereby an N-nitroso nitrolic acid derivative was formed (figure). This latter product was mutagenic" and "is unstable and rapidly reverts to the non-mutagenic nitrolic acid derivative except in the presence of excess nitrous acid." Importantly, GSK makes no mention of NDMA, which they knew, based on their own experiments, would form under these exact conditions, which they had already studied. Thus, GSK explained, "[t]here can be little doubt that the product formed under the conditions of De Flora's experiment … is the N-nitroso nitrolic acid derivative of

[5] Brittain, et al., *Safety of ranitidine*. 2 LANCET 8255, 1119 (1981).

ranitidine." Even through Drs. Brittain, Martin, Harris, and Poynter knew that ranitidine could react with high levels of nitrite (specifically at 40 mmol) under the NAP test to form high levels of NDMA, GSK did not mention NDMA. This is remarkable considering how well-established it was that NDMA was a genotoxic and mutagenic nitrosamine. Failing to disclose this information to Dr. De Flora and the rest of the medical community was misleading. Indeed, they specifically stated that mutagenic compound formed in Dr. De Flora's experiment was, with "little doubt," a N-nitroso nitrolic acid derivative that quickly reverts to non-mutagenic nitrolic acid. GSK deliberately misled the public about their findings, diverting concerns regarding nitrosation away from NDMA and toward a N-nitroso nitrolic acid derivative.

107. The results of the Brittan "N-nitroso nitrolic acid derivative" experiments were conveyed to the FDA. However, GSK deliberately did not share the NDMA data.

108. Internal documents confirm that Dr. Brittian deliberately withheld information in his response to Dr. De Flora and did not identify all the resulting products formed by nitrosating ranitidine. This would necessarily include NDMA.

109. In December 1981, GSK finally decided to respond to the inquiries from Drs. De Flora and Brambilla. The researchers requested samples of the supposed nitrosation compounds that GSK has claimed to have isolated. However,

Dr. Brittian cautioned that he did not want to disclose the products that were formed by nitrosated ranitidine to the researchers and, instead, work to convince them of ranitidine safety. He indicated that his colleagues, Drs. Jack and Poynter would handle. At no time did GSK tell these researchers about the NDMA data.

F. GSK Buries the NDMA Data and Lies to the FDA about Its Data

110. On April 6, 1982, GSK's Dr. Tanner finalized the NDMA study titled, "The Determination of N-Nitrosodimethylamine [NDMA] formed by the Reaction of Ranitidine Hydrochloride with Sodium Nitrite." The report was circulated internally at GSK to Dr. Martin, and Dr. Brittain was specifically copied. Dr. Tanner noted that "molecules with tertiary amines," like ranitidine, can "react with nitrite under certain conditions to yield N-nitrosodimethylamine (NDMA)." This is consistent the IARC literature. "[T]herefore experiments were carried out to determine whether NDMA could be formed from the drug in the presence of nitrite." Dr. Tanner used "conditions similar to those described for the WHO …NAP test" and under a simulation of "the human stomach after ingestion of a nitrite rich meal[.]" Using "gas chromatography mass spectrometry" Dr. Tanner observed "under the conditions of the WHO NAP test (Experiment 3) 232µg [232,000 ngs] NDMA were formed … equivalent to 3.1% yield based on ranitidine." "A similar quantity of NDMA, 219µg [219,000 ngs], was formed in a 10ml incubation mixture when the ranitidine concentration was raised to that of

nitrite (40mM)." This result was one of the highest NDMA conversion rates observed of a drug compound. It was 39 times greater than the 0.08% observed for the recalled drug methapyrilene pursuant to the NAP test. For the high nitrite-meal simulation experiment, it "gave a weak signal similar to that observed from a control incubation[.]" Dr. Tanner, however, did not provide the actual results of the NDMA formed to reach a "weak signal" despite the high temperatures used in the GCMS, which are known to cause NDMA formation.[6]

111. GSK did not share the Tanner study with the FDA or otherwise ever inform the FDA on information specifically about NDMA. The Tanner study was only disclosed to the FDA in December 2019, a few months before the FDA recalled ranitidine from the market.

112. A month later, on May 13, 1982, GSK presented before the FDA's Scientific Advisory Panel to specifically discuss the science and safety of ranitidine. Dr. Poynter specifically presented to the FDA on ranitidine's "mutagenicity" and "nitrosation." Dr. Jack, however, who was originally copied on the Special Report (discussed above), set the stage:

> [W]e want to focus only on the part which raises the real problem in some people's mind, namely, *the possibility of carcinogenesis with drugs of this kind*. That possibility was first raised in people's mind when Elder and his colleagues from Manchester reported that they had some patients who developed cancer of the stomach within a few months of treatment with cimetidine. Of course, any such effect must

[6] This point is critical. FDA confirmed that when ranitidine is exposed to the high temperatures in gas chromatography, it will form high levels of NDMA—i.e., millions of ngs. If Glaxo was looking for NDMA, they should have observed extremely high levels. That they fail to report this data is suspicious. GSK has since destroyed the data so there is no way to know what the testing showed.

> be the effect of a very potent and highly specific carcinogen, and *the mechanism they proposed was that cimetidine in the body might be nitrosated to this N-nitroso derivative*… So what one is saying, very simply, that even if the hypothesis about cimetidine were right, it would not apply to ranitidine, because ranitidine behaves very differently towards nitrous acid. Instead of nitrosating on nitrogen, it nitrosates on carbon, this carbon. What is formed is a nitrolic acid.

113. Then, in introducing Dr. Poynter, Dr. Jack noted that he would present data "known to be sensitive to carcinogens and *in particular to nitrosamines*, under conditions which foster the production of these substances[.]" However, when Dr. Poynter presented to the FDA, he *did not disclose the NDMA data* nor any of GSK's tests done showing NDMA formation including the recently completed Tanner Study. This, despite the FDA specifically raising concerns about the nitrosation of ranitidine in May 1980. Dr. Poynter referenced nitrosation and even the potential interaction or ranitidine with nitrite, but he was silent about NDMA. Considering the importance Dr. Jack placed on presenting issues surrounding the nitrosation and formation of N-nitroso compounds, it is clear this omission was intentional.

114. Dr. Poynter focused on the rodent carcinogenicity studies done on ranitidine and explained that there was "no evidence of ranitidine being itself carcinogenic either in the stomach or for that matter anywhere else[.]" But, in GSK's first long-term mouse study, they specifically observed "a statistically significant positive dose-response trend in tumor rates for pulmonary tumors in female mice" and that there was only 1 liver tumor in the control group, versus

seven liver tumors in mice treated with ranitidine. To state that there was "no evidence" is, at best, an exaggeration and, at worst, a falsehood. In the face of Dr. Poynter's presentation, unsurprisingly, the Committee voted to approve ranitidine.

115. A few months later, on August 10, 1982, GSK submitted a proposed Summary Basis for Approval ("SBA")—a document that the FDA issues summarizing its approval of any new drug. In the SBA, GSK specifically discusses the potential for nitrosamine formation, but limits its discussion to the N-nitroso nitrolic acid derivative experiments by Brittan et al., and *makes no mention of NDMA* or their NDMA experiments. It states that "[a]lthough N-nitroso-nitrolic acid was a potent mutagen, it is not likely to be formed in the stomach of a patient ingesting ranitidine. An unrealistic large amount of nitrite needs to be present to form and maintain the nitrosamine." By deliberately omitting the Martin or Tanner data, and by providing an explanation for the observed mutagenic effects as being a "N-nitroso-nitrolic acid," GSK was able to avoid any suspicion that ranitidine, in the presence of nitrite, could form NDMA.

116. In 1983, the FDA approved ranitidine for the short-term treatment of ulcers. However, in the final SBA issued by the FDA, they repeated, verbatim, GSK's discussion of the N-nitroso nitrolic acid derivative. The FDA, however, did note that long-term use of ranitidine could result in a balance of bacteria in the gut that would lead to elevated levels of nitrite. FDA noted, which was not in the draft

submitted by GSK in August 1982, that "[t]he 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." But, GSK specifically had that evidence, i.e., that ranitidine and nitrite could react to form NDMA in human gastric fluid, a well-established and potent nitrosamine—evidence that the FDA had *specifically* requested. By concealing this information from the FDA, the Agency concluded that because "[r]anitidine is recommended only for short-term use" the "carcinogenic risk, if any, should thus be minimized."

117. Even more alarming, however, is the fact that the FDA dismissed this concern regarding cancer because Zantac would only be used for short periods of time (two weeks) and GSK, at that time, knew that patients would use Zantac for longer periods of time. They specifically banked on this fact: "Zantac will be launched with indications for short-term duodenal ulcer … our major competitor, Tagamet, has broader indications … for long-term maintenance therapy... At first glance this may appear to be a limitation to Zantac. In reality, it is no limitation at all. … many physicians will, or their own accord, use Zantac in the same manner in which cimetidine is used." GSK knew that "the carcinogenic risk, if any" would not "be minimized" but it did not care—it needed to dominate the market.

("[W]e're out to dominate the entire product category.") (emphasis in original). In fact, GSK's marketing efforts, from day one, specifically focused on the off-label promotion of Zantac for long-term use, despite the drug's approved indication for short-term use and despite the potential risk of carcinogenicity stemming from long-term use.

G. GSK's Deception and Concealment Derail Independent Researchers from Making the Connection to NDMA

118. GSK's deception also impacted researchers who were, at this time, specifically investigating the nitrosation of ranitidine and potential nitrosamine formation. Following Dr. De Flora's original abstract, he and several other researchers published studies, after being misled by GSK.

119. In Maura (1983), researchers demonstrated that ranitidine, in the presence of nitrite, yielded "a nitroso derivative capable of inducing a dose-dependent DNA fragmentation in cultured Chinese hamster ovary cells."[7] When they evaluated the yellow oily substance created by the nitrosated ranitidine (which is exactly what NDMA looks like), the researchers assumed "the N-nitroso compound obtained was likely to be the N-nitroso nitrolic acid derivative … previously identified by Brittain." Indeed, the researchers specifically noted that "[b]ecause of the presence in ranitidine molecule of a dimethylamine group, in

[7] Maura, et al., *DNA Damage Induced by Nitrosated Ranitidine in Cultured Mammalian Cells*, 18 TOX. LETTERS 97, 87-102 (1983).

analogy with the nitrosation pattern of other tertiary amines [NDMA] formation should be also expected." But they dismissed that possibility, however, because "Brittain et al. showed that … if the concentration of [nitrite] was increased to 40 mmol, a further reaction occurred whereby an N-nitroso nitrolic acid derivative was formed" and "chromatography revealed only one major nitroso-derivative spot[.]" In other words, even though they expected NDMA to form, because they only observed one N-Nitroso compound, they assumed it was the compound presented by Brittain.

120. In another example, Dr. De Flora published his full study in 1983, where he concludes "there seems to be no doubt about the possibility of formation of genotoxic derivatives from ranitidine and an excess nitrite under in vitro conditions[.]"[8] However, in discussing what may have been causing the genotoxicity, Dr. De Flora specifically noted that the way nitrosated ranitidine caused genetic damage is similar to NDMA. But, because Maura ruled it out, so did Dr. De Flora. Indeed, Dr. De Flora deferred to Brittain regarding the chemical makeup (as did Maura) of nitrosated ranitidine, concluding that "[o]ur findings seem to be consistent[.]"

121. In yet another study, Brambilla (1983), published the same year as

[8] De Flora, et al., *Genotoxicity of nitrosated ranitidine*, 4 CARCINOGENESIS 3, 255–260 (1983).

Maura and De Flora, researchers specifically studied whether ranitidine and nitrite could induce genetic damage in a living animal.[9] And, once again, the researchers concluded, "[o]ur experimental findings have shown that simultaneous oral administration in rats of high doses of ranitidine and NaNO2 can produce DNA fragmentation either in liver or in gastric mucosa. However, this effect was found to be dependent on both gastric pH and molar ratio drug/nitrite." Remarkably, the researchers used NDMA as a positive control, showing nearly identical levels of genetic damage in animals exposed to NDMA and nitrosated ranitidine. But, in discussing what was chemically causing the genetic damage, the researchers once again relied on Brittain: "the major (or the only) nitrosation product is likely to be the mutagenic N-nitroso nitrolic acid derivative obtained by Brittain et al. (34) by reacting ranitidine with a large excess of nitrite." The NDMA connection was never made because they were misled by Brittain's published letter and their direct interactions with GSK.

H. GSK Proceeds to Aggressively Market Ranitidine; Despite Numerous Studies Linking Ranitidine to NDMA Formation, GSK Never Tests Ranitidine Again for NDMA or Discloses Its Data to the FDA

122. When ranitidine degrades into NDMA, consistent with NDMA being a yellow oily liquid, ranitidine becomes discolored. Indeed, in GSK's 2020 root-

[9] Brambilla, et al., *Genotoxic effects in rodents given high oral doses of ranitidine and sodium nitrite*, 4 CARCINOGENESIS 10, 1281–1285 (1983).

cause analysis, they observed that when ranitidine degrades into NDMA in the presence of moisture and heat, it changes color (turns yellow and then brown), breaks down, and this is directly related to NDMA content

123. On February 13, 1984, shortly after the FDA's approval of ranitidine, GSK prepared a report titled, "Preliminary Results of an Investigation into the Thermal Degradation of Ranitidine Hydrochloride. The report detailed that ranitidine would rapidly degrade in the presence of moisture and heat, and that "[a]dditional, as yet unidentified, breakdown products are also produced within the liquid mass formed as a result[.]" The authors note that increased temperature and moisture "shows considerable darkening" and that existing method "HPLC assay procedure" was unable to properly identify these "break down products." GSK did not test these unidentified breakdown products for NDMA. Had GSK tested these impurities for NDMA they would have seen it—a fact confirmed by GSK's 2020 root cause analysis and the fact that NDMA has been discovered in nearly every ranitidine pill tested.

124. Over the course of the next several decades, as GSK did not change the ranitidine molecule, GSK continued to observe discoloration in Zantac pills, and instead of testing it to figure out what was causing it, they took actions to conceal it. For example, in the 1990s, when GSK was attempting to develop an OTC product with Warner Lambert (Pfizer predecessor), they knew they had a

discoloration problem. The white pills being sold in a plastic bottle and foil packets had "significant discolouration" at "the three month test point" when stored at elevated temperatures and humidity. Because they could not avoid discoloration, the "recommendations is that we should ASAP manufacture three full scale batches with a yellow coat… if we stay with the white coat we many not be able to offer" the product in plastic bottles. That recommendation was accepted: "Due to problems with discolouration of the white 75mg tablets on stability we have decided to change the colour to the same yellow as was used for the 25mg tablets[.]" Indeed, GSK admitted this was for the purposes of masking discoloration: "Replacement batches will be manufactured incorporating the yellow dye, previously used in the 25mg tablet, in the film coat to mask any potential discoloration."

125. In later years, when GSK was considering bulk packages (500 or 1000 pills) of Zantac, they indicated that such a product would need to be peach colored because "[i]t is believed that the peach coloured coating has superior ability to mask the yellow-brown discolouration of the tablet core relative to our white coating."

126. This issue concerning discoloration lasted decades and was even reported in the literature.[10] In 2003, researchers published a paper "Stability of

[10] Vehabovic, et al., *Stability of ranitidine in injectable solutions*, 256 INT. J. PHARMA. 109, 109–115

ranitidine in injectable solutions" reporting their own independent stability testing. This study was published while Defendant Pfizer controlled the OTC Zantac NDA (although, GSK manufactured all the ranitidine drug substance used in Pfizer's OTC products) and GSK controlled the Zantac prescription NDA. The Study reported that ranitidine was unstable and at 2 months the "colour changed from light yellow to brown" and that the "amount of related substances has exceeded allowed limits even 1 month after the test." GSK researchers discussed this paper in 2008, when a GSK scientist noted concerns regarding injection forms of ranitidine turning from clear to yellow over time, remarking "we should ask how that happens. To know what we need to know the structure of the yellow metabolite/contaminant, and how it would be generated from the patent compound over time." In response, another GSK scientist stated, "I guess I am reluctant to add further information because of the limited amount of supporting information we have … I do stress the importance of noting that the colour can change over time, which is a valid point that prescribers must be aware of, since we have received many complaints, but we do not have a full analysis on this." He goes on to explain it "surely begs the question, 'if it changes with time, is it safe to use? … which we do not have sufficient supporting information on." It begs a question GSK did not want to answer. "[W]e [do] not have a full analysis of everything that

(2003).

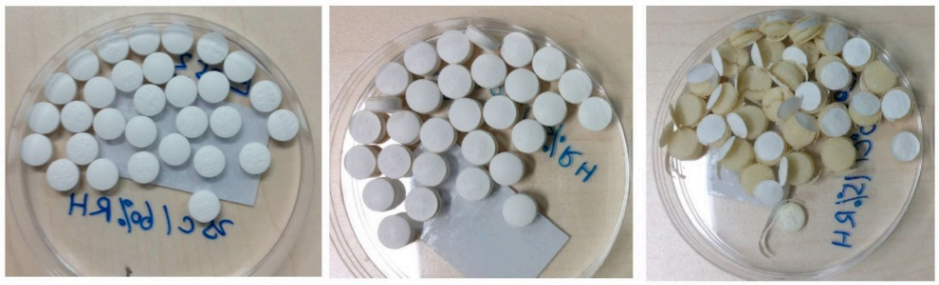
is, or is not, known at this point in time."

127. In a 2011 study titled, "Investigation into Yellow Impurities in Ranitidine HCI Sterile Injection Formulation" conducted by Andrew Searle (the GSK researcher that would later oversee the 2020 RCA of ranitidine), it states "[t]here has been a long history of yellow discolouration of Ranitidine HCI … To date, the impurities responsible for the colour have not been identified." In the study, Dr. Searle concludes that "[t]he overriding conclusion from this initial study was that the yellow discolouration was a complex phenomenon, caused by a multitude of components." Dr. Searle was unable to actually identify the yellow degradants—and, of course, he never tested for NDMA. This lack of information continued for years. "There is no knowledge on the discolouration of Zantac IV … Analytical work conducted in the past …found that the level of impurity is likely to be in the ppm level which makes it extremely difficult to identify, characterize and control."

128. In 2014, GSK conducted a Zantac Discoloration Simulation Study on Zantac tablets. "During the period from 2005 to November 2013 a number of complaints were received" regarding "tablet disintegration and discoloration as well as 9 stability …tablet discoloration." GSK systematically tested Zantac tablets under different scenarios, and concluded "color appearance and analytical results are impacted by effects of temperature and humidity. The tablet coat will

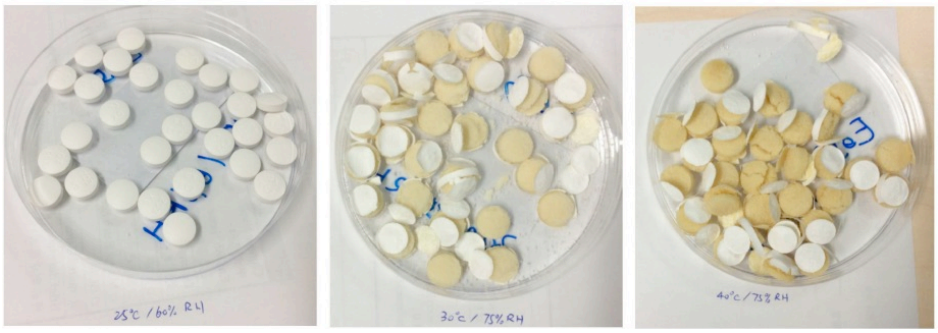
come apart and fall off and tablet will disintegrate [and] also tablet ill discolor from yellow to dark yellow, brown and finally dark drown." In the accompanying presentation, GSK provides clear visual evidence of this issue:

Day 1

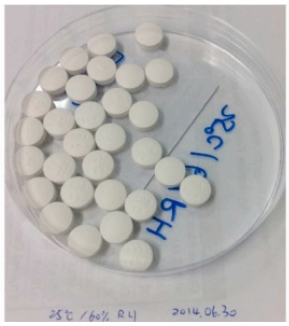


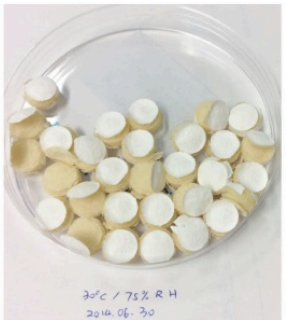
Day 2

Day 3



Day 4





2 Weeks

3 Weeks

129. While the pills at 25°C/60% RH stayed relatively intact, the 30°C/75% RH started discoloring on day 2. Peer-reviewed literature shows that temperatures routinely reach in excess of 30°C (upwards of 38°C) and relative humidity in excess of 75% (upwards of 100%) in a bathroom during a shower—the place where most people store their medications. Once again, as part of this discoloration simulation, GSK did not test for the yellow oily substances known as NDMA or identify the impurities.

130. In 2015, the Medicines and Healthcare Products Regulatory Agency ("MHRA") in the United Kingdom, inspected a GSK manufacturing facility. The MHRA identified "serious deficiencies in your operations[.]" Specifically, the MHRA cited GSK for failing to report or conduct safety assessments on batches of ranitidine that was discolored. "One issue was raised today regarding the handling of discoloured Zantac tablets identified during stability testing and through customer complaints. Inspectors are questioning why this had not been reported[.]" The MHRA noted that these deficiencies were similar to another GSK facility cited in 2014. This led to GSK, at the request of the MHRA, to conduct "a toxicology assessment of impurities that form as a result of this tablet degradation." It was also performed by Dr. Searle. He identified "[t]he structures of all impurities that have been formally characterized" and were "toxicologically assessed." These included "many previously unidentified impurity structures." In

the report, Dr. Searle represents that he ran the structures through the Derek Nexus database—a program the uses chemical structures to determine if they may be potentially genotoxic—and that they were not found to be a "cause for concern." However, internal GSK emails indicate that several of the unidentified impurities triggered alerts within the Derek system being "positive" and class "3" compounds, which were "aliphatic [oily] nitro compound." However, this was not disclosed in Dr. Searle's MHRA-ordered toxicology assessment. Instead, Dr. Searle concludes that there is no risk because "ingestion of a degraded tablets was considered unlikely to occur more than once in a lifetime."

131. At no time prior to 2019 did GSK ever test any of their discolored pills for NDMA, despite having identified this issue in 1981.

V. Pfizer and Boehringer Ingelheim Also Observed Significant Discoloration in their OTC Zantac Products and they Took No Action to Test for NDMA

132. While Pfizer controlled the Zantac OTC NDA, it repeatedly observed that its pills would degrade, turn into a yellow oily substance, exacerbated by exposure to heat and humidity. This led to Pfizer seeking to change the color of the OTC pills to specifically "mask" the discoloration and avoid consumer concerns about discolored ranitidine. These discolored pills were loaded with NDMA—as proven by numerous independent researchers—and yet, Pfizer never once tested for NDMA or disclosed this issue with the FDA or medical

community.

133. Boehringer Ingelheim saw nearly the same issues, and even studied it carefully, but never tested for NDMA.

134. From the beginning of Boehringer's control over the Zantac OTC NDA, Patheon (formerly DSM) informed Boehringer that numerous pills were failing on stability testing due to the degradation of the products into impurities caused by heat and humidity. Boehringer, in turn, took little action to identify the specific impurities being created.

135. During the period it controlled the Zantac OTC, Boehringer specifically noted that its products tended to discolor during regular transport and storage, noting in 2010 the discoloration was "exacerbated by elevated temperature and humidity conditions." This is the precise "conditions" that lead to the accelerated formation of NDMA.

136. Boehringer attempted to shift its manufacturing of the pills from Patheon to a subsidiary in Mexico—where their storage of product was not subject to any air conditioning or temperature control. But BI noted that it was having problems preventing its pills from discoloring. So, they proposed reformulating the type of dye used in their Zantac pills, which would allow it to conceal the scope of the degradation.

137. In trying to understand why this discoloration occurred, a scientist at

BI's Mexico facility identified the chemistry issue, spelling out exactly why ranitidine would form into a nitrosamine:

> The ranitidine chloralhydrate degradation components include nitro arid amino functional groups. These molecules present characteristic reactions of the functional groups from which they precede and therefore they have organic reactions. The outcome of these reactions is the formation of volatile amino compounds. The amino volatile compounds, due to its physical characteristics are not reported with a defined structure in the literature; based on that the patients could perceived a change ln the organoleptic: characteristics of the product.

138. This evaluation, however, was deemed proprietary and was not submitted to the FDA or otherwise made publicly available.

139. Shortly thereafter, Boehringer sold its control over the Zantac OTC NDA to Sanofi, i.e., released its control over the labelling, but continued to have its Mexico subsidiary manufacture the pills for Sanofi.

VI. In Addition to Discoloration, All Defendants Ignored the Accumulating Literature Linking Ranitidine to NDMA and Cancer

140. Defendants' failure to test discolored Zantac pills for NDMA is difficult to justify, especially when literature specifically identified the link to NDMA. There were numerous scientific publications linking ranitidine to NDMA—in addition to those discussed above (Maura, De Flora, and Brambilla) in 1983 noting the mutagenic effects of nitrosated ranitidine, with multiple studies comparing those effects specifically to NDMA.

141. For example, in 1990, scientists discovered that people taking

ranitidine had elevated levels of NDMA in their stomach juices compared to people with the same medical condition that did not take ranitidine or any H2 blocker.[11] This public study was available to GSK and every other Defendant as they proceeded to get involved in the manufacture and sale of RCPs.

142. That same year, researchers observed that rats treated with ranitidine for two years (lifetime) developed carcinoids in their stomach tissue, with 19 animals treated with ranitidine developing carcinoids and none in the control group.[12] This public study was available to GSK and each other Defendant as they proceeded to get involved in the manufacture and sale of RCPs.

143. In 1990, GSK published a report from their own ongoing clinical trial involving long-term maintenance use of ranitidine, indicating that people taking ranitidine daily, at either 150 or 300 mgs per day, were developing colorectal cancer a rate that twice as high as they had excepted. However, because the data was not statistically significant, they disregarded the data. This public study was available to GSK and each other Defendant as they proceeded to get involved in the manufacture and sale of RCPs.

144. Then, in 1994, GSK completed a two year follow up on that Zantac

[11] Matsuda, et al., N-*Nitrosamines in gastric juice of patients with gastric ulcer before and during treatment with histamine Hz-receptor antagonists*, 25 GASTROENTEROLOGICAL JAPONICA 2, 162–168 (1990).

[12] Havu, et al., *Enterochromaffin-Like Cell Carcinoids in the Rat Gastric Mucosa following Long-Term Administration of Ranitidine*, 45 DIGESTION 189, 189–195 (1990).

clinical trial, following patients taking ranitidine for 11 years. GSK observed that "bowel cancer was observed more frequently in the study population than would be expected (observed/expected ratio = 7/2.31 = 3.03)." It also noted that "[c]ases of prostate carcinoma arose more frequently than expected[.]" This long-term clinical trial provided a clear signal that people taking ranitidine were getting cancer a rate that was greater than expected, but GSK did not do *anything* about it. When reporting this to the FDA, GSK did not disclose whether the data was statistically significant. And, importantly, GSK never published this data. Although, this data was included in the NDAs for Zantac, including the OTC files, and thus was shared with all other Brand Drug Makers and was available for their consideration.

145. In 2003, researchers tested whether ranitidine, in combination with levels of nitrite found in stomachs after a high-nitrite meal, was genotoxic.[13] They found that "ranitidine showed" genotoxic activity. Remarkably the authors could not identify the nitrosamine that was causing the genotoxicity, but noted that their "findings are in contrast to the reported that no mutagenic nitrosation product of ranitidine is to be formed in man under any conceivable physiological conditions" as reported by Brittain. This public study was available to GSK and each other

[13] Ozhan, et al., *Genotoxic Activities of Drug-Nitrite Interaction Pro*ducts, 26 DRUG & CHEM. TOX. 4, 295–308 (2003).

Defendant as they proceeded to get involved in the manufacture and sale of RCPs.

146. In 2002, researchers identified the ability of ranitidine to combine with nitrite in water treatment to form NDMA.[14] These concerns continued throughout the 2000s, as researchers grew more and more concerned about NDMA forming in the water supply as part of water disinfecting.[15] Ranitidine reacts with chlorine to produce NDMA, noting that "Ranitidine, a pharmaceutical, showed extraordinary high conversion efficiency." These public studies were available to GSK and each other Defendant as they proceeded to get involved in the manufacture and sale of RCPs.

147. In 2011, researchers studied 20 common personal products, including ranitidine, to see how they reacted to chloramine to form NDMA: "Ranitidine shows the strongest potential to form NDMA[.]"[16] Indeed, the authors even explain how the chemical structure of ranitidine makes its susceptible to NDMA formation. This public study was available to GSK and each other Defendant as they proceeded to get involved in the manufacture and sale of RCPs.

148. In 2015, another study examined how NDMA formed following

[14] Mitch et al., *Formation of N-Nitrosodimethylamine (NDMA) from Dimethylamine during Chlorination*, 36 ENVIRON. SCI. & TECH. 4, 588–595 (2002).

[15] Sacher, et al., *Strategies for Minimizing Nitrosamine Formation During Disinfection* (Winter 2007/2008).

[16] Shen, et al., *Demonstration of 20 pharmaceutical and personal care products as nitrosamine precursors during chloramine disinfection*, 45 WATER RES. 944, 944–952 (2011).

ingestion in urine and feces, and there the authors reported that NDMA was endogenously formed from ranitidine consumption: "[T]hese results indicate that consumption of Zantac increased the loading of NDMA in urine as well as the amount of chloramine reactive NDMA precursors, which likely derived from ranitidine itself."[17] And that study was followed-up by a larger urinary study involving NDMA formation after ranitidine ingestion, which showed hundreds of thousands of ngs of NDMA in urine following ranitidine consumption.[18] This study also replicated the Tanner experiments from 1982, whereby varying amounts of nitrite were shown to react with ranitidine to form NDMA in simulated gastric fluid. Despite these studies, no Defendant tested ranitidine discoloration for NDMA nor disclosed any data concerning the link of ranitidine to NDMA until 2019.

149. There were also several studies specifically linking ranitidine to cancer, and still Defendants did not do anything. Specifically, in 2000, scientists from Kaiser published an epidemiology study using data from Northern California.[19] They observed that people taking ranitidine were more likely to

[17] Zeng, et al., *Contribution of N-Nitrosamines and Their Precursors to Domestic Sewage by Greywaters and Blackwaters*, 49 ENV. SCI. TECH. 22, 13158–13167 (2015).

[18] Zeng, et al., *Oral intake of ranitidine increases urinary excretion of N-nitrosodimethylamine*, 37 CARCINOGENESIS 6, 625–634 (2016). This study was ultimately retracted in 2021, a year after the FDA pulled ranitidine from the market. However, it remained in the published literature for years and GSK did nothing to examine NDMA formation.

[19] Habel et al., *Cimetidine Use and Risk of Breast, Prostate, and Other Cancers*, 8 PHARMACOEPIDEMOLOGY & DRUG SAFETY 149, 149–155 (2000).

develop various cancers than people not taking ranitidine.

150. In 2004, researchers looked at data collected from health professionals around the U.S.[20] They reported "an increase in bladder cancer risk among men who reported taking either" ranitidine or cimetidine (a 58% increased risk) in 1986. And, that risk remained elevated even after adjusting for potential confounders.

151. In 2008, a study was published showing that women taking ranitidine had a doubling of risk of developing breast cancer.[21]

152. Despite numerous studies linking ranitidine to NDMA and other studies linking ranitidine to cancer development, at no time did GSK test for NDMA or disclose to the FDA the truth about its experiments back in 1981.

153. Similarly, despite numerous studies linking ranitidine to NDMA and other studies linking ranitidine to cancer development, at no time did Pfizer, Boehringer, or Sanofi test for NDMA.

I. Valisure Tests Ranitidine Including the Same Tests GSK Concealed in 1981 But, Unlike GSK, Shares that Data with the FDA

154. In January 2019, FDA established a protocol for testing for NDMA in pharmaceutical products. This emerged following the discovery of NDMA contamination in Valsartan products (which Valisure was instrumental in

[20] Michaud, et al., *Gonorrhea and male bladder cancer in a prospective study*, 96 BRIT. J OF CANCER 169, 169–171 (2007).

[21] Mathes, *Relationship between Histamine^2-Receptor Antagonist Medications and Risk of Invasive Breast Cancer*, 17 CANCER EPI. BIOMARKERS & PREVENTION 1, 67–72 (2008).

exposing) that led to mass recalls of contaminated medications.[22] This process utilized Gas Chromatography ("GC") Mass Spectrometry ("MS"). GC-MS has been regarded as a "gold standard" for forensic substance identification and can be used to identify small polar molecules like NDMA.

155. In early 2019, the infant daughter of a scientist at Valisure was prescribed ranitidine. Concerned with giving his infant daughter a prescription medication, Valisure scientists tested the drug for the presence of impurities, including NDMA. The initial testing occurred in the February – March 2019 timeframe, and Valisure continued its investigation for several months.

156. Valisure tested representative samples of Zantac using the FDA's January 2019 protocol. Valisure tested whole 150 mg ranitidine tablets issued by five different distributors. Their results demonstrated exceedingly high levels of NDMA.

Sample	**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

[22] U.S. Food & Drug Administration, *GC/MS Headspace Method for Detection of NDMA in Valsartan Drug Substance and Drug Products* (Jan. 25, 2019), *available at* https://www.fda.gov/media/115965/download.

157. These tests on ranitidine pills confirmed that ranitidine was fundamentally unstable and contained the constituent components to form NDMA at an alarming rate.

158. That said, Valisure recognized that the levels of NDMA observed in ranitidine were likely inflated due to the use of heat in the FDA's GC-MS method, which required heating the ranitidine samples at 130 °C (266 °F) for fifteen minutes. This elevated temperature, itself, was likely accelerating the degradation process of ranitidine and yielding artefactually higher levels of NDMA.

159. So, Valisure developed a GC-MS method that could operate at body temperatures, i.e., 37 °C (98.6 °F). Then using this method, which was less sensitive than a traditional GC-MS approach, Valisure conducted a NAP test on ranitidine, combining ranitidine with various amounts of sodium nitrite after incubating in simulated gastric fluid. In other words, Valisure conducted the same tests that GSK had done in 1981, but concealed from the FDA.

160. Valisure obtained results similar to GSK: ranitidine produces levels of NDMA at multiples of FDA daily limits in the gastric environment.

NAP Testing Results:

Tablet Studies Lot# 77024060A	**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

161. Considering a human stomach can generate up to 3,000 ml of gastric fluid a day, this could result in millions of ngs of NDMA exposure from a single dose of ranitidine.

162. In June 2019, Valisure submitted its ranitidine data to the FDA confidentially. FDA made inquiries regarding the data, but did not seem to appreciate the importance of the findings.

J. FDA Discloses Valisure Data to Other Agencies and the Ranitidine Manufacturers, and GSK Once Again Lies to the FDA

163. FDA shared Valisure's data with the European Medicines Agency, which on July 16, 2019, reached out to GSK and other ranitidine manufacturers for information about NDMA in ranitidine.

164. On August 6, 2019, the FDA disclosed the NDMA concerns confidentially to ranitidine manufacturers, including GSK, and requested information. Specifically, FDA sent a communication to GSK:

> Recently a private analytical pharmacy and advanced laboratory notified the FDA that Zantac (ranitidine) produces a very high quantity (thousands of times higher than the FDA limits) of a probable human carcinogen N-nitrosodimethylamine (NDMA) in a single tablet of 150 mg of Zantac, when analyzed using FDA's nitrosamine test methods. The same private laboratory also found that Zantac forms high quantity of NDMA in simulated human body gastric conditions. The preliminary reports seem to indicate that in certain conditions (e.g., high temperatures and presence of nitrites) ranitidine hydrochloride (API) and ranitidine tablets degrade to form high quantities of NDMA.

165. The FDA requested specific information from GSK:

1. Are you aware of the above information?

2. Is there any potential for NDMA to be present in the Zantac tablets or ranitidine hydrochloride API? Provide a detailed explanation for your response. Include in your explanation quality information for API, excipients, manufacturing process, etc.

3. Have you tested Zantac tablets or ranitidine hydrochloride for the presence of NDMA? If you have, what were the levels of NDMA found?

4. Have you tested Zantac tablets in simulated human body conditions (including gastric conditions)? If you have, have you detected NDMA? If you did, what were the levels observed?

166. In preparing a response, GSK scientists openly conceded (before any litigation had been filed against GSK): "N-nitrosamines such as NOMA have are considered carcinogens and have been implicated in human cancers such as bladder, esophagus, stomach, and nasopharynx."

167. In response, on September 6, 2019, GSK stated that they had never tested ranitidine for NDMA. Regarding the fourth inquiry, GSK once again deflected to the Brittain study. GSK falsely stated: "There was no analysis for NDMA" because "NDMA would not have been predicted to form given the structures of the observed nitrosation products." This was a lie because not only had GSK specifically tested for NDMA in ranitidine nitrosation tests (Tanner Study), but it did so *after* predicting they would emerge based on the chemistry of the ranitidine molecule itself.

K. Valisure Files Citizen's Petition Statements from the FDA and Recalls by the Manufacturers

168. On Friday, September 13, 2019, Valisure submitted a Citizen's Petition to the FDA, disclosing the testing data.

169. The Citizen's Petition requested that the FDA take five actions:

1) request a recall and suspend sale of all lots of all products containing ranitidine. Given the drug's propensity to form the probable carcinogen NDMA, the drug is misbranded under Section 502 of the FDCA (21 U.S.C. § 352);

2) conduct examinations and investigation under Section 702 (a) of the FDCA (21 U.S.C. § 372(a)) regarding these products, their manufacturing processes, and the manufacturer submissions made for FDA approval under 704 (a) of the FDCA (21 U.S.C. § 374(a));

3) provide information to the public regarding these products under Section 705(b) of the FDCA (21 U.S.C. § 375(b));

4) in addition to the instructions for disposal and/or return in the recall notices, issue additional guidance to the public for the safe disposal of ranitidine, given the recognized potential that the drug may degrade to form the probable carcinogen NDMA in municipal wastewater treatment plants and impact the public water supply; and

5) promulgate regulations requiring robust independent chemical testing and verification of pharmaceuticals and, while these regulations are pending, issue guidance requesting such testing and verification.

170. Shortly thereafter, various personal injury and class action lawsuits were filed against GSK and other ranitidine manufacturers.

171. Within a few months, numerous voluntary recalls issued from various ranitidine manufacturers, including GSK.

172. On October 2, 2019, the FDA announced a new testing protocol for NDMA in ranitidine. Valisure's citizen's petition noted that the high levels of

NDMA formation observed in its testing were caused, in part, by the elevated temperatures used in GC-MS. So, the FDA developed and published a testing methos using Liquid Chromatography ("LC"), which did not use elevated temperatures. This special protocol was limited to testing ranitidine—the January 2019 protocol for other drug substances remained the same.

173. On November 1, 2019, FDA announced preliminary testing results on ranitidine products.

Company	**Product**	**Lots Tested**	**NDMA level ppm**	**NDMA level (micrograms-mcg/tablet or oral dose)**
Sanofi Pharmaceutical	OTC Ranitidine 150mg	19E413M, 19D554, 19A432U, 19C540, 19D431I, 19D442N, 19D423M, 19D464M,	0.07-2.38	0.01-0.36
Sanofi Pharmaceutical	OTC Ranitidine 75mg	18L012U, 9A003U, 19B006M, 18M025M, 18N023U, 19B005N, 19A002U, 18N026U	0.10-0.55	0.01-0.04

Company	Product	Lots Tested	NDMA level ppm	NDMA level (micrograms-mcg/tablet or oral dose)
Cardinal Health	OTC Ranitidine 150mg	9FE2953	1.02	0.15
Watson	Rx Nizatidine 150mg	1350798M	0.05	0.01
Watson	Rx Nizatidine 300mg	1333973A	0.04	0.01
Strides Shasun Ltd	Rx Nizatidine 150mg	7704758A	0.11	0.02
Strides Shasun Ltd	Rx Nizatidine 300mg	7704022A	0.09	0.03
Novitium	Rx Ranitidine 300mg	S18038B	2.85	0.86
Dr Reddy's	Rx Ranitidine 300mg	C805265	0.68	0.20
Strides Shasun Ltd	Rx Ranitidine 300mg	7702255A	0.11	0.03
Sandoz	Rx Ranitidine 300mg	HU2207	0.82	0.25
Strides Shasun Ltd	Rx Ranitidine 300mg	7704537A	0.02	0.00
Aurobindo	Rx Ranitidine 300mg	RA3019001-A	1.86	0.56

Company	Product	Lots Tested	NDMA level ppm	NDMA level (micrograms-mcg/tablet or oral dose)
Ajanta Pharma USA Inc	Rx Ranitidine 300mg	PA1229B	0.23	0.07
Silarx Pharma	Ranitidine 150mg Syrup	3652081-02661	1.37	0.20
Pharma Associates	Ranitidine 150mg Syrup	BE00, BF75, BF77, BF78, BDFF, COAC	0.03-0.07	0.004-0.012
Amneal Pharmaceuticals	Ranitidine 300mg	AR181795A, AR190878A, AR190876A, AR191177A, HB05819, HB06119, HL08718	0.52-2.17	0.16-0.65
Sanofi Pharmaceutical	Ranitidine 150mg	19D570, 19D428U, 19E408M	0.08-2.17	0.01-0.33

L. With Mounting Pressure of Ranitidine Litigation Looming, GSK Finally Discloses the Truth to the FDA

174. GSK was cornered. Personal injury and class action litigation was

swelling around the country, and GSK realized that, through discovery, it would no longer be able to conceal the Tanner study's existence. GSK finally disclosed the data to the FDA in December 11, 2019, but disclaimed that its prior statements to the FDA were false or misleading. This was the first time GSK had disclosed its NDMA data after nearly forty years of concealment.

M. Further Investigations Lead to a Complete Market Withdrawal of All Ranitidine-Containing Drugs by the FDA

175. On January 2, 2020, Emery Pharma submitted another citizen's petition, disclosing experiments showing that ranitidine degrades into NDMA during regular transport and storage.

176. On April 1, 2020, the FDA ordered a national withdrawal of ranitidine products. The FDA stated:

> The U.S. Food and Drug Administration today announced it is requesting manufacturers withdraw all prescription and over-the-counter (OTC) ranitidine drugs from the market immediately. This is the latest step in an ongoing investigation of a contaminant known as N-Nitrosodimethylamine (NDMA) in ranitidine medications (commonly known by the brand name Zantac). 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. As a result of this immediate market withdrawal request, ranitidine products will not be available for new or existing prescriptions or OTC use in the U.S.
>
> …
>
> NDMA is a probable human carcinogen (a substance that could cause cancer). In the summer of 2019, the FDA became aware of independent laboratory testing that found NDMA in ranitidine. Low levels of NDMA are commonly ingested in the diet, for example NDMA is present in foods and in water. These low levels would not be expected to lead to an increase in the risk of cancer. However, sustained higher levels of

> exposure may increase the risk of cancer in humans. The FDA conducted thorough laboratory tests and found NDMA in ranitidine at low levels. At the time, the agency did not have enough scientific evidence to recommend whether individuals should continue or stop taking ranitidine medicines, and continued its investigation and warned the public in September 2019 of the potential risks and to consider alternative OTC and prescription treatments.
>
> New FDA testing and evaluation prompted by information from third-party laboratories confirmed 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. The testing also showed that the older a ranitidine product is, or the longer the length of time since it was manufactured, the greater the level of NDMA. These conditions may raise the level of NDMA in the ranitidine product above the acceptable daily intake limit.

177. On that same date, the FDA issued a letter to Valisure, in formal response to the Valisure's citizen's petition, indicating that it was (1) granting its request for recall, (2) denying its request for a safe method of ranitidine disposal, and (3) denying its request that FDA issue regulatory guidance for independent testing of pharmaceutical quality and for impurities.

N. During Litigation, GSK Destroys Evidence

178. GSK's last batch of Zantac pills, Lot # 7ZP2359, was manufactured on April 3, 2017, in GSK's Zebulon, North Carolina facility. Lot 7ZP2359 consisted of 25,260 30-pill containers of 300 mg Zantac and used active pharmaceutical ingredient ("API") manufactured by Dr. Reddy's laboratories in India.

179. GSK testing has shown that products made with API from Dr. Reddy's contain more NDMA than the same products using a different API

supplier.

180. Whenever a lot is manufactured, the manufacturer is required to set aside, store, and maintain samples of that lot until 1 year after its expiration date. 21 C.F.R. § 211.170(a)(1). So, for Lot # 7ZP2359, GSK was required to maintain retained samples until at least April 30, 2020.

181. Following the one year after expiration, if there is "[a]ny evidence of reserve sample deterioration" the manufacturer is required to conduct a thorough investigation. 21 C.F.R. § 211.170(b); 21 C.F.R. § 211.192 (describing the type of investigation required and noting that "[a]ny unexplained discrepancy," like NDMA contamination, "shall be thoroughly investigated, whether or not the batch has already been distributed.").

182. GSK maintained samples of Lot # 7ZP2359 until April 30, 2020. However, in May 2020, GSK destroyed the samples and did not test the pills for NDMA. These were the *only* U.S. samples in GSK's possession and had been stored under ideal "labeled" conditions in GSK's own facilities. They would have provided powerful evidence of NDMA levels in GSK's U.S. product.

183. GSK's destruction of evidence was done despite (1) lawsuits being filed alleging NDMA contamination starting on September 13, 2019; (2) an order from a federal judge on November 19, 2019, ordering GSK to preserve "potentially relevant … tangible things within the Parties' possession, custody and/or

control[.]"; (3) an order from the MDL Court on February 6, 2020 directing GSK "to preserve evidence that may be relevant to this action" and "take reasonable steps to preserve all … tangible things[.]"; and (4) a request from the FDA on April 1, 2020, to remove all ranitidine from the market.

184. GSK violated multiple court orders and its obligations under federal and state law when it destroyed its last remaining U.S. retained samples of Zantac. And, even more vexing, GSK destroyed these pills without testing them for NDMA, in violation of federal regulations, even though it was well known at that point that ranitidine degraded into NDMA.

185. Remarkably, GSK's destruction of evidence was not limited to this last batch of pills, but it extended to the actual API used in GSK's pills. Specifically, between October 2019 and November 2020—a period of active litigation and multiple investigations into the presence of NDMA in ranitidine—GSK destroyed 9 batches of ranitidine API, which were all used in U.S. Zantac products. None of these batches of API were tested for NDMA.

186. The Discovery Referee in the state court coordinated proceeding in California explained: "[T]he idea that a routine destruction policy could go on in the face of two federal court orders is enough to make me gag. … think you're making me get a little more upset as you're defending something that's indefensible[.]"

PUNITIVE DAMAGES

187. Defendants' conduct as alleged herein was done with wanton and willful disregard for human life, oppression, and malice. Defendants were fully aware of the safety risks of Ranitidine-Containing Drugs, particularly the carcinogenic potential of Ranitidine-Containing Drugs 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.

188. This was not done by accident or through some justifiable negligence. Rather, Defendants knew they could profit by convincing consumers that Ranitidine-Containing Drugs was harmless to humans, and that full disclosure of the true risks of Ranitidine-Containing Drugs would limit the amount of money Defendants would make selling the drugs. Defendants' object was accomplished not only through a 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 Ranitidine-Containing Drugs, knowing the full risks attendant to that use. Such conduct was done with conscious indifference of Plaintiff's rights.

189. Accordingly, Plaintiff requests punitive damages against the

Manufacturer Defendants for the harms caused to Plaintiff.

EQUITIBLE TOLLING

190. 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.

191. 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.

192. 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.

193. 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 Ranitidine-Containing Drugs including the severity, duration, and frequency of risks and complications. Defendants affirmatively withheld and/or misrepresented

facts concerning the safety of Ranitidine-Containing Drugs. As a result of Defendants' misrepresentations and concealment, Plaintiff 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.

194. Given 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 Ranitidine-Containing Drugs 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.

CAUSES OF ACTION

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

196. All claims alleged herein are brought pursuant to New Jersey state law.

I. STRICT PRODUCTS LIABILITY

A. COUNT I: STRICT LIABILITY MANUFACTURING DEFECT

197. This claim is alleged against all manufacturers of RCPs, including the Brand Drug Makers and the Manufacturing Defendants. This claim is not asserted

against any Brand Drug Maker for injuries caused by use of generic versions of RCPs.

198. Defendants were involved in the manufacture, distribution, and sale of RCPs ingested by Plaintiff.

199. The manufacture of ranitidine-containing products entails a multi-step process. First, the Defendants either manufacture themselves or purchase ranitidine drug substance from a third party, nearly always in facilities outside the United States. The drug substance is then stored for some period of time and, eventually, transported—often by ship freight in heated cargo containers for months a time—to a pill manufacturing plant in the United States. Then, the drug substance is often left in storage in non-temperature controlled facilities for a period of time (can be months or years). Finally, the drug substance is combined with other excipients, using compression and other heat-generating procedures, to form tablets, pills, IV solutions, and/or syrups. For tablets, the pills are then coated, again while being exposed to heat, and then dried (more heat), before being placed in various types of containers and blister packs. Finally, those pills are left in non-temperature-controlled storage until, at some point, the products are shipped by non-temperature controlled fright truck to a distribution center, at which point the products leave the possession of the Defendants.

200. When ranitidine was first approved by the FDA in 1983, and in every

approval thereafter until November 2019, approvals did not *directly* address the presence of NDMA. However, as explained below, FDA regulations and federal law prohibit the sale of ranitidine containing NDMA and, thus, indirectly, the FDA permitted no NDMA in ranitidine. The FDA did not issue specific guidance or regulation related to NDMA and ranitidine until November 1, 2019, wherein the FDA indicated that "FDA has set the acceptable daily intake limit for NDMA at 0.096 micrograms or 0.32 ppm for ranitidine." This was formalized in an FDA guidance document in September 2020. The NDMA limits were established in July 2018 pursuant to the ICH Guidance M7(R1) Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk, which was first published in June 2017, but were not applied to ranitidine until 2019. Prior to that, there was no allowance for any NDMA in ranitidine products.

201. At the time ranitidine was approved in 1983, and ever since, the FDA has known that NDMA is a probable human carcinogen.

202. In the 1980's, FDA raised concern about the ability of ranitidine to nitrosate and form nitrosamines. FDA requested data about this potential nitrosamine formation from GSK. GSK, however, after conducting experiments demonstrating that ranitidine could nitrosate into NDMA, concealed that data from the FDA. Thus, at the time ranitidine was first approved, the FDA did not know of

the connection between ranitidine and NDMA, even though GSK and subsequent Defendants did.

203. The FDA did not know about the ability of ranitidine to degrade into NDMA until mid-2019, having been first informed about the issue by Valisure.

204. In the 1980s independent researchers raised concern about the ability of ranitidine to nitrosate and cause mutations similar to what they observed with NDMA causing mutations. However, GSK intentionally misled the scientific community by publishing fraudulent data to conceal any connection between ranitidine and NDMA. Thus, neither the independent researchers nor the FDA were made aware of the connection between ranitidine and NDMA.

205. The FDA did not approve, at any time, the sale of ranitidine-containing products with NDMA. NDMA is a degradant of ranitidine, which renders ranitidine contaminated with NDMA, under FDA regulations, adulterated and illegal for sale. Furthermore, if ranitidine is sold containing NDMA, the label for the product must indicate its presence or else the drug is misbranded. And misbranded dugs are not approvable for sale. Thus, FDA's approval of ranitidine prohibited it being sold while being contaminated with NDMA. This prohibition on the presence of NDMA has existed from the date of first approval until the FDA set limits in November 2019, and then was vacated when the FDA recalled all ranitidine products from the marketplace.

206. Additionally, when ranitidine was approved for sale, starting in 1983 and onward, each approved ranitidine-containing product was required to maintain stability, i.e., maintain purity and not form carcinogenic degradants, for the duration of its expiration date. If the ranitidine product lacked the ability to maintain stability, then that is a design of ranitidine that was not approved.

207. At the point the RCPs left Defendants' possession, custody, or control and entered the stream of commerce, they contained a manufacturing defect.

208. The RCPs differ from their intended design in that they contain NDMA. The design of RCPs does not contemplate the presence of NDMA, nor does the FDA's approval.

209. The RCPs contained NDMA because, while in the control and possession of Defendants, the ranitidine molecules degraded into NDMA, accelerated by the presence of heat and humidity. Had Defendants ensured that the ranitidine drug substance was not exposed to heat or humidity during the manufacture, sale, and distribution of their RCPs, prior to losing possession of and the RCP's entry into the stream of commerce, the RCPs would not have had a manufacturing defect.

210. Defendants did not sell the ranitidine product as it was intended, but instead sold a product that was not the same as it contained NDMA contamination, and the intended design of ranitidine-containing products do not contain NDMA.

211. Nothing under federal law limited or restricted Defendants from taking action to reduce or eliminate the RCP's exposure to heat or humidity. Taking such action would not have violated federal law in any way, nor required FDA approval in any way. Put another way, FDA permitted Defendants, in the process of manufacturing ranitidine, to avoid exposure to heat and humidity at every step.

212. Importantly, because Defendants sold RCPs with a manufacturing defect, they sold adulterated and misbranded drugs in violation of federal law, which runs parallel to the obligations imposed by state law. Indeed, to the extent that state law seeks to impose liability on Defendants that exceeds the duties imposed by federal law, Plaintiff does not seek to impose such liability.

213. This manufacturing defect exposed Plaintiff to dangerous levels of NDMA which, in turn, was a substantial factor in causing the development of cancer.

B. COUNT II: STRICT LIABILITY DESIGN DEFECT

214. This claim is alleged against all manufacturers of RCPs, including the Brand Drug Makers and the Manufacturing Defendants. This claim is not asserted against any Brand Drug Maker for injuries caused by use of generic versions of RCPs.

215. Defendants were involved in the manufacture, distribution, and sale of

RCPs ingested by Plaintiff.

216. Plaintiff's use of Defendants' RCPs is typical of any pharmaceutical product in that an ordinary consumer can form minimum safety expectations regarding the safety of RCPs and, reasonably, would assume the drug did not degrade, over time, into a potent and deadly carcinogen.

1. Traditional Design Defect Claim

217. The RCP ingested by Plaintiff was defective because the product did not perform as safely as an ordinary consumer would have expected it to perform because, the products degrade into NDMA outside and inside the body and, thus, fail to perform as safely as an ordinary consumer would have expected it to perform.

218. The design of ranitidine-containing products caused Plaintiff to be exposed to dangerous levels NDMA, which in turn are capable of causing cancer.

219. Although ranitidine-containing products are approved for sale by the FDA, the FDA did not know about the faulty design of ranitidine because the Defendants concealed it from them. Once FDA became aware of the defective design, it recalled the products from the market.

220. The Defendants, not the FDA, are responsible for the design of their drugs, and are prevented by FDA regulations and federal law from selling a drug who's design subject users to undisclosed risks, including exposure to NDMA and

the development of cancer. Thus, by selling defectively designed ranitidine-containing products, Defendants violated both state law and parallel federal law.

221. This design defect was a substantial cause of Plaintiff's injuries.

222. This claim would apply to all morphologies of ranitidine.

2. Alternative Design Defect Claim (Crystal Morphology)

223. The RCP ingested by Plaintiff was defective because the product did not perform as safely as an ordinary consumer would have expected it to perform because the product would degrade into NDMA from the point of manufacture until it was ingested.

224. From 1983 onward, the FDA approved the sale of ranitidine-containing products that used ranitidine drug substance that contained a columnar crystal morphology. The FDA also approved the sale of ranitidine-containing products that used ranitidine drug substance that did not have a columnar crystal morphology.

225. Thus, Defendants were permitted, by the FDA, to manufacture and/or use ranitidine drug substance that contained a columnar crystal morphology, which reduces the ability of RCPs to degrade and form into NDMA.

226. Manufacturing / using ranitidine drug substance with a columnar crystal morphology could be done without prior FDA approval. In fact, it always approved.

227. Because Defendants sold RCPs with a design defect, they sold adulterated and misbranded drugs in violation of federal law, which runs parallel to the obligations imposed by state law. Indeed, to the extent that state law seeks to impose liability on Defendants that exceeds the duties imposed by federal law, Plaintiff does not seek to impose such liability.

228. The excess degradation of RCP into NDMA was reasonably foreseeable when the RCP products were used or misused in a reasonably foreseeable manner, i.e., used, stored, and transported in the ways medications are normally used, stored, and transported.

229. Plaintiff was harmed by being exposed to Defendants' defective RCPs because they were exposed to additional amounts of NDMA which, in turn, played a substantial factor in causing Plaintiff to develop cancer.

C. COUNT III: STRICT LIABILITY DESIGN DEFECT (PRE-APPROVAL ASCORBIC ACID)

230. This claim is alleged against the Brand Drug Makers. This claim is not asserted against any Brand Drug Maker for injuries caused by use of generic versions of RCPs.

231. Defendants were involved in the manufacture, distribution, and sale of RCPs ingested by Plaintiff.

232. Plaintiff's use of Defendants' RCPs is typical of any pharmaceutical product in that an ordinary consumer can form minimum safety expectations

regarding the safety of RCPs and, reasonably, would assume the drug did not degrade into a potent and deadly carcinogen after ingestion.

233. The RCP ingested by Plaintiff was defective because the product did not perform as safely as an ordinary consumer would have expected it to perform because the product would rapidly convert into NDMA after ingestion, especially when ingested along with foods that contain high levels of nitrite; which are the types of food that would normally lead consumers to take an antacid medication like RCPs.

234. This endogenous formation of RCPs into NDMA was reasonably foreseeable when the RCP products were used or misused in a reasonably foreseeable manner, i.e., consumed with meals containing high levels of nitrite. Indeed, prior to ranitidine's first approval in 1983, independent scientists informed the medical community that ranitidine should not be consumed closed to meals and should be consumed along with ascorbic acid (Vitamin C), which was shown to neutralize the NDMA reaction with ranitidine and nitrite.

235. These Defendants should have disclosed their own data showing the possibility of NDMA formation from ranitidine and nitrite in gastric fluids to the FDA. And, prior to seeking approval of ranitidine for sale, Defendants should have proposed RCPs containing ascorbic acid, which would have substantially reduced the formation of NDMA following ingestion of ranitidine. Such a design

was feasible and was specifically recommended by independent scientists in 1981. The FDA would have approved such a design as it would have rendered the medication safer for consumers. However, because Defendants did not seek this design, pre-approval, the RCPs that were ultimately manufactured, distributed, and sold by these Defendants were defective in their design.

236. This claim does not allege that these Defendant should have added ascorbic acid to ranitidine without FDA approval or made a major change to the drug post-approval. This claim alleges that the design defect could have been cured had Defendants acted pre-approval. Moreover, over the years, these Defendants would seek new approvals of RCPs, and in each instance, they could have proposed a different design that would have been approved by the FDA and resulted in the products, thereafter, no longer having this design defect.

237. Plaintiff was harmed by being exposed to Defendants defective RCPs because they were exposed to additional amounts of NDMA endogenously which, in turn, played a substantial factor in causing Plaintiff to develop cancer.

D. COUNT IV: STRICT LIABILITY FAILURE TO WARN

238. This claim is alleged against the Brand Drug Makers. This claim is not asserted against any Brand Drug Maker for injuries caused by use of generic versions of RCPs.

239. Defendants were involved in the manufacture, distribution, and sale of

RCPs ingested by Plaintiff.

240. RCPs, at all times, have the ability to degrade into NDMA exogenously and endogenously and expose users to NDMA. This issue was known and/or knowable in light of scientific and medical knowledge that was generally accepted within the scientific community (even if that data was hidden and concealed from the medical community) starting in 1983 through the present.

241. This issue of NDMA exposure presented a substantial danger to users when RCPs were used or misused in a reasonably foreseeable manner, i.e., under expected storage and transport conditions and consumed with meals containing high levels of sodium nitrite.

242. Ordinary consumers would not have recognized or expected that RCPs would exposed them to NDMA or cause cancer. Plaintiff relied upon the skill, superior knowledge, and judgment of Defendants to know about and disclose any health risks associated with using RCPs.

243. Defendants had a duty to warn of the risks associated with the use of RCPs. Specifically, Defendants were obligated to warn consumers that RCPs exposed them to NDMA and/or was capable of increasing the risk of developing various cancers.

244. Defendants failed to warn consumers, directly or indirectly, of the risks posed by ingestion of RCPs.

245. Defendants knew or through the exercise of due care should have known that the minimal warnings disseminated with their RCPs 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 or misuses.

246. 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 avoid using the drug. 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 RCPs; continued to aggressively promote the efficacy of their products, even after they knew or Defendants knew or through the exercise of due care 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 RCPs.

247. This alleged failure to warn is not limited to the information contained on RCP's labeling. Defendants were able, in accord with federal law, to comply with relevant state law by disclosing the known risks associated with RCPs

through other 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.

248. With repeated new scientific information arising, including information that has been specifically suppressed from disclosure to FDA, Defendants were able to cite new information or new analysis of previous information to justify a label change that complied with Federal law and state law, without prior FDA approval.

249. Had Defendants provided adequate warnings and instructions and properly disclosed and disseminated the risks associated with their RCPs, Plaintiff could have avoided the risk of developing injuries and could have obtained or used alternative medication. However, as a result of Defendants' concealment of the dangers posed by their RCPs, Plaintiff could not have averted their injuries.

250. 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 RCPs, and suppressed this knowledge from the general public. Defendants made conscious decisions not to warn or inform the unsuspecting public. Defendants' reckless conduct warrants an award of punitive damages.

251. The Defendants' lack of adequate warnings and instructions

accompanying their RCPs were a substantial factor in causing Plaintiff's / Decedent's injuries.

252. As a direct and proximate result of the Defendants' failure to provide an adequate warning of the risks of RCPs, 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 past and future medical expenses, lost income, and other damages.

II. NEGLIGENCE

A. COUNT V: NEGLIGENT FAILURE TO WARN

253. This claim is alleged against the Brand Drug Makers. This claim includes injuries caused by use of generic versions of RCPs, i.e., warning label liability.

254. Defendants were involved in the manufacture, distribution, and sale of the brand name RCPs ingested by Plaintiff and controlled the labeling of the generic RCPs ingested by Plaintiff.

255. RCPs, at all times, have the ability to degrade into NDMA exogenously and endogenously and expose users to NDMA when used or misused in a reasonably foreseeable manner. Indeed, this issue of NDMA exposure presented a substantial danger to users when RCPs were used or misused in a reasonably foreseeable manner, i.e., under expected storage and transport

conditions and consumed with meals containing high levels of sodium nitrite. This issue was known and/or through the exercise of due care should have known by the Defendants since 1983 until the present.

256. Defendants knew or through the exercise of due care should have known that users of RCPs would not be able to realize the risk of NDMA exposure or cancer absent a warning from the Defendants. Plaintiff relied upon the skill, superior knowledge, and judgment of Defendants to know about and disclose any health risks associated with using RCPs.

257. Defendants had a duty to warn of the risks associated with the use of RCPs. Specifically, Defendants were obligated to warn consumers that RCPs exposed them to NDMA and/or was capable of increasing the risk of developing various cancers.

258. Defendants failed to warn and/or adequately instruct consumers, directly or indirectly, of the risks posed by ingestion of RCPs, how to prevent the exogenous / endogenous formation of NDMA, or any risk of developing cancer.

259. Defendants knew or through the exercise of due care should have known that the minimal warnings disseminated with their RCPs 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 or misuses.

260. 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 avoid using the drug. 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 RCPs; continued to aggressively promote the efficacy of their products, even after they knew or through the exercise of due care 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 RCPs.

261. Defendants were able, in accord with federal law, to comply with relevant state law by disclosing the known risks associated with RCPs through other mediums, i.e., promotion, advertisements, public service announcements, and/or public information sources, in addition to the label. But the Defendants did not disclose these known risks through any medium.

262. With new scientific information arising, including information that was specifically suppressed from disclosure to FDA, Defendants were able to cite new information or new analysis of previous information to justify a label change

that complied with Federal law and state law, without prior FDA approval.

263. If Defendants had appropriately issued a warning for their RCPs, by operation of federal law, all generic RCPs would have changed their labels to match.

264. Defendants breach their standard of care by failing to use the amount of care in warning consumers about RCPs that a reasonably careful drug maker would use in similar circumstances to avoid exposing others to a foreseeable risk of harm.

265. Had Defendants provided adequate warnings and instructions and properly disclosed and disseminated the risks associated with their RCPs, Plaintiff could have avoided the risk of developing injuries and could have obtained or used alternative medication. However, as a result of Defendants' concealment of the dangers posed by their RCPs, Plaintiff could not have averted their injuries.

266. A reasonable drug maker, under similar circumstances of these Defendants, would have warned of the risk posed by RCPs.

267. 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 RCPs, and suppressed this knowledge from the general public. Defendants made conscious decisions not to warn or inform the unsuspecting public. Defendants' reckless conduct warrants an

award of punitive damages.

268. Defendants' negligence proximately caused all generic RCPs to be inadequately warned. Indeed, as noted above, due to this negligence, all RCPs were misbranded under federal law.

269. Defendants' lack of adequate warnings and instructions accompanying their RCPs were a substantial factor in causing Plaintiff's / injuries.

270. As a direct and proximate result of the Defendants' failure to provide an adequate warning of the risks of RCPs, 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 past and future medical expenses, lost income, and other damages.

B. COUNT VI: GENERAL NEGLIGENCE

271. This claim is alleged against the Brand Drug Makers. Additionally, the "Negligent Exposure to Heat, Humidity, and Time" claim, alleged below, is asserted against the Manufacturing Defendant. This claim is not asserted against any Brand Drug Maker or Manufacturing Defendant for injuries caused by use of generic versions of RCPs unless they also manufactured/ supplied/distributed the ranitidine drug substance and/or pills used in a generic RCP.

272. Defendants were involved in the design, manufacture, and supply of the brand name RCPs ingested by Plaintiff and/or involved in the manufacture and

supply of the ranitidine drug substance used in another's RCPs.

273. Defendants were negligent, i.e., failed to act in a way that a reasonable drug maker would act under similar circumstances to avoid harm to others, as specified below:

1. Negligent Manufacture

274. Defendants knew or through the exercise of due care should have known that manufacturing ranitidine drug substance using a columnar crystal morphology would reduce the ability of ranitidine drug substance to degrade into NDMA.

275. From 1983 onward, the FDA approved the sale of ranitidine-containing products that used ranitidine drug substance that contained a columnar crystal morphology. The FDA also approved the sale of ranitidine-containing products that used ranitidine drug substance that did not have a columnar crystal morphology.

276. Thus, Defendants were permitted, by the FDA, to manufacture and/or use ranitidine drug substance that contained a columnar crystal morphology, which reduces the ability of RCPs to degrade and form into NDMA.

277. Manufacturing / using ranitidine drug substance with a columnar crystal morphology could be done without prior FDA approval. In fact, it was always approved.

278. A reasonable drug maker, under similar circumstances, would have ensured that they manufactured ranitidine drug substance with a columnar crystal morphology to reduce consumer exposures to NDMA and avoid exposing others a foreseeable risk of harm.

279. Thus, each Defendant had a duty to manufacture ranitidine drug substance with columnar crystal morphology to reduce consumer exposure to NDMA.

280. Defendants breached that duty by not manufacturing ranitidine drug substance using a columnar crystal morphology for the RCP products Plaintiff ingested.

281. From 1983 onward, the FDA approved the sale of ranitidine-containing products that used ranitidine drug substance that contained a columnar crystal morphology. The FDA also approved the sale of ranitidine-containing products that used ranitidine drug substance that did not have a columnar crystal morphology.

282. Thus, Defendants were permitted, by the FDA, to manufacture and/or use ranitidine drug substance that contained a columnar crystal morphology, which reduces the ability of RCPs to degrade and form into NDMA.

283. Manufacturing / using ranitidine drug substance with a columnar crystal morphology could be done without prior FDA approval. In fact, it always approved.

284. Compliance with these duties imposed by state law did make it impossible to comply with Federal law.

285. Had Defendants manufactured and supplied ranitidine drug substance with columnar crystal morphology, it would have reduced Plaintiff's exposure to NDMA.

286. The excess NDMA exposure Plaintiff was exposed to, was a substantial factor in causing Plaintiff's cancer and injury.

2. Negligent Exposure to Heat, Humidity, and Time

287. Defendants knew or through the exercise of due care should have known that exposing ranitidine drug substance and RCPs to heat / humidity / or excess time, would cause it to degrade into NDMA and expose consumers to NDMA upon ingestion.

288. A reasonable drug maker, under similar circumstances, would have taken steps to ensure the ranitidine drug substance used in their RCPs, and the RCPs themselves, were not exposed to excess heat, humidity, or time before ingestion by a consumer, to reduce consumer exposures to NDMA and avoid exposing others a foreseeable risk of harm.

289. Thus, each Defendant had a duty to ensure their ranitidine drug substance and/or their RCPs were manufactured, supplied, and provided to consumers without exposure to excess heat, humidity, or time.

290. Defendants breached that duty by failing to properly reduce ranitidine drug substances and/or RCPs to heat, humidity, and time before being consumed by Plaintiff. This includes, *inter alia*, failure to use proper temperature controls in manufacturing facilities, failing to hire distributors that would have ensured minimal exposure to heat and humidity, streamlining supply chain to ensure minimal delay between manufacture and ingestion, etc. Defendants breached their duty to Plaintiff by failing to properly store and transport RCPs supplied to Plaintiff, leading to dangerous levels of NDMA accumulating in the drugs that harmed Plaintiff.

291. At all relevant times, Defendants were permitted, by the FDA and under federal law, to ensure that ranitidine drug substances and/or RCPs were limited in their exposure to heat, humidity, and time before being consumed by consumers. Compliance with the duties imposed by state law did make it impossible to comply with Federal law.

292. Had Defendants manufactured, supplied, and sold ranitidine drug substance and/or RCPs without exposing them to excess heat, humidity, and time, it would have reduced Plaintiff's exposure to NDMA.

293. The excess NDMA exposure Plaintiff was exposed to was a substantial factor in causing Plaintiff's cancer and injury.

3. Pre-Approval Design Negligence

294. Plaintiff's / Decedent's use of Defendants' RCPs is typical of any pharmaceutical product in that an ordinary consumer can form minimum safety expectations regarding the safety of RCPs and, reasonably, would assume the drug did not degrade into a potent and deadly carcinogen after ingestion.

295. The RCP ingested by Plaintiff was defective because the product did not perform as safely as an ordinary consumer would have expected it to perform because the product would rapidly convert into NDMA after ingestion, especially when ingested along with foods that contain high levels of nitrite; which are the types of food that would normally lead consumers to take an antacid medication like RCPs.

296. This endogenous formation of RCPs into NDMA was known and/or through the exercise of due care should have known that when the RCP products were used or misused in a reasonably foreseeable manner, i.e., consumed with meals containing high levels of nitrite. Indeed, prior to ranitidine's first approval in 1983, independent scientists informed the medical community that ranitidine should not be consumed closed to meals and should be consumed along with

ascorbic acid (Vitamin C), which was shown to neutralize the NDMA reaction with ranitidine and nitrite.

297. Defendants should have disclosed their own data showing the possibility of NDMA formation from ranitidine and nitrite in gastric fluids to the FDA. And, prior to seeking approval of ranitidine for sale, Defendants should have proposed RCPs containing ascorbic acid, which would have substantially reduced the formation of NDMA following ingestion of ranitidine. Such a design was feasible and was specifically recommended by independent scientists in 1981. The FDA would have approved such a design as it would have rendered the medication safer for consumers. However, because Defendants did not seek this design, pre-approval, the RCPs that were ultimately manufactured, distributed, and sold by these Defendants were defective in their design.

298. Defendants owed a duty to design a safer drug and seek its approval by the FDA. A reasonable drug maker, under similar circumstances, would have sought such a design pre-approval to avoid exposing consumers to a foreseeable, indeed foreseen, risk of harm.

299. Defendants breached their duty by failing to seek, pre-approval, a safer design of RCPs that would have reduced the likelihood of endogenous formation of NDMA.

300. This claim does not allege that Defendants should have added ascorbic acid to ranitidine without FDA approval or made a major change to the drug post-approval. This claim alleges that the design defect could have been cured had Defendants acted pre-approval. However, over the years, Defendants would seek new approvals of RCPs pursuant to multiple NDAs and sNDAs, and in each instance, they could and should have proposed a different design that would have been approved by the FDA and resulted in the products, thereafter, no longer having this foreseeable risk of harm.

301. Plaintiff was harmed by being exposed to Defendants defective RCPs because they were exposed to additional amounts of NDMA endogenously which, in turn, played a substantial factor in causing Plaintiff to develop cancer.

302. Defendants' negligence, as alleged above, was a proximate cause of the injuries sustained by Plaintiff. It caused significant and serve injuries.

JURY TRIAL DEMAND

303. Plaintiff demands a trial by jury on all the triable issues within this pleading.

PRAYER FOR RELIEF

304. WHEREFORE, Plaintiff requests the Court to enter judgment in Plaintiff's favor and against the Defendants for:

a. actual or compensatory damages in such amount to be determined at

trial and as provided by applicable law;

b. damages permitted under pertinent wrongful, death and survival statutes, if applicable.

c. exemplary and punitive damages sufficient to punish and deter the Defendants and others from future wrongful practices;

d. pre-judgment and post-judgment interest;

e. costs including reasonable attorneys' fees, court costs, and other litigation expenses; and

f. any other relief the Court may deem just and proper.

Dated: June 2, 2025

CONAWAY-LEGAL LLC

/s/ *Bernard G. Conaway*
Bernard G. Conaway, Esquire (DE 2856)
1007 North Orange Street, Suite 400
Wilmington, DE 19801
Tele: (302) 428-9350
Email: bgc@conaway-legal.com

OF COUNSEL:

Jennifer A. Moore, Esquire
California Bar ID No.: 206779
MOORE LAW GROUP, PLLC
1473 South 4th Street
Louisville, KY 40208
Tele: (502) 717-4080
Email: jennifer@moorelawgroup.com

Attorneys for the Plaintiff