CANADA

PROVINCE OF QUEBEC
DISTRICT OF MONTREAL

NO: 500-06-001023-197

(Class Action)
SUPERIOR COURT

M. ROYER

and

P. FAUVEL

Petitioners

-vs.-

SANOFI CONSUMER HEALTH INC.
and
GLAXOSMITHKLINE INC.
and

PFIZER CANADA SRI, legal person duly constituted, having its head office at 17300 Rte TransCanada, City of Kirkland, Province of Quebec, H9J 2M5

and

JOHNSON & JOHNSON INC., legal person duly constituted, having its head office at 88 McNabb Street, City of Markham, Province of Ontario, L3R 5L2

and
SANDOZ CANADA INCORPORATED
and
PHARMASCIENCE INC.
and
APOTEX INC.
and
PRO DOC LTÉE
and
SANIS HEALTH INC.
and
SIVEM PHARMACEUTICALS ULC
and

DOMINION PHARMACAL, legal person duly constituted, having its head office at 6111 Royalmount Avenue, Suite 100, City of Montreal, Province of Quebec, H4P 2T4

and

LABORATOIRE RIVA INC., legal person duly constituted, having its head office at 660 boul. Industriel, City of Blainville, Province of Quebec, J7C 3V4

and

SUN PHARMA CANADA INC. (FORMERLY KNOWN AS RANBAXY PHARMACEUTICALS CANADA INC.), legal person duly constituted, having its head office at 126 East Drive, City of Brampton, Province of Ontario, L6T 1C1

and

TEVA CANADA LIMITED, legal person duly constituted, having its head office at 30 Novopharm Court, City of Toronto, Province of Ontario, M1B 2K9

and

VITA HEALTH PRODUCTS INC., legal person duly constituted, having its head office at 155 Wellington Street West, City of Toronto, Province of Ontario, M5V 3J7

Respondents

AMENDED APPLICATION TO AUTHORIZE THE BRINGING OF A CLASS ACTION & TO APPOINT THE PETITIONERS AS REPRESENTATIVE PLAINTIFFS
(Art. 574 C.C.P and following)

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TO THE HONOURABLE MADAM JUSTICE COURCHESNE OF THE SUPERIOR COURT, SITTING IN AND FOR THE DISTRICT OF MONTREAL, YOUR PETITIONERS STATE AS FOLLOWS:

I. GENERAL PRESENTATION

A) The Action

1. Petitioners wish to institute a class action on behalf of the following class, of which they are (…) members, namely:

    - All persons residing in Canada who purchased and/or ingested the drug, RANITIDINE (sold under the brand name ZANTAC® as well as under various generic names) and their successors, assigns, family members, and dependants, or any other group to be determined by the Court;

    Alternatively (or as a subclass)

    - All persons residing in Quebec who purchased and/or ingested the drug, RANITIDINE (sold under the brand name ZANTAC® as well as under various generic names) and their successors, assigns, family members, and dependants, or any other group to be determined by the Court;

2. "ZANTAC" is the brand name version of the generic drug containing the active ingredient ranitidine (ranitidine hydrochloride), which is used to treat gastrointestinal conditions such as acid indigestion, heartburn, sour stomach, and gastroesophageal reflux disease;

3. Unless the context indicates otherwise, the word "ZANTAC" as used herein will be understood to mean both the brand name drug Zantac as well as the generic drugs containing ranitidine;

4. The Respondents developed, designed, manufactured, tested, marketed, labelled, packaged, promoted, advertised, imported, distributed, and/or sold ZANTAC as safe and/or effective despite a wealth of existing knowledge that consumption of the drugs exposed users to unsafe levels of the carcinogen *N*-Nitrosodimethylamine (NDMA);

4.1 The types of cancer that have been linked to the ingestion or injection of ranitidine include, but are not limited to:

- Bladder cancer
- Brain cancer
- Breast cancer

- Colorectal cancer
- Esophageal/throat/nasal cancer
- Intestinal cancer
- Kidney cancer
- Liver cancer
- Lung cancer
- Ovarian cancer
- Pancreatic cancer
- Prostate cancer
- Stomach cancer
- Testicular cancer
- Thyroid cancer
- Uterine cancer

(the "Ranitidine-Induced Cancer(s)");

5. The Petitioners contend that Respondents represented to the medical and healthcare community, to Health Canada, and to the Class Members that they had developed, designed, manufactured, and tested ZANTAC and that it had been found to be safe and/or effective for its intended uses. In addition, the Respondents concealed their knowledge of ZANTAC's defects from the medical and healthcare community, Health Canada and from Class Members;

6. In short, the Respondents' liability rests on (i) inadequate warning that the consumption of ranitidine exposed humans to unsafe levels of NDMA, (ii) failure to notify of the full scope of risks known to be associated with and caused by ranitidine, and (iii) safety misrepresentations;

7. Respondents continue to market, label, package, promote, advertise, import, distribute, and/or sell ranitidine throughout Canada, including within the province of Quebec, with inadequate warnings as to the associated exposure to unsafe levels of the carcinogen, NDMA;

B) The Respondents

8. Respondent Sanofi Consumer Health Inc. ("Sanofi") is a Canadian pharmaceutical corporation, with its head office in Laval, Quebec. Sanofi is involved in the development, design, manufacture, testing, marketing, labelling, packaging, promotion, advertising, importation, distribution, and/or sale of 2 varieties of ZANTAC as an over-the-counter medicine. Its ZANTAC products were sold in the formats of 75 mg and 150 mg, from March 21, 2017 until their recall on October 18, 2019. It does business throughout Canada, including within the province of Quebec, the whole as appears more fully from a copy of an extract from the *Registraire des enterprises* and from copies of extracts from Health Canada's website at www.healthycanadians.gc.ca, produced herein *en liasse* as **Exhibit R-1**;

9. Respondent Sanofi is the current owner of the following trade-marks:

   (a) “ZANTAC 75” (TMA535314), which was filed on August 3, 1998,

   (b) “ZANTAC 150” (TMA778793), which was filed on August 8, 2006,

   (c) “ZANTAC PILL AND SWIRL DESIGN” (TMA725162), which was filed on October 2, 2008,

   The whole as appears more fully from copies of said trade-marks from the CIPO database, produced herein *en liasse* as **Exhibit R-2**;

10. Respondent GlaxoSmithKline Inc. (“GlaxoSmithKline”), is a Canadian pharmaceutical corporation, with its head office in Mississauga, Ontario. GlaxoSmithKline or its predecessors had previously been involved in the development, design, manufacture, testing, marketing, labelling, packaging, promotion, advertising, importation, distribution, and/or sale of ZANTAC as both a prescription and over-the-counter medicine from 1982 until February 12, 1999 when it was transferred to a division of Respondent Pfizer. Its ZANTAC products were sold in the formats of 15 mg, 25 mg, 75 mg, 150 mg, 300 mg, and 400 mg. It does business throughout Canada, including within the province of Quebec, the whole as appears more fully from a copy of an extract from the *Registraire des enterprises*, produced herein as **Exhibit R-3**;

10.1 Respondent Pfizer Canada SRI (“Pfizer”) is a Canadian pharmaceutical corporation with its head office in Kirkland, Quebec. Pfizer or its predecessor was involved in the development, design, manufacture, testing, marketing, labelling, packaging, promotion, advertising, importation, distribution, and/or sale of ZANTAC from January 17, 2001 until January 23, 2007 when it was sold to McNeil Consumer Healthcare, an entity within the Johnson & Johnson healthcare products group of companies, the whole as appears more fully from a copy of an extract from the *Registraire des entreprises*, produced herein as **Exhibit R-31**;

10.2 Respondent Johnson & Johnson Inc. (“J&J”) is a Canadian pharmaceutical corporation with its head office in Markham, Ontario. J&J or a division thereof was involved in the development, design, manufacture, testing, marketing, labelling, packaging, promotion, advertising, importation, distribution, and/or sale of ZANTAC from January 23, 2007 until March 21, 2017 when it was transferred to Respondent Sanofi, the whole as appears more fully from a copy of an extract from the Corporations Canada website, produced herein as **Exhibit R-32**;

11. ZANTAC has been marketed and sold by prescription in Canada since as early as December 31, 1982 by either GlaxoSmithKline, Pfizer, J&J, or Sanofi;

12. Respondent Sandoz Canada Incorporated ("Sandoz") is a Canadian pharmaceutical corporation, with its head office in Boucherville, Quebec. Sandoz is involved in the development, design, manufacture, testing, marketing, labelling, packaging, promotion, advertising, importation, distribution, and/or sale of 4 varieties of RANITIDINE as both an over-the-counter and a prescription medicine. It has been marketing RANITIDINE in Canada since as early as May 15, 2001. Its RANITIDINE products were sold in the formats of 50 mg/2 ml, 150 mg, and 300 mg, 2 of which were recalled on September 17, 2019 and 1 of which was cancelled pre-market on June 16, 2017. It does business throughout Canada, including within the province of Quebec, the whole as appears more fully from a copy of an extract from the *Registraire des enterprises* and from copies of extracts from Health Canada's website at www.healthycanadians.gc.ca, produced herein *en liasse* as **Exhibit R-4**;

13. Respondent Pharmascience Inc. ("Pharmascience") is a Canadian pharmaceutical corporation, with its head office in Montreal, Quebec. Pharmascience is involved in the development, design, manufacture, testing, marketing, labelling, packaging, promotion, advertising, importation, distribution, and/or sale of 8 varieties of RANITIDINE as both an over-the-counter and a prescription medicine including under the brand names Atoma, Biomedic, Compliments, Co-op Care+, Equate, Exact, Health One, Kirkland Signature, Life Brand, London Drugs, Option+, Personnelle, Pharmasave, Preferred Pharmacy, Rexall and Selection. It has been marketing RANITIDINE in Canada since as early as April 25, 2000. Its RANITIDINE products were sold in the formats of 75 mg, 150 mg, and 300 mg. Both Respondents Pharmascience and Dominion Pharmacal (described below) are wholly-owned by non-party Joddes Limited. 5 of Pharmascience's RANITIDINE products were recalled on October 23, 2019, 2 had been cancelled post market on September 8, 2014 and 1 had not been marketed. Pharmascience does business throughout Canada, including within the province of Quebec, the whole as appears more fully from a copy of an extract from the *Registraire des enterprises* and from copies of extracts from Health Canada's website at www.healthycanadians.gc.ca, produced herein *en liasse* as **Exhibit R-5**;

14. Respondent Apotex Inc. ("Apotex") is a Canadian pharmaceutical corporation, with its head office in Toronto, Ontario. Apotex is involved in the development, design, manufacture, testing, marketing, labelling, packaging, promotion, advertising, importation, distribution, and/or sale of 5 varieties of RANITIDINE as both an over-the-counter and a prescription medicine. It has been marketing RANITIDINE in Canada since as early as December 31, 1987. Its RANITIDINE products were sold in the formats of 15 mg/ml, 75 mg, 150 mg, and 300 mg. It also manufactured the Equate and Selection brands of RANITIDINE in the 150 mg format. 4 of Apotex's RANITIDINE products were recalled on September 24, 2019 and 1 had gone "dormant" on August 4, 2017. It does business throughout Canada, including within the province of Quebec, the whole as

appears more fully from a copy of an extract from the *Registraire des enterprises* and from copies of extracts from Health Canada's website at www.healthycanadians.gc.ca, produced herein *en liasse* as **Exhibit R-6**;

15. Respondent Pro Doc Ltée. ("Pro Doc") is a Canadian pharmaceutical corporation, with its head office in Laval, Quebec. Pro Doc is involved in the development, design, manufacture, testing, marketing, labelling, packaging, promotion, advertising, importation, distribution, and/or sale of 2 varieties of RANITIDINE as a prescription medicine. It has been marketing RANITIDINE in Canada since as early as December 31, 1988. Its RANITIDINE products were sold in the formats of 150 mg and 300 mg, until their recall on September 24, 2019. It does business throughout Canada, including within the province of Quebec, the whole as appears more fully from a copy of an extract from the *Registraire des enterprises* and from copies of extracts from Health Canada's website at www.healthycanadians.gc.ca, produced herein *en liasse* as **Exhibit R-7**;

16. Respondent Sanis Health Inc. ("Sanis") is a Canadian pharmaceutical corporation, with its head office in Fredericton, New Brunswick. Sanis is involved in the development, design, manufacture, testing, marketing, labelling, packaging, promotion, advertising, importation, distribution, and/or sale of 2 varieties of RANITIDINE as a prescription medicine. It has been marketing RANITIDINE in Canada since as early as June 18, 2010. Its RANITIDINE products were sold in the formats of 150 mg and 300 mg, until their recall on September 24, 2019. It does business throughout Canada, including within the province of Quebec, the whole as appears more fully from a copy of an extract from the *Registraire des enterprises* and from copies of extracts from Health Canada's website at www.healthycanadians.gc.ca, produced herein *en liasse* as **Exhibit R-8**;

17. Respondent Sivem Pharmaceuticals ULC ("Sivem") is a Canadian pharmaceutical corporation, with its head office in Vancouver, British Columbia. Sivem is involved in the development, design, manufacture, testing, marketing, labelling, packaging, promotion, advertising, importation, distribution, and/or sale of 2 varieties of RANITIDINE as a prescription medicine. It has been marketing RANITIDINE in Canada since as early as June 8, 2012. Its RANITIDINE products were sold in the formats of 150 mg and 300 mg, until their recalls on September 24, 2019 and on October 17, 2019. It does business throughout Canada, including within the province of Quebec, the whole as appears more fully from a copy of an extract from the *Registraire des enterprises* and from copies of extracts from Health Canada's website at www.healthycanadians.gc.ca, produced herein *en liasse* as **Exhibit R-9**;

17.1 Respondent Dominion Pharmacal is a Canadian Pharmaceutical corporation with its head office in Montreal, Quebec. Dominion Pharmacal was involved in the development, design, manufacture, testing, marketing, labelling,

packaging, promotion, advertising, importation, distribution, and/or sale of 3 varieties of RANITIDINE as both an over-the-counter and a prescription medicine, including under the brand name Personnelle (sold at Jean Coutu). It has been marketing RANITIDINE in Canada since as early as January 8, 2001. Its RANITIDINE products were in the formats of 150 mg and 300 mg, 2 of which went "dormant" on August 3, 2017 and 1 of which was recalled on October 23, 2019, which has since then been cancelled post market on May 5, 2020, the whole as appears more fully from a copy of an extract from the *Registraire des enterprises* and from copies of extracts from Health Canada's website at www.healthycanadians.gc.ca, produced herein *en liasse* as **Exhibit R-33**;

17.2 Respondent Laboratoire Riva Inc. ("Riva") is a Canadian Pharmaceutical corporation with its head office in Blainville, Quebec. Riva was involved in the development, design, manufacture, testing, marketing, labelling, packaging, promotion, advertising, importation, distribution, and/or sale of 4 varieties of RANITIDINE as both an over-the-counter and a prescription medicine, including under the brand names Biomedic, Circle K, and Option+ (sold at Familiprix, Circle K, and Uniprix). It has been marketing RANITIDINE in Canada since as early as August 7, 1998. Riva's RANITIDINE products were in the formats of 75 mg, 150 mg and 300 mg until their recall on October 24, 2019 and 1 additional one had been cancelled post market on June 13, 2017, the whole as appears more fully from a copy of an extract from the *Registraire des enterprises* and from copies of extracts from Health Canada's website at www.healthycanadians.gc.ca, produced herein *en liasse* as **Exhibit R-34**;

17.3 Respondent Sun Pharma Canada Inc. (formerly Ranbaxy Pharmaceuticals Canada Inc.) ("Sun Pharma") is a Canadian Pharmaceutical corporation with its head office in Brampton, Ontario. On April 6, 2014, Sun Pharma acquired Ranbaxy in a USD$4 billion landmark transaction. Sun Pharma was involved in the development, design, manufacture, testing, marketing, labelling, packaging, promotion, advertising, importation, distribution, and/or sale of 4 varieties of ranitidine as a prescription medicine. It has been marketing ranitidine in Canada since as early as October 23, 2009. Two of Sun Pharma's ranitidine products were in the formats of 150 mg and 300 mg until their recall on September 25, 2019 and the other two were only approved, the whole as appears more fully from a copy of an extract from the *Registraire des enterprises*, from a copy of the Sun Pharma Press Release entitled "Sun Pharma to acquire Ranbaxy in a US$ 4 billion landmark transaction" dated April 6, 2014, and from copies of extracts from Health Canada's website at www.healthycanadians.gc.ca, produced herein *en liasse* as **Exhibit R-35**;

17.4 Respondent Teva Canada Limited ("Teva") is a Canadian Pharmaceutical corporation with its head office in Toronto, Ontario. Teva was founded as Novopharm in 1965 and was acquired by Teva Pharmaceuticals Industries in 2000, when it was renamed as Teva Novopharm. The Novopharm name was dropped in 2010, the whole as appears more fully from a copy of the Teva

Press Release entitled “Novopharm Limited becomes Teva Canada Limited” dated February 16, 2010, produced herein as **Exhibit R-36**;

17.5 Teva was involved in the development, design, manufacture, testing, marketing, labelling, packaging, promotion, advertising, importation, distribution, and/or sale of 6 varieties of RANITIDINE as a prescription medicine. It has been marketing RANITIDINE in Canada since as early as December 31, 1989. Teva’s RANITIDINE products were in the formats of 25 mg/ml, 75 mg/ml, 150 mg, and 300 mg. 2 were recalled on October 17, 2019, 3 had been cancelled post market on June 22, 2018 and on June 10, 2020 and 1 had been cancelled pre market on October 16, 2015, the whole as appears more fully from a copy of an extract from the *Registraire des enterprises* and from copies of extracts from Health Canada’s website at www.healthycanadians.gc.ca, produced herein *en liasse* as **Exhibit R-37**;

17.5 Respondent Vita Health Products Inc. (“Vita”) is a Canadian Pharmaceutical corporation with its head office in Toronto, Ontario. Vita was involved in the development, design, manufacture, testing, marketing, labelling, packaging, promotion, advertising, importation, distribution, and/or sale of 3 varieties of RANITIDINE as an over-the counter medicine. It has been marketing RANITIDINE in Canada since as early as March 31, 2006. Vita’s RANITIDINE products were in the formats of 75 mg and 150 mg. 2 were recalled on October 24, 2019 and 1 had been cancelled post market on August 6, 2009, the whole as appears more fully from a copy of an extract from the *Registraire des enterprises* and from copies of extracts from Health Canada’s website at www.healthycanadians.gc.ca, produced herein *en liasse* as **Exhibit R-38**;

18. All Respondents have either directly or indirectly developed, designed, manufactured, tested, marketed, labelled, packaged, promoted, advertised, imported, distributed, and/or sold ZANTAC to distributors and retailers for resale to or, directly to physicians, hospitals, medical practitioners and to the general public throughout Canada, including within the province of Quebec;

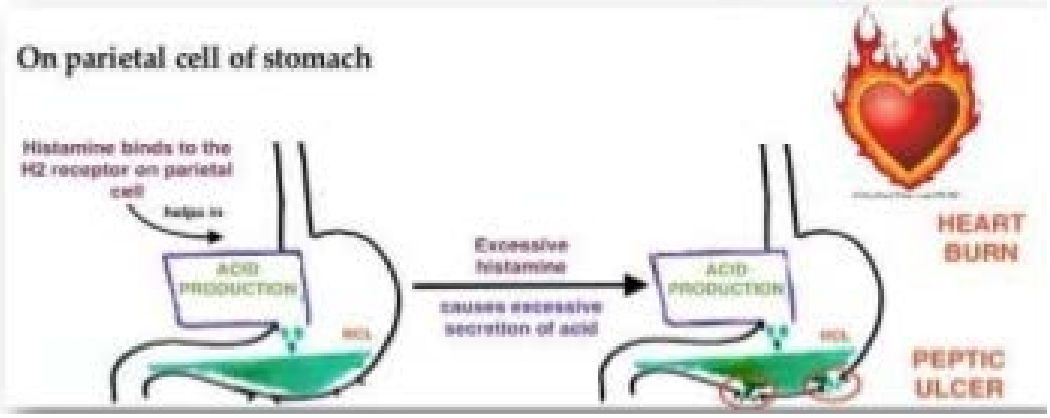
19. Given the close ties between the Respondents and considering the preceding, all Respondents are solidarily liable for the acts and omissions of the other;

C) The Situation

I. What is Ranitidine?

20. Ranitidine belongs to a group of medicines called Histamine 2 (H_2) Blockers, also known as Histamine 2 Receptor Antagonists (H_2RAs). This group of drugs helps relieve heartburn symptoms by reducing the amount of acid your stomach produces in response to histamine, the whole as appears more fully from a copy of an extract from Respondent Sanofi's website at www.zantac.ca, produced herein as **Exhibit R-10**;

21. In more technical terms, H_2 blockers are a class of medications that block the action of histamine at the histamine H_2 receptors of the parietal cells in the stomach – this decreases the production of stomach hydrochloric acid, which relieves heartburn, ulcers (duodenal and gastric), and certain conditions, such as Zollinger-Ellison disease, in which the stomach produces too much acid. In over-the-counter (OTC) strengths, these medicines are used to relieve and/or prevent gastric ulcers, heartburn, acid indigestion, (…) sour stomach, and other gastrointestinal conditions. H2-blockers may also be used for other conditions as determined by a physician, the whole as appears more fully from a copy of an extract from the Mayo Clinic website at www.mayoclinic.org and from a copy of an extract from the Drugs.com website at www.drugs.com, produced herein *en liasse* as **Exhibit R-11**;



22. There are several H_2 blockers on the market. In Canada, there are four brand names on the market; (i) ranitidine (ZANTAC), (ii) cimetidine, (iii) famotidine (Pepcid), and (iv) nizatidine; there are also generic forms available, the whole as appears more fully from a copy of an extract from the International Foundation for Gastrointestinal Disorders' website at www.aboutgerd.org, produced herein as **Exhibit R-12**;

23. According to Respondent Sanofi (Exhibit R-10), Ranitidine's mechanism of action is as follows:

    - Your stomach produces excess acid – This acid is produced in response to histamine released in the stomach. Histamine interacts with the cells in your stomach, known as the parietal cells, stimulating the production of acid.

    - Your esophagus is irritated – You feel heartburn when acid from your stomach escapes your stomach and irritates your esophagus.

    - The H2 Blockers take effect – H2 Blockers such as ZANTAC® interrupt the process by which histamine interacts with the cells in your stomach that produce acid.

    - There is less acidity – Reducing the production of acid, in turn, decreases the amount of acid that can be regurgitated during reflux, bringing acid production control for up to 12 hours.

24. ZANTAC is available in 3 forms, (i) ZANTAC 75 Regular Strength, (ii) ZANTAC 150 Maximum Strength, and (iii) ZANTAC 150 Cool Mint Maximum Strength. The key difference between the three is the amount of ranitidine they contain, ZANTAC 75 contains 75mg of ranitidine and ZANTAC 150 contains 150 mg of ranitidine, the whole as appears more fully from copies of extracts from Respondent Sanofi's website at www.zantac.ca, produced herein *en liasse* as **Exhibit R-13**;

24.1 Ranitidine can be taken orally, by injection into a muscle or a vein;

25. Ranitidine was discovered in 1976 by a predecessor of Respondent GlaxoSmithKline and it is the generic version of ZANTAC. Ranitidine was approved for sale in Canada in 1981 and marketed as ZANTAC. In 1982, Respondent GlaxoSmithKline began selling ZANTAC in Canada, the whole as appears more fully from a copy of the "Factum of the Respondent on Appeal/ Appellant on Cross-Appeal (Redacted)" in *Her Majesty the Queen* v. *GlaxoSmithKline Inc.*, Court File No. 33874 and from a copy of the SCC decision in *Canada* v. *GlaxoSmithKline Inc.*, [2012] 3 SCR 3, 2012 SCC 52[1], produced herein *en liasse* as **Exhibit R-14**;

25.1 On September 13, 1979, the patent from ZANTAC was filed and on June 21, 1983, it was issued as CA 1202638 "AMINOALKYLFURAN DERIVATIVES", the whole as appears more fully from a copy of the patent documents from CIPO, produced herein as **Exhibit R-39**;

26. Since then, ZANTAC has become the best-selling drug in history as a result of a shrewd, multifaceted marketing strategy that has enabled the product to dominate the acid marketplace, the whole as appears more fully from a copy of the Journal of Healthcare Marketing article entitled "How Zantac Became the Best-Selling Drug in History" dated winter 1996, produced herein as **Exhibit R-15**;

27. ZANTAC is one of the most popular tablet brands of acid inhibitors in the world and in Canada. However, ZANTAC's popularity and enormous sales were only made possible because of a deception perpetrated by the drug's manufacturers on consumers who have purchased Zantac since it hit the market in 1982;

II. The Introduction of the Various Ranitidine Products in Canada

27.1 ZANTAC was first introduced in Canada in 1982 by a predecessor to GlaxoSmithKline and was owned by Glaxo Wellcome Inc. and then Glaxo Canada Inc. until February 12, 1999 when it was transferred to Warner Lambert Canada Inc., a division of Respondent Pfizer. From January 23, 2007 until March 21, 2017, ZANTAC was owned by a division of Respondent J&J, until it was eventually transferred to Respondent Sanofi, the whole as appears more fully from copies of extracts from Health Canada's website at https://health-products.canada.ca, produced herein *en liasse* as **Exhibit R-40**;

27.2 Initially, ZANTAC was only available by prescription; on September 15, 1997, it became available over-the-counter in tablet dosages of 75 mg and 150 mg (Exhibit R-40);

[1] *Canada* v. *GlaxoSmithKline Inc*., [2012] 3 SCR 3, 2012 SCC 52 is the first ruling of the Supreme Court of Canada that deals with issues involving transfer pricing and how they are treated under the *Income Tax Act*.

27.3 A copy of the list of all manufacturers that were given permission from Health Canada to manufacture and market ranitidine since January 26, 1994 is produced herein as **Exhibit R-41**;

27.5 On December 31, 1987 Respondent Apotex was granted permission by Health Canada to manufacture and market ranitidine (Exhibit R-6), the whole the whole as appears more fully from copies of extracts from Health Canada's website at https://health-products.canada.ca, produced herein *en liasse* as **Exhibit R-42**;

27.6 On December 31, 1988, Respondent Pro Doc was granted permission by Health Canada to manufacture and market ranitidine (Exhibit R-7), the whole the whole as appears more fully from copies of extracts from Health Canada's website at https://health-products.canada.ca, produced herein *en liasse* as **Exhibit R-43**;

27.7 On December 31, 1989, Respondent Teva was granted permission by Health Canada to manufacture and market ranitidine (Exhibit R-37), the whole the whole as appears more fully from copies of extracts from Health Canada's website at https://health-products.canada.ca, produced herein *en liasse* as **Exhibit R-44**;

27.8 On August 7, 1998 Respondent Riva was granted permission by Health Canada to manufacture and market ranitidine, the whole the whole as appears more fully from copies of extracts from Health Canada's website at https://health-products.canada.ca, produced herein *en liasse* as **Exhibit R-45**;

27.9 On April 25, 2000, Respondent Pharmascience was granted permission by Health Canada to manufacture and market ranitidine (Exhibit R-5), the whole the whole as appears more fully from copies of extracts from Health Canada's website at https://health-products.canada.ca, produced herein *en liasse* as **Exhibit R-46**;

27.10 On January 8, 2001, Respondent Dominion Pharmacal was granted permission by Health Canada to manufacture and market ranitidine (Exhibit R-33), the whole the whole as appears more fully from a copy of an extract from Health Canada's website at https://health-products.canada.ca, produced herein as **Exhibit R-47**;

27.11 On May 15, 2001, Respondent Sandoz was granted permission by Health Canada to manufacture and market ranitidine (Exhibit R-4), the whole the whole as appears more fully from copies of extracts from Health Canada's website at https://health-products.canada.ca, produced herein *en liasse* as **Exhibit R-48**;

27.12 On October 23, 2009, Respondent Sun Pharma was granted permission by Health Canada to manufacture and market ranitidine, the whole the whole as appears more fully from copies of extracts from Health Canada's website at https://health-products.canada.ca, produced herein *en liasse* as **Exhibit R-49**;

27.12 On June 18, 2010, Respondent Sanis was granted permission by Health Canada to manufacture and market ranitidine, the whole the whole as appears more fully from copies of extracts from Health Canada's website at https://health-products.canada.ca, produced herein *en liasse* as **Exhibit R-50**;

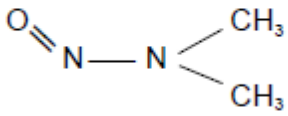
27.13 On June 11, 2012, Respondent Sivem was granted permission by Health Canada to manufacture and market ranitidine (Exhibit R-9), the whole the whole as appears more fully from copies of extracts from Health Canada's website at https://health-products.canada.ca, produced herein *en liasse* as **Exhibit R-51**;

III. *N*-Nitrosodimethylamine (NDMA)

28. The Respondents never disclosed to consumers that the drug has a critical defect: when ingested, ranitidine produces in the human body high quantities of NDMA, a chemical that the World Health Organization has described as "clearly carcinogenic", the whole as appears more fully from a copy of the World Health Organization's Concise International Assessment Document for *N*-Nitrosodimethylamine, produced herein as **Exhibit R-16**;

28.1 NDMA is the simplest dialkylnitrosamine, with a molecular formula of $C_2H_6N_2O$ and a molecular weight of 74.08 g/mol. NDMA is also known as dimethylnitrosamine, dimethylnitrosoamine, *N,N*-dimethylnitrosamine, *N*-methyl-*N*-nitrosomethanamine, *N*-nitroso-*N,N*-dimethylamine, DMN and DMNA (Exhibit R-53), the whole as appears more fully from a copy of the Toxicological Profile for *N*-Nitrosodimethylamine from the Agency for Toxic Substances and Disease Registry (ATSDR) U.S. Public Health Service dated December 1989, produced herein as **Exhibit R-52**;

FIGURE 1 Chemical structure of NDMA



28.2 NDMA was used to make rocket fuel, but this use was stopped after unusually high levels of this compound were found in air, water, and soil samples collected near a rocket fuel manufacturing plant. NDMA is, however, unintentionally formed during various manufacturing processes at many industrial sites and in air, water and soil from reactions involving other chemicals called alkylamines. Alkylamines are both natural and man-made

compounds which are found widely distributed throughout the environment (Exhibit R-52);

28.3 Experiments in animals have shown that after being given by mouth, NDMA enters the bloodstream and goes to many organs of the body in a matter of minutes. In the liver, NDMA is broken down into other substances, most of which leave the body within 24 hours in air exhaled from the lungs and in urine, along with the NDMA that is not broken down (Exhibit R-52);

28.4 When rats, mice, hamsters, and other animals ate food, drank water, or breathed air containing lower levels of NDMA for periods more than several weeks, liver cancer and lung cancer as well non-cancerous liver damage occurred. The high level short-term and low-level long-term exposures that caused non-cancerous liver damage and/or cancer in animals also usually resulted in internal bleeding and death (Exhibit R-52);

29. The primary sources of human exposure to NDMA are tobacco smoke, chewing tobacco, diet (cured meats [particularly bacon], beer, fish, cheese, and other food items), toiletry and cosmetic products (for example, shampoos and cleansers), interior air of cars, and various other household goods, such as detergents and pesticides. In addition, NDMA can form in the stomach during digestion of alkylamine containing foods. Alkylamines are naturally occurring compounds which are found in some drugs and in a variety of foods, the whole as appears more fully from a copy of the Agency for Toxic Substances and Disease Registry's public health statement regarding NDMA dated December 1989, produced herein as **Exhibit R-17**;

30. The dangers of NDMA have been publicly known for over 40 years. NDMA itself belongs to a family of chemicals called N-nitrosamines, which Health Canada classifies as a "probable human carcinogen", the whole as appears more fully from a copy of The New York Times' article entitled "Personal Health" dated October 3, 1979 and from a copy of the Health Canada Press Release entitled "Health Canada assessing NDMA in ranitidine" dated September 13, 2019, produced herein *en liasse* as **Exhibit R-18**;

30.1 When scientists want to study tumors in experimental animals, the toxin of choice to induce tumors in the animals is often NDMA. Unfortunately, the manufacturers of the ranitidine products have been poisoning consumers with extremely high levels of NDMA for over 35 years. A single dose of ranitidine has been shown to break down inside the body into over three million nanograms of NDMA. This is over 30,000 times higher than the threshold level of 96 nanograms per day;

30.2 Based upon laboratory studies in which tumours have been induced in all species examined at relatively low doses, NDMA is clearly carcinogenic, with a very strong likelihood that the mode of action for the induction of tumours

involves direct interaction with genetic material. 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, the whole as appears more fully from a copy of Environment Canada's Priority Substances List Assessment Report[2] for *N*-Nitrosodimethylamine (NDMA) under the *Canadian Environmental Protection Act, 1999*, produced herein as **Exhibit R-53**;

30.3 NDMA is assessed as "toxic" as defined in section 64 of the *Canadian Environmental Protection Act*, 1999, which provides as follows:

Substance toxique 64 Pour l'application de la présente partie et de la partie 6, mais non dans le contexte de l'expression « toxicité intrinsèque », est toxique toute substance qui pénètre ou peut pénétrer dans l'environnement en une quantité ou concentration ou dans des conditions de nature à : a) avoir, immédiatement ou à long terme, un effet nocif sur l'environnement ou sur la diversité biologique; b) mettre en danger l'environnement essentiel pour la vie; c) c) constituer un danger au Canada pour la vie ou la santé humaines.	Toxic substances 64 For the purposes of this Part and Part 6, except where the expression "inherently toxic" appears, a substance is toxic if it is entering or may enter the environment in a quantity or concentration or under conditions that (a) have or may have an immediate or long-term harmful effect on the environment or its biological diversity; (b) constitute or may constitute a danger to the environment on which life depends; or (c) constitute or may constitute a danger in Canada to human life or health.

30.4 NDMA appears on Environment Canada's List of Toxic Substances found at Schedule 1 of the *Canadian Environmental Protection Act, 1999*;

30.5 According to Environment Canada, since NDMA is likely to be carcinogenic to humans at relatively low levels of exposure and is not currently used in commerce in Canada, it is recommended that the manufacture, import and use

[2] The *Canadian Environmental Protection Act, 1999* requires the federal Ministers of Environment and of Health to develop and publish a Priority Substances List (PSL) that identifies substances, including chemicals, groups of chemicals, effluents and wastes, that may be harmful to the environment or constitute a danger to human health.

of the substance be banned in order to prevent its introduction into the Canadian market (Exhibit R-53);

30.6 Since 1975, efforts have been made to reduce the potential for exposure to NDMA in foodstuffs in Canada through continued reduction of allowable nitrite levels during preservation and suspension of the use of nitrate for certain food groups made through changes to the *Food and Drugs Regulations*, CRC, c 870 (Exhibit R-53);

31. In December 1989, the Agency for Toxic Substances and Disease Registry published the following (Exhibit R-17):

> "NDMA is very harmful to the liver of animals and humans. People who were intentionally poisoned on one or several occasions with unknown levels of NDMA in beverage or food died of severe liver damage accompanied by internal bleeding. Animals that ate food, drank water, or breathed air containing high levels of NDMA over a period of days or several weeks also developed serious, noncancerous, liver disease. When rats, mice, hamsters, and other animals ate food, drank water, or breathed air containing lower levels of NDMA for periods more than several weeks, liver cancer and lung cancer as well as non-cancerous liver damage occurred. The high level short-term and low level long-term exposures that caused noncancerous liver damage and/or cancer in animals also usually resulted in internal bleeding and death.
>
> Although there are no reports of NDMA causing cancer in humans, it is reasonable to expect that exposure to NDMA by eating, drinking, or breathing could cause cancer in humans.";

32. Recent scientific testing conducted by Valisure LLC and ValisureRX LLC (collectively "Valisure") "has detected extremely high levels of NDMA in all lots [of ranitidine] tested, across multiple manufacturers of ranitidine products," including ZANTAC, the whole as appears more fully from a copy of the Valisure Citizen Petition to the U.S. Food and Drug Administration dated September 9, 2019 and from a copy of The Wall Street Journal article entitled "FDA Finds Probable Carcinogen in Some Versions of Zantac" dated September 13, 2019, produced herein *en liasse* as **Exhibit R-19**;

33. The tests conducted by Valisure show that "ranitidine can react with itself in standard analysis conditions…at high efficiency to produce NDMA at dangerous levels well in excess of the permissible daily intake limit for this probable carcinogen" (Exhibit R-19);

34. Valisure's testing – which employs the U.S. FDA's own gas chromatography/ mass spectrometry ("GC/MS") protocol – detected 2,511,469 ng of NDMA per

150 mg tablet of Zantac, which is 26,000 times greater than the amount that can be safely ingested daily (Exhibit R-19);

35. The U.S. National Institutes of Health provided the following: "The typical recommended dose of ranitidine for therapy of peptic ulcer disease in adults is 150 mg twice daily or 300 mg once nightly for 4 to 8 weeks, and maintenance doses of 150 mg once daily." Moreover, chronic use of the drug is common "for therapy of heartburn and indigestion", the whole as appears more fully from a copy of the U.S. National Institutes of Health website at livertox.nih.gov, produced herein as **Exhibit R-20**;

36. Thus, a typical consumer who is taking ranitidine over the course of eight weeks to treat peptic ulcer disease is exposed to more than 280,000,000 ng (or 0.28 grams) of NDMA. A consumer who takes a 150 mg maintenance dose of Zantac once daily is exposed to 889,000,000 ng (0.889 grams) of NDMA over the course of a year. Again, the U.S. FDA's permissible intake limit of NDMA is 96 ng per day, which translates to just 0.000034 grams per year;

37. Ranitidine is used not only by adults, but is also given to infants, children, and teenagers to treat gastroesophageal reflux, among other things;

38. In addition, when ZANTAC was tested "in conditions simulating the human stomach," the quantity of NDMA detected was as high as 304,500 ng per tablet – 3,171 times more than the amount that can be safely ingested daily (Exhibit R-19);

IV. The Scientific Literature

39. Recent peer-reviewed scientific literature has demonstrated the existence of dangerous levels of NDMA in the urine of those who have taken ranitidine, the whole as appears more fully from a copy of the Oxford article entitled "Oral intake of ranitidine increases urinary excretion of *N*-nitrosodimethylamine" dated March 18, 2016, produced herein as **Exhibit R-21**;

40. The Respondents knew or should have known that ranitidine exposes users to unsafe levels of the carcinogen NDMA. During and even before the time periods that the Respondents manufactured and distributed the drug (outlined above), numerous scientific studies were published showing, among other things, that ranitidine forms NDMA when placed in drinking water and that a person who consumes ranitidine has a 400-fold increase of NDMA (Exhibit R-21), such as:

(a) Massimiliano Sgroi, *et al*., N-Nitrosodimethylamine (NDMA) and its precursors in water and wastewater: A review of formation and removal, 191 CHEMOSPHERE 685 (Oct. 15, 2017), produced herein as **Exhibit R-22**;

(b) Yong Dong Liu, *et al*., Formation Mechanism of NDMA from Ranitidine, Trimethylamine, and Other Tertiary Amines during Chloramination: A Computational Study, 48 ENVTL. SCI. & TECHNOLOGY 8653 (June 26, 2014), produced herein as **Exhibit R-23**;

(c) Julien Le Roux, *et al*., Chloramination of nitrogenous contaminants (pharmaceuticals and pesticides): NDMA and halogenated DBPs formation, 45 WATER RESEARCH 3164 (Mar. 26, 2011), produced herein as **Exhibit R-24**;

(d) Ruqiao Shen & Susan A. Andrews, Demonstration of 20 pharmaceuticals and personal care products (PPCPs) as nitrosamine precursors during chloramine disinfection, 45 WATER RESEARCH 944 (Oct. 13, 2010), produced herein as **Exhibit R-25**;

(e) Giovanni Brambilla & Antonietta Martelli, Update on genotoxicity and carcinogenicity testing of 472 marketed pharmaceuticals, 681 MUTATION RESEARCH 209 (Sept. 19, 2008), produced herein as **Exhibit R-26**;

(f) Giovanni Brambilla & Antonietta Martelli, Genotoxic and carcinogenic risk to humans of drug–nitrite interaction products, 635 MUTATION RESEARCH 17 (Dec. 6, 2006), produced herein as **Exhibit R-27**;

(g) J.M. Barnes, & P.N. Magee, Some toxic properties of dimethylnitrosamine. 11 BR. J. IND. MED. 167–174 (1954), produced herein as **Exhibit R-54**;

(h) P.N. Magee & J.M. Barnes, Induction of kidney tumours in the rat with dimethylnitrosamine (N-nitrosodimethylamine), 84 J. PATHOL. BACTERIOL. 19–31 (1962), produced herein as **Exhibit R-55**;

(i) B. Terracini, *et al*., Carcinogenicity of dimethylnitrosamine in Swiss mice. 20 BR. J. CANCER 871–876 (1966), produced herein as **Exhibit R-56**;

(j) V.A. Alexandrov, Blastomogenic effect of dimethylnitrosamine on pregnant rats and their offspring, 218 NATURE 280–281 (1968), produced herein as **Exhibit R-57**;

(k) R.L. Carter, W.H. Percival, & F.J.C. Roe., Exceptional sensitivity of mink to the hepatotoxic effects of dimethylnitrosamine, 97 J. PATHOL. 79–88 (1969), produced herein as **Exhibit R-58**;

(l) A.E.M. McLean and P.N. Magee, Increased renal carcinogenesis by dimethyl nitrosamine in protein deficient rats. 51 BR. J. EXP. PATHOL. 587–590 (1970), produced herein as **Exhibit R-59**;

(m) N.K. Clapp & R.E. Toya, Sr., Effect of cumulative dose and dose rate on dimethylnitrosamine oncogenesis in RF mice, 45 J. NATL. CANCER INST. 495–498 (1970), produced herein as **Exhibit R-60**;

(n) G.C. Hard and W.H. Butler, Cellular analysis of renal neoplasia: light microscope study of the development of interstitial lesions induced in the rat kidney by a single carcinogenic dose of dimethylnitrosamine, 30 CANCER RES. 2806–2815 (November 1970), produced herein as **Exhibit R-61**;

(o) A. Ayanaba, & M. Alexander, Transformation of methylamines and formation of a hazardous product, dimethylnitrosamine, in samples of treated sewage and lake water, 3 J. ENVIRON. QUAL. 83–89 (January 1974), produced herein as **Exhibit R-62**;

(p) J. Althoff, *et al*., Transplacental effects of nitrosamines in Syrian hamsters, 90 Z. KREBSFORSCH 79–86 (1977), produced herein as **Exhibit R-63**;

(q) Linda A. Ferraro, Richard E. Wolke & Paul P. Yevich, Acute toxicity of water-borne dimethylnitrosamine (DMN) to Fundulus heteroclitus, 10 L. J. FISH. BIOL. 203–209 (1977), produced herein as **Exhibit R-64**;

(r) Consuelo Agrelo, *et al.*, Studies on the gastrointestinal absorption of N-nitrosamines: effect of dietary constituents, 10 TOXICOLOGY 159–167 (1978), produced herein as **Exhibit R-65**;

(s) K. Terao, T. Aikawa & K. Kera, A synergistic effect of nitrosodimethylamine on sterigmatocystin carcinogenesis in rats, 16 FOOD COSMET. TOXICOL. 591–596 (1978), produced herein as **Exhibit R-66**;

(t) Lucy M. Anderson, Loretta J. Priest & John M. Budinger, Lung tumorigenesis in mice after chronic exposure in early life to a low dose of dimethylnitrosamine, 62 J. NATL. CANCER INST. 1553–1555 (1979), produced herein as **Exhibit R-67**;

(u) Mayasuki Arai, *et al*., Long-term experiment of maximal non-carcinogenic dose of dimethylnitrosamine for carcinogenesis in rats, 70 GANN 549–558 (August 1979), produced herein as **Exhibit R-68**;

(v) Alfred C. Draper & William S. Brewer, Measurement of the aquatic toxicity of volatile nitrosamines, 5 J. TOXICOL. ENVIRON. HEALTH 985–993 (1979), produced herein as **Exhibit R-69**;

(w) Tadao Kakizoe, *et al*., Volatile *N*-nitrosamines in the urine of normal donors and of bladder cancer patients, 39 CANCER RES. 829–832 (March 1979), produced herein as **Exhibit R-70**;

(x) V.V. Khudoley & J.J. Picard, Liver and kidney tumours induced by Nnitrosodimethylamine in Xenopus borealis (Parker), 25 INT. J. CANCER 679–683 (1980), produced herein as **Exhibit R-71**;

(y) L. Lakritz, *et al*., N-Nitrosodimethylamine in human blood, 18 FOOD COSMET. TOXICOL. 77–79 (1980), produced herein as **Exhibit R-72**;

(z) Deborah C. Herron and Ronald C. Shank, Methylated purines in human liver DNA after probable dimethylnitrosamine poisoning, 40 CANCER RES. 3116–3117 (September 1980), produced herein as **Exhibit R-73**;

(aa) G. Brambilla, *et al*., Quantitative correlation among DNA damaging potency of six Nnitroso compounds and their potency in inducing tumor growth and bacterial mutations, 2 CARCINOGENESIS 425–429 (March 11, 1981), produced herein as **Exhibit R-74**;

(bb) G. Brambilla, M. Cavanna, & S. De Flora, Genotoxic Effects of Drugs: Experimental Findings Concerning Some Chemical Families of Therapeutic Relevance, Nicolini C. (eds) Chemical Carcinogenesis. NATO Advanced Study Institutes Series (Series A: Life Sciences), Vol 52. Springer, Boston, MA (1982), produced herein as **Exhibit R-75**;

(cc) Giovanni Brambilla, *et al.*, Genotoxic effects in rodents given high oral doses of ranitidine and sodium nitrite, 4:10 CARCINOGENESIS 1281-1285 (1983), produced herein as **Exhibit R-76**;

(dd) Paul G. Brantom, Dose-Response Relationships in Nitrosamine Carcinogenesis, DOCTORAL THESIS, UNIVERSITY OF SURREY (1983), produced herein as **Exhibit R-77**;

(ee) Alain Barbin, Jean-Claude Béréziat & Helmut Bartsch., Evaluation of DNA damage by the alkaline elution technique in liver, kidneys and lungs of rats and hamsters treated with N-nitrosodialkylamines, 4 CARCINOGENESIS 541–545 (March 21, 1983), produced herein as **Exhibit R-78**;

(ff) William Lijinsky & Melvin D. Reuber, Carcinogenesis in rats by nitrosodimethylamine and other nitrosomethylalkylamines at low doses, 22 CANCER LETT. 83–88 (1984), produced herein as **Exhibit R-79**;

(gg) Peter F. Swann, Angela M. Coe, & Raymond Mace, Ethanol and dimethylnitrosamine and diethylnitrosamine metabolism and disposition in the rat. Possible relevance to the influence of ethanol on human cancer incidence, 5:10 CARCINOGENESIS 1337–1343 (1984), produced herein as **Exhibit R-80**;

(hh) H.A. Risch, *et al*., Dietary factors and the incidence of cancer of the stomach, 122 AM. J. EPIDEMIOL. 947–957 (1985), produced herein as **Exhibit R-81**;

(ii) Stephen R. Dunn, John W. Pensabene & Michael L. Simenhoff, Analysis of human blood for volatile Nnitrosamines by gas chromatography–chemiluminescence detection, 377 J. CHROMATOGR. 35–47 (1986), produced herein as **Exhibit R-82**;

(jj) Lucy M. Anderson, *et al*., Tissue levels and biological effects of Nnitrosodimethylamine in mice during chronic low or high dose exposure with or without ethanol, 14:6 DRUG METAB. DISPOS. 733–739 (1986), produced herein as **Exhibit R-83**;

(kk) Ismael Parsa, Stanley Friedman, & Cathleen M. Cleary, Visualization of O6-methylguanine in target cell nuclei of dimethylnitrosamine-treated human pancreas by a murine monoclonal antibody, 8 CARCINOGENESIS 839–846 (1987), produced herein as **Exhibit R-84**;

(ll) Lucy M. Anderson, Increased numbers of *N*-nitrosodimethylamine-initiated lung tumours in mice by chronic co-administration of ethanol, 9 CARCINOGENESIS 1717–1719 (1988), produced herein as **Exhibit R-85**;

(mm) A. Tanaka, *et al*., A comparison of the carcinogenicity of N-nitrosodiethylamine and N-nitrosodimethylamine after intratracheal instillation into Syrian golden hamsters, 26 FOOD CHEM. TOXICOL. 847–850 (1988), produced herein as **Exhibit R-86**;

(nn) C. Bolognesi, L. Rossi & L. Santi, A new method to reveal the genotoxic effects of Nnitrosodimethylamine in pregnant mice, 207 MUTAT. RES. 57–62 (1988), produced herein as **Exhibit R-87**;

(oo) P.E. Martino, *et al*., Studies on the mechanism of the acute and carcinogenic effects of *N*-nitrosodimethylamine on mink liver, 23 J. TOXICOL. ENVIRON. HEALTH 183–192 (1988), produced herein as **Exhibit R-88**;

(pp) Lucy M. Anderson, *et al.*, Transplacental initiation of liver, lung, neurogenic, and connective tissue tumors by N-nitroso compounds in mice, FUNDAM. APPL. TOXICOL. 12: 604–620 (1989), produced herein as **Exhibit R-89**;

(qq) Tadashi Ogawa, Masumi Kimoto, & Kei Sasaoka, Purification and Properties of a New Enzyme, N^G,N^G-Dimethylarginine Dimethylaminohydrolase, from Rat Kidney, 264:17 THE JOURNAL OF

BIOLOGICAL CHEMISTRY 10205-10209 (June 15, 1989), produced herein as **Exhibit R-90**;

(rr) Beatrice L. Pool, *et al*., Employment of adult mammalian primary cells in toxicology: in vivo and in vitro genotoxic effects of environmentally significant N-nitrosodialkylamines in cells of the liver, lung, and kidney, 15 ENVIRON. MOL. MUTAGEN. 24–35 (1990), produced herein as **Exhibit R-91**;

(ss) Helen G. Haggerty & Michael P. Holsapple, Role of metabolism in dimethylnitrosamine-induced immunosuppression: a review, 63 TOXICOLOGY 1–23 (1990), produced herein as **Exhibit R-92**;

(tt) R.G. Klein, *et al*., Effects of long-term inhalation of N-nitrosodimethylamine in rats, 105 IARC SCI. PUBL. 322–328 (1991), produced herein as **Exhibit R-93**;

(uu) Richard Peto, *et al*. Effects on 4080 rats of chronic ingestion of N-nitrosodiethylamine or Nnitrosodimethylamine: a detailed dose–response study, 51 CANCER RES. 6415–6451 (December 1, 1991), produced herein as **Exhibit R-94**;

(vv) Richard Peto, *et al*. Dose and time relationships for tumor induction in the liver and esophagus of 4080 inbred rats by chronic ingestion of N-nitrosodiethylamine or Nnitrosodimethylamine, 51 CANCER RES. 6452–6469 (December 1, 1991), produced herein as **Exhibit R-95**;

(ww) Richard Desjardins, *et al.*, Immunosuppression by chronic exposure to N-nitrosodimethylamine (NDMA) in mice, 37 J. TOXICOL. ENVIRON. HEALTH 351–361 (1992), produced herein as **Exhibit R-96**;

(xx) Marc T. Goodman, *et al.*, High-fat foods and the risk of lung cancer, 3 EPIDEMIOLOGY 288–299 (1992), produced herein as **Exhibit R-97**;

(yy) Lucy M. Anderson, *et al.*, Reduced blood clearance and increased urinary excretion of N-nitrosodimethylamine in patas monkeys exposed to ethanol or isopropyl alcohol, 52 CANCER RES. 1463–1468 (March 15, 1992), produced herein as **Exhibit R-98**;

(zz) Lucy M. Anderson, *et al.*, Characterization of ethanol's enhancement of tumorigenesis by N-nitrosodimethylamine in mice, 13 Carcinogenesis 2107–2111 (1992), produced herein as **Exhibit R-99**;

(aaa) Carlos A. González, *et al*., Nutritional factors and gastric cancer in Spain, 139 AM. J. EPIDEMIOL. 466–473 (1994), produced herein as **Exhibit R-100**;

(bbb) Mary A.M. Rogers, *et al.*, Consumption of nitrate, nitrite, and nitrosodimethylamine and the risk of upper aerodigestive tract cancer. 4 CANCER EPIDEMIOL. BIOMARKERS PREV. 29–36 (1995), produced herein as **Exhibit R-101**;

(ccc) Dominique Pobel, *et al*., Nitrosamine, nitrate and nitrite in relation to gastric cancer: A case–control study in Marseille, France, 11 EUR. J. EPIDEMIOL. 67–73 (1995), produced herein as **Exhibit R-102**;

(ddd) Lucy M. Anderson, *et al.*, *N*-Nitrosodimethylaminederived O6-methylguanine in DNA of monkey gastrointestinal and urogenital organs and enhancement by ethanol, 66 INT. J. CANCER 130–134 (1996), produced herein as **Exhibit R-103**;

(eee) Eduardo De Stefani, *et al*., Dietary nitrosodimethylamine and the risk of lung cancer: a case–control study from Uruguay. 5 CANCER EPIDEMIOL. BIOMARKERS PREV. 679–682 (September 1996), produced herein as **Exhibit R-104**;

(fff) H. Biaudet, L. Mouillet & G. Debry, Migration of nitrosamines from condoms to physiological secretions, 59 BULL. ENVIRON. CONTAM. TOXICOL. 847–853 (1997), produced herein as **Exhibit R-105**;

(ggg) Paul Knekt, *et al*., Risk of colorectal and other gastro-intestinal cancers after exposure to nitrate, nitrite and N-nitroso compounds: a follow-up study, 80 INT. J. CANCER, 852–856 (1999), produced herein as **Exhibit R-106**;

(hhh) William A. Mitch, *et al*., *N*-Nitrosodimethylamine (NDMA) as a Drinking Water Contaminant: A Review, 20 ENVIRONMENTAL ENGINEERING SCIENCE 5 (2003), produced herein as **Exhibit R-107**;

(iii) Dominique S. Michaud, *et al*, Peptic ulcer disease and the risk of bladder cancer in a prospective study of male health professionals, 13 CANCER EPIDEMIOL BIOMARKERS PREV. 2, 250-254 (February 2004), produced herein as **Exhibit R-108**;

(jjj) Yun Zhu, *et al*., Dietary N-nitroso compounds and risk of colorectal cancer: a case-control study in Newfoundland and Labrador and Ontario, Canada, 111:6 BR J NUTR. 1109-1117 (March 28, 2014), produced herein as **Exhibit R-109**;

(kkk) Teng Zeng & William A. Mitch, Oral Intake of Ranitidine Increases Urinary Excretion of N-Nitrosodimethylamine 37:6 CARCINOGENESIS 625 (2016), produced herein as **Exhibit R-110**;

40.1 Relevant epidemiological studies include case–control investigations in which the potential risks of cancer of the stomach (Risch *et al*., Exhibit R-81; González *et al*., Exhibit R-100; Pobel *et al*., Exhibit R-102), upper digestive tract (Rogers *et al*. – Exhibit R-101), and lung (Goodman *et al*., Exhibit R-97; De Stefani et al. – Exhibit R-104) associated with the ingestion of NDMA have been assessed. In some of these reports (Goodman *et al*., Exhibit R-97; González *et al*., Exhibit R-100; Pobel *et a*l., Exhibit R-102), the estimated intake of NDMA was based upon recollection of an individual's typical diet consumed in the year preceding the onset of illness, as well as the reported levels of this nitrosamine in the foodstuffs consumed. In the studies conducted by De Stefani *et al*. (Exhibit R-104) and Rogers *et al*. (Exhibit R-ZI), subjects were asked to recall their typical diet in the 5 and 10 years, respectively, prior to the onset of illness, the whole as appears more fully from a copy of the Background document for development of WHO Guidelines for Drinking-water Quality entitled "N-Nitrosodimethylamine in drinking-water" dated 2006, produced herein as **Exhibit R-111**;

40.2 On December 30, 1991, the first adverse reaction connecting ranitidine to liver cancer was reported to Health Canada. Thereafter, only one other individual was able to make the connection until after the news broke regarding the carcinogenic dangers of NDMA, when 3 more people have come forward to report having gotten cancer subsequent to the use of ranitidine, the whole as appears more fully from a copy of Health Canada's list of adverse reaction reports and from a copy of the actual reports, produced herein *en liasse* as **Exhibit R-112**;

V. Regulatory Reaction

41. On September 13, 2019, Health Canada issued a press release (Exhibit R-18) to inform Canadians of the presence of NDMA in some ranitidine drugs;

42. On September 17 and again on September 25, 2019, Health Canada released press releases requesting that companies stop distributing ranitidine drugs in Canada while it assesses NDMA, the whole as appears more fully from a copy of the Health Canada press release entitled "Health Canada requests that companies stop distributing ranitidine drugs in Canada while it assesses NDMA; additional products being recalled" dated September 25, 2019, to which the September 17, 2019 press release is appended, produced herein as **Exhibit R-28**;

42.1 On November 1, 2019, the United States Food and Drug Administration ("U.S. FDA") posted its laboratory results in its testing of NDMA in ranitidine; NMDA was present in all samples tested. The U.S. FDA has set the acceptable daily intake limit for NDMA at 0.096 micrograms or 0.32 ppm for ranitidine, the whole as appears more fully from a copy of the U.S. FDA's Laboratory Results and

from a copy of the testing method document entitled "Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS) Method for the Determination of NDMA in Ranitidine Drug Substance and Solid Dosage Drug Product" dated October 17, 2019, produced herein *en liasse* as **Exhibit R-113**;

42.2 Of the Respondents' ranitidine products, the following levels of NDMA were found:

Respondent	Product	NMDA level ppm	NDMA level mcg/tablet or oral dose
Sanofi	OTC Ranitidine 150 mg	0.07-2.38	0.01-0.36
	OTC Ranitidine 75 mg	0.10-0.55	0.01-0.04
	Ranitidine 150 mg	0.08-2.17	0.01-0.33
Sandoz	Rx Ranitidine 300 mg	0.82	0.25

43. Despite the weight of scientific evidence showing that ranitidine exposed users to unsafe levels of the carcinogen NDMA, none of the Respondents disclosed this risk to consumers, healthcare professionals and the public. Had Defendants disclosed that consumption of ZANTAC and its generic versions containing ranitidine results in unsafe levels of NDMA in the human body, no person, let alone a reasonable person, would have purchased and consumed ZANTAC or the generic equivalent containing ranitidine;

44. Copies of the various product monographs are produced herein *en liasse* as **Exhibit R-29**;

VI. The Respondents' Knowledge of the Dangers of NDMA and their Ranitidine Products

44.1 During the time that the Respondents developed, designed, manufactured, tested, marketed, labelled, packaged, promoted, advertised, imported, distributed, and/or sold the ranitidine products in Canada, i.e. from 1982 until their recalls in September-October 2019, there was a wealth of scientific evidence that consumption of ranitidine exposed humans to unsafe levels of NDMA. The Respondents failed to disclose this risk to Class Members, to their physicians, and to Health Canada, whether on the product labelling, on the product monograph (Exhibit R-29) or by any other means;

44.2 Even before ZANTAC entered the market in 1982, there was research showing elevated levels of NDMA when properly and independently tested;

44.3 Drug manufacturers, such as the Respondents (and referred to as Market Authorization Holders (MAH) by Health Canada), are required to prepare and submit annual summary reports (ASRs) and, when requested issue-related summary reports (IRSRs). An ASR is a comprehensive assessment of all known safety information for a marketed drug or natural health product. It is prepared by the MAH to provide an update on the worldwide safety profile at defined intervals post-authorization. An IRSR is a concise, critical analysis, requested by the Minister, of a specific safety or effectiveness issue. It is prepared by the MAH at the request of Health Canada, the whole as appears more fully from a copy of the Health Canada Guidance Document for Preparing and Submitting Summary Reports for Marketed Drugs and Natural Health Products, dated May 23, 2018, produced herein as **Exhibit R-114**;

44.4 In accordance with section C.01.018 of the *Food and Drug Regulations*, in preparing the ASR, the MAH must determine whether there has been a significant change in what is known about the risks and benefits of the drug. If the MAH concludes from the ASR that there has been a significant change, they must inform Health Canada immediately in a letter sent to the Office of Submissions and Intellectual Property:

Rapport de synthèse annuel et fiches d'observation	Annual Summary Report and Case Reports
C.01.018 (1) Le fabricant prépare un rapport de synthèse annuel sur les renseignements concernant les réactions indésirables à une drogue et les réactions indésirables graves à une drogue dont il a reçu communication ou a eu connaissance au cours des douze derniers mois.	C.01.018 (1) The manufacturer shall prepare an annual summary report of all information relating to adverse drug reactions and serious adverse drug reactions to the drug that it received or became aware of during the previous 12 months.
(2) Le rapport de synthèse annuel comprend une analyse critique et concise des réactions indésirables à une drogue et des réactions indésirables graves à une drogue.	(2) The annual summary report shall contain a concise, critical analysis of the adverse drug reactions and serious adverse drug reactions to the drug.
(3) Dans le cadre de la préparation du rapport de synthèse annuel, le fabricant évalue, en se fondant sur l'analyse visée au paragraphe (2), si ce qui est connu à propos des risques et avantages associés à la drogue a changé de façon importante	(3) In preparing the annual summary report, the manufacturer shall determine, on the basis of the analysis referred to in subsection (2), whether there has been a significant change in what is known about the risks and benefits of the drug during the period covered by the report and

durant la période visée par le rapport et fait état de ses conclusions à cet égard dans son rapport. (4) Lorsque, dans le cadre de la préparation du rapport de synthèse annuel, le fabricant conclut à un changement important, il en informe sans tarder le ministre par écrit, si ce n'est déjà fait.	shall include its conclusions in this regard in the summary report. (4) If, in preparing the annual summary report, the manufacturer concludes that there has been a significant change, it shall notify the Minister without delay, in writing, unless this has already been done.

44.5 The Respondents did not follow these regulations when they chose to disregard the existing scientific evidence, to not provide Health Canada with the relevant studies, and not disclose or report the significant information and new information affecting the safety of the ranitidine products;

44.6 In a 1981 study published by GlaxoSmithKline, the metabolites of ranitidine in urine were studied using liquid chromatography. Many metabolites were listed, though there is no indication that NDMA was looked for; likely this was intentional; a ploy to avoid detecting a carcinogen in their product, the whole as appears more fully from a copy of the study entitled "Determination of ranitidine and its metabolites in human urine by reversed-phase ion-pair high-performance liquid chromatography" dated 1981, produced herein as **Exhibit R-115**;

44.7 By 1987, after numerous studies raised concerns over ranitidine and cancerous nitroso compounds (discussed previously), GlaxoSmithKline published a clinical study investigating gastric contents in human patients and N-nitroso compounds. This study indicated that there were no elevated levels of N-nitroso compounds (of which NDMA is one). However, the study was designed to fail. It used an analytical system called a "nitrogen oxide assay" for the determination of N-nitrosamines, which was developed for analyzing food indirectly and non-specifically, the whole as appears more fully from a copy of the study entitled "Effects of one year's treatment with ranitidine and of truncal vagotomy on gastric contents" dated 1987, produced herein as **Exhibit R-116**;

44.8 Further, in addition to this approach being less accurate, GlaxoSmithKline also removed all gastric samples that contained ranitidine out of concern that samples with ranitidine would contain high concentrations of N-nitroso compounds being recorded:

> N-nitroso compounds were assayed by measurement of nitrogen oxide evolved under special conditions. The assays were restricted to ranitidine free samples because the presence of ranitidine in gastric juice may result in falsely high concentrations of N-nitroso compounds being recorded (Exhibit R-116 at page 730).

Logically, without the chemical being present in any sample, any degradation into NDMA could not, by design, be observed. This spurious "test" was again intentionally designed to mask any potential cancer risk and to instead protect the Respondents' profit margins;

44.9 There are various alternatives to ranitidine that do not pose the same carcinogenic risk, such as Cimetidine (Tagamet), Nizatidine (Axid), Famotidine (Pepcid), Omeprazole (Prilosec), Esomeprazole (Nexium), Omeprazole (Losec), and Lansoprazole (Prevacid);

VII. The Recalls to Date

44.10 On September 17, 2019 Sandoz recalled the following ranitidine products:

Product Name/ Active Pharmaceutical Ingredient	DIN	Strength
Sandoz Ranitidine	02243229	150 mg
Sandoz Ranitidine	02243230	300 mg

The whole as appears more fully from a copy of the Health Canada recall dated September 17, 2019, produced herein as **Exhibit R-117**;

44.11 On September 24, 2019 Apotex recalled the following ranitidine products:

Product Name/ Active Pharmaceutical Ingredient	DIN	Strength
Acid Reducer (ranitidine) sold under the brand names Equate and Selection	02296160	150 mg
Apo-Ranitidine Oral Solution	02280833	75 mg/5 mL
Apo-Ranitidine Tablet 150mg	00733059	150 mg
Apo-Ranitidine Tablet 300mg	00733067	300 mg

Sanis recalled the following ranitidine products:

Product Name/ Active Pharmaceutical Ingredient	DIN	Strength
Ranitidine	02353016	150 mg
Ranitidine	02353024	300 mg

and Sivem recalled the following ranitidine products[3]:

Product Name/ Active Pharmaceutical Ingredient	DIN	Strength
Ranitidine	02385953	150 mg
Ranitidine	02385961	300 mg

[3] On October 17, 2019 Sivem issued a second recall for the same ranitidine products.

The whole as appears more fully from a copy of the Health Canada recalls dated September 24, 2019 and October 17, 2019, produced herein *en liasse* as **Exhibit R-118**;

44.12 On September 25, 2019, Sun Pharma (Ranbaxy) recalled the following ranitidine products[4]:

Product Name/ Active Pharmaceutical Ingredient	DIN	Strength
Ran-Ranitidine	02336480	150 mg
Ran-Ranitidine	02336502	300 mg

The whole as appears more fully from copies of the Health Canada recalls dated September 25, 2019 and October 24, 2019, produced herein *en liasse* as **Exhibit R-119**;

44.13 On October 17, 2019, Teva recalled the following ranitidine products:

Product Name/ Active Pharmaceutical Ingredient	DIN	Strength
ACT-Ranitidine	02248570	150 mg
ACT-Ranitidine	02248571	300 mg

The whole as appears more fully from a copy of the Health Canada recall dated October 17, 2019, produced herein as **Exhibit R-120**;

44.14 On October 18, 2019, Sanofi recalled the following ranitidine products:

Product Name/ Active Pharmaceutical Ingredient	DIN	Strength
Zantac (ranitidine)	02230287	75 mg
Zantac Maximum Strength Non-Prescription (ranitidine)	02277301	150 mg

The whole as appears more fully from a copy of the Health Canada recall dated October 18, 2019, produced herein as **Exhibit R-121**;

44.15 On October 23, 2019, Dominion Pharmacal recalled the following ranitidine product:

Product Name/ Active Pharmaceutical Ingredient	DIN	Strength
Maximum Strength Acid Reducer Without Prescription (ranitidine) sold under the brand name Personnelle	02407523	150 mg

and Pharmascience recalled the following ranitidine products:

[4] On October 24, 2019, Sun Pharma issued a second recall for the same ranitidine products.

Product Name/ Active Pharmaceutical Ingredient	DIN	Strength
PMS-Ranitidine 150 mg	02242453	150 mg
PMS-Ranitidine 300 mg	02242454	300 mg
Acid Reducer (ranitidine) sold under the brand names Atoma, Biomedic, Compliments, Exact, Life Brand, London Drugs, Option+, Personnelle, Pharmasave, Preferred Pharmacy, Rexall and Selection	02247551	75 mg
Maximum Strength Acid Reducer Without Prescription (ranitidine) sold under the brand names Atoma, Biomedic, Compliments, Co-op Care+, Equate, Exact, Health One, Kirkland Signature, London Drugs, Option+, Personnelle, Pharmasave, Rexall and Selection	02293471	150 mg
Acid Reducer (ranitidine) sold under the brand names Exact and Life Brand	02400103	150 mg

The whole as appears more fully from copies of the Health Canada recalls dated October 23, 2019, produced herein *en liasse* as **Exhibit R-122**;

44.16 On October 24, 2019, Pro Doc recalled the following ranitidine products:

Product Name/ Active Pharmaceutical Ingredient	DIN	Strength
Ranitidine - 150	00740748	150 mg
Ranitidine - 300	00740756	300 mg

and Riva recalled the following ranitidine products:

Product Name/ Active Pharmaceutical Ingredient	DIN	Strength
Riva-Ranitidine 150	02247814	150 mg
Riva-Ranitidine 300	02247815	300 mg
Acid Reducer (ranitidine) sold under the brand names Biomedic, Circle K and Option+	02452464	75 mg

The whole as appears more fully from copies of the Health Canada recalls dated October 24, 2019, produced herein *en liasse* as **Exhibit R-123**;

44.17 On October 25, 2019, Vita recalled the following ranitidine products:

Product Name/ Active Pharmaceutical Ingredient	DIN	Strength
Acid Reducer (ranitidine) sold under the brand names Equate, iPharma, Stanley and Western Family	02298740	75 mg
Maximum Strength Acid Reducer (ranitidine) sold under the brand names Equate, iPharma and Western Family	02298902	150 mg

The whole as appears more fully from a copy of the Health Canada recall dated October 25, 2019, produced herein as **Exhibit R-124**;

44.18 On April 1, 2020, the U.S. FDA announced that it was requesting manufacturers to withdraw all prescription and over-the-counter ranitidine drugs from the market immediately. The agency 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, the whole as appears more fully from a copy of the U.S. FDA Press Release entitled "FDA Requests Removal of All Ranitidine Products (Zantac) from the Market" dated April 1, 2020, produced herein as **Exhibit R-125**;

VIII. The Respondents' Liability

45. The Respondents have either not adequately studied ranitidine or have failed to make public the results of any studies or investigations that they might have conducted;

46. Despite evidence that ingestion of ranitidine produces in the human body high quantities of NDMA, the Respondents have either failed to investigate or conduct any studies on the safety of ranitidine and/or failed to make public the results of any studies or investigations that they might have conducted;

47. A reasonably prudent drug developer, designer, manufacturer, tester, marketer, labeller, packager, promotor, advertiser, distributer, and/or seller in the Respondents' positions would have adequately warned both doctors and patients of the risks associated with the use of ranitidine;

48. Despite a clear signal, the Respondents failed to either alert the public and the scientific and medical community or to perform further investigation into the safety of ranitidine;

49. The Respondents were negligent in the development, design, manufacture, testing, marketing, labelling, packaging, promotion, advertising, distribution, and/or sale of the ranitidine products in one or more of the following respects:

    a. They knew or should have known that consumption of (…) ranitidine results in unsafe levels of NDMA in the human body;

    b. They failed to ensure that their ranitidine products were not dangerous to consumers;

c. They failed to conduct appropriate testing to determine whether and to what extent the ingestion, injection, and/or use of ranitidine poses serious risks, including the production of unsafe levels of NDMA;

d. They failed to adequately test their ranitidine products prior to placing them on the market;

e. They failed to adequately test their ranitidine products in a manner that would fully disclose the production in the human body high quantities of NDMA;

f. They failed to use care in developing, designing and manufacturing their ranitidine products so as to avoid posing unnecessary health risks to users of such product;

g. They failed to conduct adequate pre-clinical and clinical testing, post-marketing surveillance and follow-up studies to determine the safety of the drug;

h. They failed to advise that the ingestion, injection, and/or use of ranitidine produces in the human body high quantities of NDMA;

i. They failed to advise the medical and scientific communities of the exposure to users to unsafe levels of the carcinogen NDMA;

j. They failed to provide adequate and timely warnings or sufficient indications about the increased potential health risks associated with the use of ranitidine;

k. They failed to provide Class Members and their physicians with adequate warnings or sufficient indications of inherent risks associated with ranitidine;

l. They failed to provide adequate updated and current information to Class Members and their physicians respecting the risks of ranitidine as such information became available;

m. They failed to provide prompt warnings of potential hazards of ranitidine in the product monographs and in the product labelling;

n. They failed to warn Class Members and their physicians that the risks associated ranitidine would exceed the risks of other available acid reducing drugs;

o. They falsely stated and/or implied that ranitidine was safe when they knew or ought to have known that this representation was false;

p. They failed to accurately and promptly disclose to Health Canada information relating to the exposure to NDMA associated with ranitidine and to modify (…) the associated product monographs and product labelling accordingly in a timely manner;

q. They deprived patients of a chance for safe, effective and/or successful alternative treatments; and

r. In all circumstances of this case, they applied callous and reckless disregard for the health and safety of their consumers;

50. The Respondents concealed and failed to disclose their knowledge that consumption of (…) ranitidine exposed users to unsafe levels of the carcinogen NDMA as well as their knowledge that they had failed to fully test or study the drug;

IX. The U.S. Litigation

50.1 On February 6, 2020, the U.S. Judicial Panel on Multidistrict Litigation ("JPML") consolidated pretrial proceedings for *In Re: Zantac (Ranitidine) Products Liability Litigation*, MDL No. 2924 in the United States District Court for the Southern District of Florida (the "U.S. MDL Court"), the whole as appears more fully from a copy of the Transfer Order in *In Re: Zantac (Ranitidine) Products Liability Litigation*, MDL No. 2924 dated February 6, 2020, produced herein as **Exhibit R-126**;

50.2 On June 22, 2020, a Master Personal Injury Complaint was filed in the U.S. MDL Court, the whole as appears more fully from a copy of the Master Personal Injury Complaint in *In Re: Zantac (Ranitidine) Products Liability Litigation*, MDL No. 2924 dated June 22, 2020, produced herein as **Exhibit R-127**;

X. Summative Remarks

50.3 Despite the vast availability of knowledge clearly indicating that ranitidine is causally-related to Ranitidine-Induced Cancer, the Respondents not only failed to warn Class Members, but instead incongruously promoted and marketed their ranitidine products as safe and effective, effectively appropriating the ability of doctors and patients to make informed decisions regarding their health;

50.4 The Respondents concealed and failed to completely disclose their knowledge that the ranitidine products were associated with or could cause Ranitidine-Induced Cancer as well as their knowledge that they had failed to fully or properly test or study said risk;

50.5 The Respondents ignored the association between the use of the ranitidine products and the risk of Ranitidine-Induced Cancer;

50.6 The Respondents developed, designed, manufactured, tested, marketed, labelled, packaged, promoted, advertised, imported, distributed, and/or sold the ranitidine products with active misrepresentations about their safety;

50.7 The Respondents failed to disclose and/or actively concealed, despite a wealth of longstanding knowledge, that the ranitidine products are defective and unsafe in order to increase their profits;

50.8 Feasible and suitable alternatives to the ranitidine products exist that do not present the same frequency or severity of risks as do the ranitidine products;

50.9 The ranitidine products were at all times utilized and ingested in a manner foreseeable to the Respondents;

50.10 The Petitioners and Class Members would not have purchased and ingested the ranitidine products had they known they were unsafe;

50.11 The Respondents concealed material information regarding the truth about the existence and nature of the health risks from the medical and health community, Health Canada, the Petitioners, the Class Members, and the public in general at all times, even though they knew or should have known about the dangers, including Ranitidine-Induced Cancer and knew or should have known that this information would be important to a reasonable person;

II. FACTS GIVING RISE TO INDIVIDUAL ACTIONS BY THE PETITIONERS

A. Petitioner Royer

51. Over the course of decades, (…) Petitioner Royer has purchased and ingested ZANTAC as well as generic ranitidine products on a daily basis;

51.1 Petitioner Royer took ZANTAC to sooth his heartburn and acid reflux, a condition that he suffered from even as a young child;

51.2 Petitioner Royer would purchase and ingest ZANTAC and the ranitidine products in the 300 mg tablet format;

51.3 Petitioner Royer would purchase ZANTAC and the ranitidine products at many different locations including, but not limited to pharmacies, grocery stores, and gas stations. Most often he would purchase ZANTAC, but if there was a big price difference between the generic, he would opt for that instead;

52. At no time prior to the recalls in September 2019 was (…) Petitioner Royer made aware that when ingested, ZANTAC (ranitidine) produces, in the human body, high quantities of NDMA;

52.1 When Petitioner Royer learned of the recalls and of the carcinogenic effect of ranitidine, he immediately stopped taking ZANTAC and the generic ranitidine products;

53. Had the Respondents properly disclosed this fact, Petitioner Royer would not have purchased and ingested ZANTAC;

54. Petitioner Royer is aware that several lawsuits were filed in the United States due to the defects associated with ZANTAC and due to the Respondents' conduct related thereto, as appears more fully from a copy of the U.S. Complaints, produced herein *en liasse* as **Exhibit R-30**;

55. As a result of the Respondents' conduct, (…) Petitioner Royer suffered damages including, but not limited to physical and mental/emotional injuries, including pain, suffering, anxiety (…), fear, loss of quality and enjoyment of life, (…), loss of income, (…) and the apportioned cost of ZANTAC and the ranitidine products;

B. Petitioner Fauvel

55.1 Over the course of 10 to 15 years, Petitioner Fauvel has purchased and ingested ZANTAC as well as generic ranitidine products approximately 2 times per week in the 150 mg tablet format (usually before coaching football games as he would otherwise get acid reflux while nervous);

55.2 He would normally purchase generic ranitidine from Uniprix Sylvie Delisle – at 358 boul. Chemin de la Grande-Côte, in Boisbriand, Quebec and at the Walmart Supercentre at 401 Boul Labelle, in Rosemère, Quebec. While taking ZANTAC, Petitioner Fauvel would normally purchase it from Costco Wholesale at 3600 Avenue des Grandes Tourelles, in Boisbriand, Quebec;

55.3 In January 2019, he went to his family doctor for his yearly check up and to get his biannual bloodwork done at the Boisbriand Medical Clinic at 877 boulevard Grande Allée, in Boisbriand, Quebec. As Petitioner Fauvel had noticed that he had been going to the bathroom more often than normal, he mentioned this to his doctor who ordered a stool sample. Upon analysis, his stool sample contained blood;

55.4 As such, on February 26, 2019, Petitioner Fauvel underwent a colonoscopy at the Hospital of Saint-Eustache located at 520 Boulevard Arthur-Sauvé, in Saint-Eustache, Quebec. That same day, he was diagnosed with stage 4 colorectal cancer, which had metastasized to his liver;

55.5 Petitioner Fauvel was prescribed chemotherapy by his oncologist and he began the FOLFOX regimen[5], which consisted of undergoing intravenous chemotherapy every other week for 3 months at the Saint-Eustache Hospital's Cancer Clinic. He stopped the chemotherapy 7 weeks before his scheduled operation on August 17, 2019 to remove the cancer from his colon and from his liver. At this point, Petitioner Fauvel's blood tests, CAT scans and MRIs indicated that he was stable;

55.6 On August 17, 2019, Petitioner Fauvel underwent a 10.5-hour operation at the *Centre hospitalier de l'Université de Montréal*, whereby he had 23 centimetres of his colon removed and his cancerous masses were removed from his liver;

55.7 After his operation, Petitioner Fauvel's cancerous masses on his liver responded aggressively and he was then prescribed chemotherapy on the FOLFIRI regimen, which again consisted of undergoing intravenous chemotherapy every second week for 5 months at the Saint-Eustache Hospital's Cancer Clinic;

55.8 In approximately March 2020, Petitioner Fauvel underwent testing to see his progress from the two sequences of chemotherapy that he had underwent. The testing revealed that the masses were growing again on his liver

55.9 Petitioner Fauvel was then prescribed Lonsurf (trifluridine and tipitacil) tablets, which is an oral chemotherapy prescription medicine used to treat people with colon, rectal, or stomach cancer that has spread to other parts of the body and who have been have been previously treated with certain chemotherapy medicines, the whole as appears more fully from a copy of an extract from the Lonsurf website at www.lonsurf.com, produced herein as **Exhibit R-128**;

55.10 Petitioner Fauvel took Lonsurf for 14 days on and then 14 days off for 3 months after 3 months, testing revealed that his cancerous masses were getting bigger and that the cancerous proteins in his blood were elevated;

55.11 Petitioner was then prescribed Stivarga (Regorafenib), which is an oral chemotherapy prescription medicine taken to shrink tumors and decrease symptoms of colon cancer and is not commonly given with the goal of cure. He is taking 4 Stivarga pills per day for 21 days per month, the whole as appears more fully from a copy of an extract from the Chemo Experts website www.chemoexperts.com, produced herein as **Exhibit R-129**;

55.12 After Petitioner Fauvel's cancer diagnosis, he continued taking ZANTAC and generic ranitidine products until approximately May 2020, when he went to his pharmacy, Uniprix, and was informed that ZANTAC had been recalled – he

[5] FOLFOX is the abbreviation for a combination chemotherapy regimen that is used to treat colorectal cancer. It includes the drugs leucovorin calcium (folinic acid), fluorouracil, and oxaliplatin.

was informed that the reason for the recall had to do with a Chinese root that was being reformulated;

55.13 Petitioner Fauvel never made the connection between his cancer and ranitidine, until July 5, 2020, when he was watching television on an American station and saw a commercial about the lawsuit in the United States, which described how ZANTAC and other ranitidine could cause his type of cancer;

55.14 Had Petitioner Fauvel not been watching television that day, he would never have otherwise made the connection between ranitidine and cancer;

55.15 Petitioner Fauvel always lead a very good, active, and healthy lifestyle;

55.16 Petitioner Fauvel suffered damages including, but not limited to physical and mental/emotional injuries, including developing cancer, undergoing an extensive operation, chemotherapy, pain, suffering, anxiety, fear, loss of quality and enjoyment of life, and the apportioned cost of ZANTAC and the ranitidine products;

56. Petitioners' damages are a direct and proximate result of their use of the ranitidine products, Respondents' negligence and/or lack of adequate warnings, wrongful conduct, and the unreasonably dangerous and defective characteristics of ZANTAC;

57. In consequence of the foregoing, the Petitioners are justified in claiming damages;

III. FACTS GIVING RISE TO AN INDIVIDUAL ACTION BY EACH OF THE MEMBERS OF THE GROUP

58. Every member of the Class has purchased and/or ingested/injected ZANTAC or is the successor, family member, assign, and/or dependant of a person who purchased, ingested, and/or used ZANTAC;

59. The Class Members' damages would not have occurred, but for the acts, omissions and/or negligence of the Respondents in failing to ensure that the ranitidine products were safe to use, for failing to provide adequate warning of the unreasonable risks associated with using the drug, for false or misleading representations and for omitting to disclose important information to Class Members, to their physicians, and to Health Canada;

60. In consequence of the foregoing, each member of the Class is justified in claiming at least one or more of the following as damages:

a. Physical and psychological injuries, including pain, suffering, anxiety, fear, loss of quality and enjoyment of life, increased risk of Ranitidine-Induced Cancer, (…);

b. Out-of-pocket expenses incurred or to be incurred, including those connected with hospital stays, medical treatment, life care, medications, medical monitoring services, and the diagnosis and treatment of (…) the Ranitidine-Induced Cancer;

c. Refund of the purchase price of the ranitidine products or alternatively, the incremental costs of the ranitidine products as paid for by the Class Members and/or by the *Régie de l'assurance maladie du Québec*, the Ontario Health Insurance Plan, and other provincial health insurers; and

d. Punitive damages;

61. As a direct result of the Respondents' conduct, the users' family members and dependants have, had, and/or will suffer damages and loss including:

a. Out-of-pocket expenses, including debts accrued and/or paying or providing nursing, housekeeping and other services;

b. Loss of income and loss of future income; and

c. Loss of support, guidance, care, consortium, and companionship that they might reasonably have expected to receive if the injuries had not occurred;

62. All of these damages to the Class Members are a direct and proximate result of the use of the ranitidine products and the Respondents' conduct, negligence and reckless failure to adequately disclose necessary information and the risks associated with the drug;

IV. CONDITIONS REQUIRED TO INSTITUTE A CLASS ACTION

A) The composition of the Class makes it difficult or impracticable to apply the rules for mandates to sue on behalf of others or for consolidation of proceedings

63. The Petitioners are unaware of the specific number of persons who ingested, injected and/or purchased the ranitidine products, which information is confidential; however, it is safe to estimate that it is in the hundreds of thousands;

64. Class Members are numerous and are scattered across the entire province and country;

65. In addition, given the costs and risks inherent in an action before the courts, many people will hesitate to institute an individual action against the Respondents. Even if the Class Members themselves could afford such individual litigation, it would place an unjustifiable burden on the courts. Furthermore, individual litigation of the factual and legal issues raised by the conduct of the Respondents would increase delay and expense to all parties and to the court system;

66. Also, a multitude of actions instituted in different jurisdictions, both territorial (different provinces) and judicial districts (same province), risks having contradictory judgments on questions of fact and law that are similar or related to all members of the Class;

67. These facts demonstrate that it would be impractical, if not impossible, to contact each and every member of the Class to obtain mandates and to join them in one action;

68. In these circumstances, a class action is the only appropriate procedure for all of the members of the Class to effectively pursue their respective rights and have access to justice;

B) The claims of the members of the Class raise identical, similar or related issues of law or fact

69. Individual issues, if any, pale by comparison to the numerous common issues that are significant to the outcome of the litigation;

70. The damages sustained by the Class Members flow, in each instance, from a common nucleus of operative facts, namely, Respondents' misconduct;

71. The claims of the members raise identical, similar or related issues of fact or law, namely:

    a) Does the ingestion of ranitidine expose users to unsafe levels of NDMA?

    b) Did the Respondents fail to adequately test the ranitidine products both before and/or after placing them on the market?

    c) Did the Respondents adequately and sufficiently advise/ warn the Class Members, Health Canada, and/or their physicians about the production of NDMA in the human body from the ingestion of ranitidine?

    d) Did the Respondents know or should they have known about the risks associated with the use of ranitidine?

e) In the affirmative to any of the above questions, did the Respondents' conduct engage their solidary liability toward the members of the Class?

f) Are the Defendants liable to pay compensatory damages to the Class Members?

g) Are the Defendants liable to pay aggravated or punitive damages and, if so, in what amount?

72. The interests of justice favour that this application be granted in accordance with its conclusions;

V. NATURE OF THE ACTION AND CONCLUSIONS SOUGHT

73. The action that the Petitioners wish to institute on behalf of the members of the Class is an action in damages (…) and declaratory judgment;

74. The conclusions that the Petitioners wish to introduce by way of an application to institute proceedings are:

GRANT the class action of the Plaintiffs and each of the members of the Class;

DECLARE that the Defendants failed to provide adequate warnings that ranitidine exposed users to unsafe levels of the carcinogen NDMA;

RESERVE the right of each of the members of the Class to claim future damages related to the use of ranitidine;

DECLARE the Defendants solidarily liable for the damages suffered by the Petitioners and each of the members of the Class;

CONDEMN the Defendants to pay to each member of the Class a sum to be determined in compensation of the damages suffered, and ORDER collective recovery of these sums;

CONDEMN the Defendants to pay to each of the members of the Class, punitive damages, and ORDER collective recovery of these sums;

CONDEMN the Defendants to pay interest and additional indemnity on the above sums according to law from the date of service of the application to authorize a class action;

ORDER the Defendants to deposit in the office of this Court the totality of the sums which forms part of the collective recovery, with interest and costs;

ORDER that the claims of individual Class Members be the object of collective liquidation if the proof permits and alternately, by individual liquidation;

CONDEMN the Defendants to bear the costs of the present action including expert and notice fees;

RENDER any other order that this Honourable Court shall determine and that is in the interest of the members of the Class;

A) The Petitioners request that they be attributed the status of representatives of the Class

75. Petitioners are (…) members of the Class;

76. Petitioners are ready and available to manage and direct the present action in the interest of the members of the Class that they wish to represent and are determined to lead the present dossier until a final resolution of the matter, the whole for the benefit of the Class, as well as, to dedicate the time necessary for the present action before the Courts and the *Fonds d'aide aux actions collectives*, as the case may be, and to collaborate with their attorneys;

77. Petitioners have the capacity and interest to fairly, properly, and adequately protect and represent the interest of the members of the Class;

78. Petitioners have given the mandate to their attorneys to obtain all relevant information with respect to the present action and intend to keep informed of all developments;

79. Petitioners, with the assistance of their attorneys, is ready and available to dedicate the time necessary for this action and to collaborate with other members of the Class and to keep them informed;

80. Petitioners have given instructions to their attorneys to put information about this class action on its website and to collect the coordinates of those Class Members that wish to be kept informed and participate in any resolution of the present matter, the whole as will be shown at the hearing. To date, a total of 8,865 potential Class Members have inputted their contact information in order to be kept informed about the status of the case (4015 of which were from Quebec), the whole as appears more fully from copies of redacted charts of potential Class Members who have inputted their information through the CLG webpage, produced herein *en liasse* as **Exhibit R-130**;

81. Petitioners are in good faith and has instituted this action for the sole goal of having his rights, as well as the rights of other Class Members, recognized and protected so that they may be compensated for the damages that they have suffered as a consequence of the Respondents' conduct;

82. Petitioners understand the nature of the action;

83. Petitioners' interests are not antagonistic to those of other members of the Class;

84. Petitioners are prepared to be examined out-of-court on his allegations (as may be authorized by the Court) and to be present for Court hearings, as may be required and necessary;

85. Petitioners have spent time researching this issue on the internet and meeting with their attorneys to prepare this file. In so doing, they are convinced that the problem is widespread;

B) The Petitioners suggest that this class action be exercised before the Superior Court of Justice in the district of Montreal

86. A great number of the members of the Cass reside in the judicial district of Montreal and in the appeal district of Montreal;

87. The Petitioners' attorneys practice their profession in the judicial district of Montreal;

88. The present application is well founded in fact and in law.

FOR THESE REASONS, MAY IT PLEASE THE COURT:

GRANT the present application;

AUTHORIZE the bringing of a class action in the form of an application to institute proceedings in damages (…) and declaratory relief;

ASCRIBE the Petitioners the status of representatives of the persons included in the class herein described as:

- All persons residing in Canada who purchased and/or ingested the drug, RANITIDINE (sold under the brand name ZANTAC® as well as under various generic names) and their successors, assigns, family members, and dependants, or any other group to be determined by the Court;

Alternatively (or as a subclass)

- All persons residing in Quebec who purchased and/or ingested the drug, RANITIDINE (sold under the brand name ZANTAC® as well as under various generic names) and their successors,

assigns, family members, and dependants, or any other group to be determined by the Court;

IDENTIFY the principle issues of fact and law to be treated collectively as the following:

a) Does the ingestion of ranitidine expose users to unsafe levels of NDMA?

b) Did the Respondents fail to adequately test the ranitidine products both before and/or after placing them on the market?

c) Did the Respondents adequately and sufficiently advise/ warn the Class Members, Health Canada, and/or their physicians about the production of NDMA in the human body from the ingestion of ranitidine?

d) Did the Respondents know or should they have known about the risks associated with the use of ranitidine?

e) In the affirmative to any of the above questions, did the Respondents' conduct engage their solidary liability toward the members of the Class?

f) Are the Defendants liable to pay compensatory damages to the Class Members?

g) Are the Defendants liable to pay aggravated or punitive damages and, if so, in what amount?

IDENTIFY the conclusions sought by the class action to be instituted as being the following:

GRANT the class action of the Plaintiffs and each of the members of the Class;

DECLARE that the Defendants failed to provide adequate warnings that ranitidine exposed users to unsafe levels of the carcinogen NDMA;

RESERVE the right of each of the members of the Class to claim future damages related to the use of ranitidine;

DECLARE the Defendants solidarily liable for the damages suffered by the Petitioners and each of the members of the Class;

CONDEMN the Defendants to pay to each member of the Class a sum to be determined in compensation of the damages suffered, and ORDER collective recovery of these sums;

CONDEMN the Defendants to pay to each of the members of the Class, punitive damages, and ORDER collective recovery of these sums;

CONDEMN the Defendants to pay interest and additional indemnity on the above sums according to law from the date of service of the application to authorize a class action;

ORDER the Defendants to deposit in the office of this Court the totality of the sums which forms part of the collective recovery, with interest and costs;

ORDER that the claims of individual Class Members be the object of collective liquidation if the proof permits and alternately, by individual liquidation;

CONDEMN the Defendants to bear the costs of the present action including expert and notice fees;

RENDER any other order that this Honourable Court shall determine and that is in the interest of the members of the Class;

DECLARE that all members of the Class that have not requested their exclusion, be bound by any judgment to be rendered on the class action to be instituted in the manner provided for by the law;

FIX the delay of exclusion at thirty (30) days from the date of the publication of the notice to the Class Members, date upon which the members of the Class that have not exercised their means of exclusion will be bound by any judgment to be rendered herein;

ORDER the publication of a notice to the members of the group in accordance with article 579 C.C.P. within sixty (60) days from the judgment to be rendered herein in The Globe and Mail, the National Post, La Presse, and the Montreal Gazette;

ORDER that said notice be available on the Respondents' websites, Facebook page(s), and twitter accounts with a link stating "Notice to RANITIDINE (ZANTAC) prescribers and users";

RENDER any other order that this Honourable Court shall determine and that is in the interest of the members of the Class;

THE WHOLE with costs, including all publication fees.

Montreal, July 17, 2019

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