UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

DANIEL HUDSON AND STEPHANIE HUDSON, Plaintiffs, v. ASTRAZENECA PHARMACEUTICALS LP; ASTRAZENECA LP; & MERCK & CO. INC. D/B/A MERCK, SHARP & DOHME CORPORATION, Defendants.	**Case No.: 2:19-cv-11900** **COMPLAINT AND DEMAND FOR JURY TRIAL**

COMPLAINT

Plaintiffs, Daniel Hudson and Stephanie Hudson, by way of Complaint against Defendants, AstraZeneca Pharmaceuticals LP, AstraZeneca LP, and Merck & Co. Inc. d/b/a Merck, Sharp & Dohme Corporation (collectively "Defendants) alleges as follows:

NATURE OF THE ACTION

1. This action is brought on behalf of Plaintiff, Daniel Hudson, who used esomeprazole, sold under the brand names of Nexium, and Nexium 24HR for treatment of Plaintiff's gastroesophageal reflux disorder (GERD).

2. Plaintiffs seek compensatory damages as a result of Plaintiff's use of esomeprazole which has caused the Plaintiff to suffer, and continue to suffer, from stomach cancer as well as other severe personal injuries which are permanent and lasting in nature, physical pain and mental anguish, including diminished enjoyment of life, markedly decreased life expectancy, as well as

the need for remaining 'lifelong' medical treatment, monitoring and/or medications, surgery, fear of developing any of additional health consequences and significant past, present and future economic loses included lost wages and earning capacity.

3. Defendants, AstraZeneca Pharmaceuticals LP, AstraZeneca LP and Merck & Co. Inc. d/b/a Merck, Sharp & Dohme Corporation, (hereinafter collectively referred to as "Defendants") designed, researched, manufactured, tested, advertised, promoted, marketed, sold, and distributed esomeprazole.

4. When warning of the safety and risks of esomeprazole, Defendants negligently represented to the medical, healthcare, regulatory community, the Plaintiff's prescribing and treating physicians, and the public in general, that esomeprazole had been tested and found to be safe and/or effective for its indicated use in treating peptic disorders.

5. Defendants concealed their knowledge of esomeprazole's defects, specifically the fact that it causes clinically significant hypergastrinemia and gastric cancer, from Plaintiff's treating physicians, hospitals, pharmacies, the public in general and/or the medical and regulatory community.

6. These representations were made by Defendants with the intent of defrauding and deceiving the Plaintiff's physicians, the public in general, and the medical and healthcare community in particular, and were made with the intent of inducing the public in general, and the medical community in particular, to recommend, dispense and/or purchase esomeprazole for the treatment of peptic disorders which include 'heartburn', gastroesophageal reflux disease (GERD), peptic ulcer disease, and nonsteroidal anti-inflammatory drug induced gastropathy, all of which evinced a callous, reckless, willful, depraved indifference to health, safety and welfare of the Plaintiff herein.

7. As a result of the foregoing acts and omissions, the Plaintiff was and still is caused to suffer serious and dangerous side effects including, *inter alia*, Stage III gastric cancer, as well as other severe and personal injuries which are permanent and lasting in nature, physical pain and mental anguish, including diminished enjoyment of life, loss of income, as well as the need for lifelong medical treatment, monitoring and/or medications, and fear of developing any additional health consequences.

8. Consequently, Plaintiffs seek compensatory damages as a result of Plaintiff's use of esomeprazole, which has caused Plaintiff to suffer from gastric cancer, as well as other severe and personal injuries which are permanent and lasting in nature, physical pain and mental anguish, including diminished enjoyment of life, as well as the need for lifelong medical treatment, monitoring and/or medications, and fear of developing any of the above named health consequences.

PARTIES

9. Plaintiff, Daniel Hudson, is a citizen of the United States of America, and is a citizen of Box Springs, Georgia.

10. Plaintiff, Daniel Hudson, was born on October 16, 1965.

11. Plaintiff, Daniel Hudson, first began using prescription brand Nexium in or about April 12, 2004, and Plaintiff used prescription brand Nexium up through October 14, 2014.

12. Plaintiff, Daniel Hudson, first began using esomeprazole in or about June 11, 2015, and Plaintiff continues to use esomeprazole today.

13. As result of Plaintiff's ingestion of Defendants' esomeprazole, Plaintiff has suffered and continues to suffer from gastric cancer, diagnosed on or about April 23, 2018, as

well as any and all of its sequelae including, but not limited, to attendant pain, suffering, and emotional distress.

14. The injuries and damages sustained by Plaintiff were caused by Defendants' esomeprazole and their unlawful conduct with respect to its design, manufacture, marketing and sale.

15. Plaintiff Stephanie Hudson is a citizen of the United States of America and is a resident of the State of Georgia and is the lawful spouse of Daniel Hudson.

16. Defendant AstraZeneca Pharmaceuticals LP is and, at all times relevant to this action, has been a Delaware limited partnership having a principal place of business at 1800 Concord Pike, Wilmington, DE 19850.

17. Defendant AstraZeneca LP is and, at all times relevant to this action, has been a Delaware limited partnership having a principal place of business at 1800 Concord Pike, Wilmington, DE 19850.

18. Defendant AstraZeneca LP's sole general partner is AstraZeneca Pharmaceuticals LP. Defendant AstraZeneca LP has no limited partners. AstraZeneca Pharmaceutical LP's general partner is AstraZeneca AB, a corporation incorporated under the laws of the nation of Sweden with its principal place of business in Sweden. AstraZeneca Pharmaceutical LP's sole limited partner is Zeneca Inc., a corporation incorporated under the laws of the State of Delaware with its principal place of business in Delaware.

19. Defendant AstraZeneca Pharmaceuticals LP and Defendant AstraZeneca LP and are referred to collectively herein as the "AstraZeneca Defendants."

20. Each of the AstraZeneca Defendants was the agent and employee of the other AstraZeneca Defendants and, in doing the things alleged, was acting within the course and scope

of such agency and employment and with the other AstraZeneca Defendants' actual and implied permission, consent, authorization and approval.

21. The AstraZeneca Defendants, in collaboration amongst themselves, designed, tested, researched and developed the prescription and non-prescription over-the counter esomeprazole products.

22. As a part of their business and at all relevant times, the AstraZeneca Defendants have been involved in the design, research, manufacture, testing, advertisement, promotion, marketing, sale and distribution of both prescription and over-the-counter esomeprazole products.

23. In 1982, the AstraZeneca Defendants entered a joint venture with Defendant Merck to design and develop the first proton pump inhibitor.

24. The result of this joint venture was the development of omeprazole, which was ultimately marketed and sold under the brand name Prilosec.

25. In September 1989, the FDA approved Prilosec for healing of erosive esophagitis, maintenance of healing erosive esophagitis and treatment of GERD.

26. In anticipation of the expiration of the patent for prescription Prilosec, the AstraZeneca Defendants launched an internal program called Operation Shark Fin for the purpose of developing a second PPI Product in order to capitalize on the market for PPI Products. The result of Operation Shark Fin was the development of Nexium (esomeprazole).

27. In December 1999, Defendant AstraZeneca Pharmaceutical LP submitted its first NDA for a Nexium product, NDA 021153, to the FDA for approval to market Nexium in the United States.

28. In December 2000, the FDA simultaneously approved Nexium, NDA 021153, and Nexium Delayed Release, NDA 021154, for healing of erosive esophagitis, maintenance of healing

erosive esophagitis, treatment of symptomatic GERD and *H. pylori* eradication to reduce the risk of duodenal ulcer recurrence (as part of a triple therapy with amoxicillin and clarithromycin).

29. Defendant AstraZeneca Pharmaceuticals LP is also the holder of approved NDAs 021957 and 022010 for Nexium Delayed-Release Oral Suspension, and NDAs 022101 and 021689 for Nexium Injection Solution.

30. The AstraZeneca Defendants manufacture and market each of the aforementioned esomeprazole formulations in the United States.

31. In 2003, the AstraZeneca Defendants spent $260 million alone in promoting and marketing esomeprazole products to American consumers, the largest amount spent on marketing a single brand of pharmaceutical to that date.

32. In an agreement reached in 2012, the AstraZeneca Defendants licensed to the Pfizer Defendants the exclusive right to market an over-the-counter version of Nexium (esomeprazole), known as Nexium 24HR, which was launched in 2014.

33. According to the agreement between the Pfizer Defendants and the AstraZeneca Defendants, the AstraZeneca Defendants receive royalty payments from the Pfizer Defendants on product launches and sales.

34. The AstraZeneca Defendants have transacted and conducted business related to esomeprazole in each of the States and Territories of the United States.

35. The AstraZeneca Defendants have derived substantial revenue from esomeprazole used in each of the States and Territories of the United States. For example, in 2003 alone, sales of Nexium in the United States were $2.7 billion and world-wide was $3.9 billion.

36. The AstraZeneca Defendants have expected or should have expected their acts to have consequences within each of the States and Territories of the United States, and derived

substantial revenue from interstate commerce in each of the States and Territories of the United States related to esomeprazole.

37. Defendant Merck & Co. Inc. d/b/a Merck, Sharp & Dohme Corporation (hereinafter "Defendant Merck") is and, all times relevant to this action, has been a New Jersey corporation having a principal place of business at One Merck Drive, Whitehouse Station, New Jersey 08889.

38. In 1982, Defendant Merck entered into an agreement with the AstraZeneca Defendants, under the terms of which Defendant Merck developed and marketed the AstraZeneca Defendants' products, including esomeprazole products, under a royalty-bearing license.

39. In 1993, Merck's total sales of the AstraZeneca Defendants' products reached a level that triggered the first step in the establishment of a joint venture business (the "Joint Venture") in which Defendant Merck and the AstraZeneca Defendants each owned a 50% share. This Joint Venture, formed in 1994, was called Astra Merck Inc. and was responsible for the sale of Prilosec and other of the AstraZeneca Defendants' products.

40. Until 2014, Defendant Merck had a contractual and ownership interest in the Joint Venture. Through these interests, between 2009 and 2014, Defendant Merck earned at least $7 billion, based on the sales of prescription and over-the-counter formulations of Nexium (esomeprazole) and Prilosec (omeprazole).

41. Defendant Merck currently has, and will continue to have until 2018, a financial interest in esomeprazole products.

42. As a part of their business and at all relevant times, Defendant Merck has been and is involved in the design, research, manufacture, testing, advertisement, promotion, marketing, sale and distribution of esomeprazole products.

43. Defendant Merck has had a contractual, ownership and financial interest in the

following FDA approved forms of Nexium: Delayed-Release Capsule Pellets, NDA 021153; Delayed-Release Oral Suspension, NDAs 02195 and 022010; and Intravenous Injectable Solution, NDA 021689.

44. Defendant Merck manufactures and markets esomeprazole in the United States.

45. Defendant Merck has transacted and conducted business related to esomeprazole in each of the States and Territories of the United States.

46. Defendant Merck has derived substantial revenue from esomeprazole in each of the States and Territories of the United States.

47. Defendant Merck has expected or should have expected its acts to have consequence within each of the States and Territories of the United States and derived substantial revenue from interstate commerce in each of the States and Territories of the United States related to esomeprazole.

48. Defendants AstraZeneca LP, AstraZeneca Pharmaceuticals LP, and Defendant Merck & Co. Inc. d/b/a Merck, Sharp & Dohme Corporation shall herein be collectively referred to as "Defendants."

JURISDICTION AND VENUE

49. This Court has subject matter jurisdiction over this action pursuant to 28 U.S.C. § 1332(a)(1) because this case is a civil action where the matter in controversy exceeds $75,000, exclusive of interest and costs, and is between citizens of different States.

50. Venue is proper in this District pursuant to 28 U.S.C. § 1391(b) as a substantial part of the events and/or omissions giving rise to the Plaintiff's claims emanated from activities within this jurisdiction and Defendants transact substantial business within this jurisdiction.

51. Consistent with the Due Process Clause of the Fifth and Fourteenth Amendments, the Court has personal jurisdiction over Defendants, because Defendants are present in the State of New Jersey, such that the exercise of jurisdiction does not offend traditional notions of fair play and substantial justice.

52. This Court has personal jurisdiction over Defendants pursuant to and consistent with the Constitutional requirements of Due Process because Defendants, acting through their agents or apparent agents, committed one or more of the following: transaction of business within the state of New Jersey; making of contracts within the state; the commission of a tortious act within this state; and the ownership, use, or possession of any real estate situated within this state as well as registered as foreign partnerships to do business within the state and maintaining a registered agent for service of process.

53. Requiring Defendants to litigate these claims in New Jersey does not offend traditional notions of fair play and substantial justice and is permitted by the United States Constitution. All of Plaintiff's claims arise in part from conduct Defendants purposefully directed to the State of New Jersey. Upon information and belief, Defendants' esomeprazole products are sold at hundreds of local and national pharmacies, including, but not limited to Wal-Mart, Target, CVS, and Walgreens throughout the Plaintiff's state of residency and the State of New Jersey.

54. Upon information and belief, Defendants avail themselves of numerous advertising and promotional materials regarding their defective esomeprazole products specifically intended to reach consumers in Plaintiff's home state and the State of New Jersey, including but not limited to advertisements on local television programs, advertisements on local radio broadcasts, advertisements on billboards and advertisements in print publications delivered to consumers in Plaintiff's home state of and the State of New Jersey.

55. Plaintiff's claims arise out of Defendants' design, marketing and/or sale of esomeprazole products in the State of New Jersey.

56. Defendants regularly conduct or solicit business and derive substantial revenue from goods used or consumed in, inter alia, the State of New Jersey.

57. At all relevant times, Defendants were present and doing business in the State of New Jersey.

58. At all times relevant hereto, Defendants transacted, solicited, and conducted business in the State of New Jersey and derived substantial revenue from such business.

59. At all relevant times, Defendants placed esomeprazole products ingested by Plaintiff into the stream of interstate commerce.

60. At all relevant times, Defendants expected or should have expected that their acts and omissions would have consequences within the United States, including Plaintiff's state of residency and the State of New Jersey in particular.

61. Defendants regularly file patent infringement claims against non-New Jersey Corporations in New Jersey Federal Court thereby availing themselves of the benefits of New Jersey courts, laws and jurisdiction. (See AstraZeneca Pharmaceuticals LP, et al. v. Teva Pharmaceuticals, Case 1:17-CV-02448-RMB-KMW, filed April 10, 2017.)

62. Defendants have obtained a Certificate of Registration with the New Jersey Department of Health Drug and Medical Devices, Registration No. 5003966; 5003887.

63. Defendants maintain a registered agent in Trenton, New Jersey.

64. Defendants, by and through their actions stated above, have consented to jurisdiction in state of New Jersey.

65. Defendants, by and through their actions stated above, are judicially estopped from

challenging jurisdiction in New Jersey State and Federal Courts under the doctrine of Judicial Estoppel.

66. Defendants named herein are conclusively presumed to have been doing business in this state and are subject to New Jersey long arm jurisdiction.

FACTUAL BACKGROUND

67. This action seeks, among other relief, general and special damages and equitable relief due to Plaintiff Daniel Hudson suffering stomach cancer caused by Plaintiff's ingestion of esomeprazole.

68. Upon information and belief, the AstraZeneca Defendants began marketing and selling prescription brand Nexium (esomeprazole) in 2001.

69. Plaintiff began taking prescription brand Nexium (esomeprazole) in or about April 12, 2004.

70. At all relevant times, Defendants heavily marketed esomeprazole and to treat peptic disorders, including but not limited to gastroesophageal reflux disease (GERD), peptic ulcer disease, and nonsteroidal anti-inflammatory drug induced gastropathy.

71. Defendants' marketing of esomeprazole and included advertisements, press releases, web site publications, sales representative pitches and other communications.

72. Materials including advertisements, press releases, webs site publications and other communications regarding esomeprazole are part of the labeling of the drug and could be altered by Defendants without prior FDA approval.

A. General Background: Proton Pump Inhibitors

73. Proton pump inhibitors ("PPIs") are one of the most commonly prescribed

medications in the United States.

74. PPIs were introduced in 1989 with the development of Prilosec (omeprazole).

75. PPIs are indicated for the treatment of conditions such as: gastroesophageal reflux disease (GERD), dyspepsia (indigestion), acid peptic disease, Zollinger-Ellison syndrome, acid reflux, and peptic or stomach ulcers.

76. More than 15 million Americans used prescription PPIs in 2013, costing more than $10 billion.

77. However, it has been estimated that between 25% and 70% of these prescriptions have no appropriate indication.

78. Up to 70% of PPIs may be used inappropriately for indications or durations that were never tested or approved.

79. Further, 25% of long-term PPI users could discontinue therapy without developing any symptoms.

80. Esomeprazole is a PPI which works by inhibiting the secretion of stomach acid. Proton pump inhibitors diminish acid production of the active acid pumps in the stomach thereby reducing hydrochloric acid in the stomach. The drug binds with the proton pump which inhibits the ability of the gastric parietal cell to secrete gastric acid.

81. Early, it was recognized that PPIs induced hypergastrinemia and ECL cell hyperplasia.[1] Like in the early test rats, where the tumorigenesis began with hyperplasia and then developed into neoplasia of increasing malignancy, the same initial event has been found in man and has been attributed to the hypergastrinemia caused by omeprazole and all subsequent PPIs. Indeed, a study from Finland found that patients with high gastrin values in samples from the

[1] Waldum HL, Fossmark R. Proton pump inhibitors and gastric cancer: a long- expected side effect finally reported also in man. Gut. Published Online First: 20 Nov 2017. doi:10.1136/gutjnl-2017-315629.

eighties had increased risk of gastric cancer.[2]

82. During the period in which PPI products have been sold in the United States, hundreds of reports of injuries, including stomach cancer, have been submitted to the FDA in association with ingestion of esomeprazole products and other PPIs.

83. Defendants have had notice of serious adverse health outcomes regarding stomach cancer associated with PPI products through case reports, clinical studies and post-market surveillance.

84. As such, these numerous reports of stomach cancer put Defendants on notice as to the excessive risks of gastric injuries related to the use of esomeprazole.

A. The Stomach and Digestion

85. The core function of the human stomach is as an aid to digestion for which it has four key components, (1) its function as a reservoir, (2) acid secretion, (3) enzyme secretion and, (4) its role in gastrointestinal motility.

86. Acid secretion is a very important non-immunological defense against invading pathogens as well as being an important mechanism allowing for more complex diets. The regulation of acid secretion is a complex milieu of neurological, endocrine and paracrine factors to maintain an optimal acid output. Excessive acid secretion is toxic and irritant to the digestive mucosa.

87. The stomach is also an important endocrine organ producing an array of peptide hormones important for both enteric and non-enteric physiology including ghrelin and leptin.

88. In addition to the reservoir function, the stomach also plays an important motility role as a pump, which anatomically is provided by the distal two thirds of the corpus, the antrum

[2] Murphy G, Abnet CC, Choo-Wosoba H, et al. Serum gastrin and cholecystokinin are associated with subsequent development of gastric cancer in a prospective cohort of Finnish smokers. Int J Epidemiol 2017;46:914–23.

and the pylorus.

B. Physiological Balance between Gastric Acidity and Gastrin

89. Gastrin, a peptide hormone, is involved physiologically in secretion of gastric acid and growth of the gastrointestinal tract. Gastrin is released from 'G cells' in the stomach antrum, or body, during normal physiologic digestion of food and serves as a major stimulator of gastric acid secretion from the stomach parietal cells. Gastrin, once released from the G cells, travels through the bloodstream to the corpus, or body, of the stomach, where enterochromaffin-like (ECL) cells are stimulated to secrete histamine which, in turn, stimulates the parietal cells to secrete hydrochloric acid (HCl). Excessive gastrin release, with concomitant elevated levels within the blood stream, is referred to *hypergastrinemia*.

90. Cholecystokinin (CCK) is another peptide/hormone, this one produced by I-cells in the lining of the duodenum and is also released by some neurons in the brain. It acts on two types of receptors found throughout the gut and central nervous system. Its most recognized functions are also in digestion and appetite.

91. The gastrointestinal peptides gastrin and CCK have been implicated in various regulatory functions; as neurotransmitters in the brain; and in the regulation of various functions of the gastrointestinal tract, primarily at the level of the stomach, pancreas, and gallbladder.[3] In addition, they can act as physiological growth factors in most parts of the gastrointestinal tract[4,5,6]

[3] Walsh, J. H. Gastrin. in: J. H. Walsh and 0.J. Dockray (eds.). Gut Peptides: Biochemistry and Physiology, 75-121.New York: Raven Press, 1994.
[4] Hakanson, R., and Sundler, F. Trophic effects of gastrin. Scand. J. Gastroenterol., 26 (Suppl. 180): 130-136, 1991
[5] Johnson, L. R. The trophic action of gastrointestinal hormones. Gastroenterology, 70:278-288, 1976.
[6] Johnson, L. R. Trophic effects of gut peptides. in: G. M. Makhlouf (ed), Handbook of Physiology, Section 6, pp. 291-310. Bethesda, MD: American Physiological Society, 1989.

and as stimulatory growth factors in several neoplasms, such as colonic and gastric cancers.[7,8,9] The actions of CCK and gastrin are mediated by two different receptor types, CCK-A (also known as CCK1R) and CCK-B (also known as CCK2R)[10,11], which can be distinguished pharmacologically by their low (CCK-A) versus high (CCK-B) affinity for gastrin.

92. CCK-A and CCK-B/gastrin receptors have been identified in several normal tissues; CCK-B/gastrin receptors are present in the gut mucosa and in the brain.[3,12,13] The presence of receptors for gastrin and CCK in tumors has also been reported.[14] In the gastric body of the proximal stomach, the receptor mediates acid secretion as well as growth and differentiation of the epithelium.[15,16,17] In addition, CCK-B is upregulated in the gastric cardia of mice with Barrett's metaplasia, and this effect is enhanced with administration of bile acids.[18] Studies in animal models of gastrointestinal cancer have demonstrated that CCK-B signaling can accelerate tumorigenesis

[7] Smith, J. P., and Solomon, T. E. Effects of gastrin, proglumide, and somatostatin on growth of human colon cancer. Gastroenterology, 95: 1541-15481, 1988.
[8] Watson, S., Durrant, L. G., and Moths, D. Gastrin: growth-enhancing effects on human gastric and colonic tumor cells. Br. J. Cancer, 59: 554-558, 1989.
[9] Rehfeld, J. F., and van Solinge, W. W. The tumor biology of gastrin and cholecystokinin. Adv. Cancer Res., 63: 295-347,1994.
[10] Wank, S. A., Pisegna, J. R., and de Weerth, A. Brain and gastrointestinal cholecystokinin receptor family: structure and functional expression. Proc. Nati. Acad. Sci. USA, 89: 8691-8695, 1992.
[11] Kopin, A. S., Lee, Y., McBride, et al. Expression, cloning and characterization of the canine parietal cell gastrin receptor. Proc. Nail. Acad. Sd. USA, 89: 3605-3609, 1992.
[12] Mantyh, C. R.. Pappas, T. N., and Vigna, S. R. Localization of cholecystokinin A and cholecystokinin B/gastrin receptors in the canine upper gastrointestinal tract. Gastroenterology, 107: 1019-1030, 1994.
[13] Nakamura, M., Oda, M., Kaneko, K., Akaiwa, Y., Tsukada, N., Komatsu, H., and Tsuchiya, M. Autoradiographic demonstration of gastrin-releasing peptide-binding sites in the rat gastric mucosa. Gastroenterology, 94: 968-976,1988.
[14] Reubi JC, Schaer JC, Waser B. Cholecystokinin(CCK)-A and CCK-B/gastrin receptors in human tumors. Cancer Res. 1997 Apr 1;57(7):1377-86.
[15] Dockray GJ, Varro A, Dimaline R, Wang T. The gastrins: their production and biological activities. Annual review of physiology. 2001; 63:119–39.
[16] Koh TJ, Goldenring JR, Ito S, Mashimo H, Kopin AS, Varro A, Dockray GJ, Wang TC. Gastrin deficiency results in altered gastric differentiation and decreased colonic proliferation in mice. Gastroenterology. 1997; 113:1015–25.
[17] Nagata A, Ito M, Iwata N, et al. G protein-coupled cholecystokinin-B/gastrin receptors are responsible for physiological cell growth of the stomach mucosa in vivo. Proceedings of the National Academy of Sciences of the United States of America. 1996; 93:11825–30.
[18] Quante M, Bhagat G, Abrams JA, et al. Bile acid and inflammation activate gastric cardia stem cells in a mouse model of Barrett-like metaplasia. Cancer cell. 2012;21:36–51.

in vivo, such as in gastrin-overexpressing INS-GAS mice that develop proximal gastric cancers.[19]

93. Goetze et al[20], in 2013, evaluated 20 patients with gastric adenocarcinoma who underwent partial or total gastrectomy. In samples from each carcinoma, gastrin peptides were characterized, using a library of sequence-specific immunoassays. Expression was also demonstrated by immunohistochemistry. In addition, the gastrin and gastrin/CCK-B receptor gene expression was quantitated using real-time PCR, and the receptor protein demonstrated by western blotting. α-Amidated gastrins were detectable in 16 of 20 carcinomas. Moreover, progastrin and non-amidated processing intermediates, including glycine-extended gastrins, were detected in 19 carcinomas. Immunohistochemistry corroborated gastrin expression in the carcinoma cells. The gastrin/CCK-B receptor mRNA and protein were detected in all tumors leaving these researchers to conclude the results show that "…*the elements for a local loop of α-amidated gastrins and their receptor are detectable in 80% of human gastric adenocarcinomas. Therefore, the results support the contention that locally expressed gastrin may be involved in the tumorigenesis of gastric adenocarcinomas*."

94. Studies in animal models of gastrointestinal cancer have demonstrated that CCK-B signaling can accelerate tumorigenesis *in vivo*, such as in gastrin-overexpressing INS-GAS mice that develop proximal gastric cancers.[21]

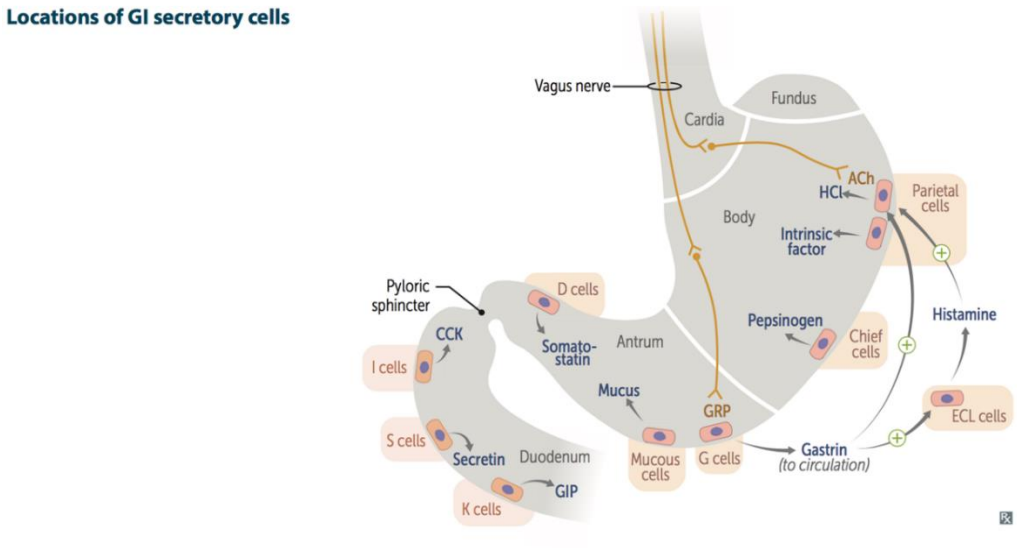
95. Hypergastrinemia, by definition, is the presence of serum gastrin levels above the normal range (~150 pg/mL). Before the 1970s, chronic hypergastrinemia was an infrequent occurrence, but when identified, it garnered considerable attention because of its level of elevation

[19] Takaishi S, Cui G, Frederick DM, et al. Synergistic inhibitory effects of gastrin and histamine receptor antagonists on Helicobacter-induced gastric cancer. Gastroenterology. 2005; 128:1965–83.
[20] Goetze JP, Eiland S, Svendsen LB, Vainer B, Hannibal J, Rehfeld JF. Characterization of gastrins and their receptor in solid human gastric adenocarcinomas. Scand J Gastroenterol. 2013 Jun;48(6):688-95. doi: 10.3109/00365521.2013.783101. Epub 2013 Apr 2.
[21] Lee Y, Urbanska AM, Hayakawa Y, et al. Gastrin stimulates a cholecystokinin-2-receptor-expressing cardia progenitor cell and promotes progression of Barrett's-like esophagus.

(~1,000 pg/mL) and association with Zollinger-Ellison syndrome and pernicious anemia. By the late 1980s, chronic hypergastrinemia was recognized with increasing frequency due to its association with gastric infection with Helicobacter pylori and, more importantly, to the widespread availability of proton pump inhibitors.

96. Gastrin induces gastric acid secretion by binding to CCK2 receptors on enterochromaffin-like cells of the gastric corpus/fundus to cause the release of histamine, which in turn stimulates the gastric parietal cells to secrete H^+ ions.

97. Once physiological levels of HCl are reached, feedback to 'D cells' within the antrum results in the release of somatostatin which 'turns off' the gastrin release.



Gastrin ↑ acid secretion primarily through its effects on enterochromaffin-like (ECL) cells (leading to histamine release) rather than through its direct effect on parietal cells.

98. This 'turning off' of gastrin release is an important physiological step for it decreases the exposure of the stomach and esophageal walls to the trophic effects of too much gastrin or hypergastrinemia.

99. Gastrin is also an important growth factor for the developing and adult digestive system, and is, in fact, trophic to the entire gastrointestinal tract. However, gastrin has also been

shown to play an important role in the stimulation of growth of several gastrointestinal cancers, including gastric and esophageal adenocarcinomas. Esophageal cancers have received more scrutiny after gastrin was found to increase COX-2 activation in Barrett's esophagus. This activation of COX-2 was shown to inhibit apoptosis, stimulate cell proliferation, promote angiogenesis, and stimulate invasion by cancer cells. The esophagus also possesses CCK2 receptors, to which gastrin can bind, and promotes tumor growth.

100. This well-recognized trophic effect of gastrin includes an effect upon the ECL cells, which are distributed throughout the *oxyntic*, or acid secreting, mucosa. ECL cells have been shown to proliferate in experimental and pathologic states associated with hypergastrinemia.

101. Since gastrin secretion is inhibited by gastric acidity, medications like H2 blockers and PPIs tend to cause hypergastrinemia. PPIs directly inhibit hydrogen ion exchange and inhibit secretion in response to all stimulatory agents, by irreversibly blocking the proton pump.

102. Proton pump inhibitors have been developed to facilitate healing of peptic ulcer disease and gastroesophageal reflux disease. Because this class of medications is very effective in suppressing acid, a consequence of long-term acid suppression can be the increase of serum gastrin levels, resulting from the interruption of the normal feedback mechanisms. Profound acid suppressive therapy leads to *hypergastrinemia* in nearly all patients.

103. For several decades there has been immense interest in the pathophysiology of gastrin, due to the increasing and extensive use of PPIs and the resulting hypergastrinemia. PPI'S are available over the counter and are used indiscriminately for treating dyspepsia, acid reflux, gastritis and peptic ulcers without appropriate indication.

104. Since the development of PPIs in the late 1980s, the significance of hypergastrinemia has become a worldwide topic of research and clinical concern.

105. H. pylori infection can, in general, also raise gastrin levels and it has become one of the most common reasons for hypergastrinemia. As a result, studies have raised concerns about the associated occurrence of neoplasms of the stomach.

106. PPIs are better inhibitors of gastric acid secretion than H2 receptor blockers and are therefore associated with higher gastrin levels.

107. Prilosec (omeprazole) has been shown to cause a 2- to 6-fold increase in serum gastrin levels in 80%–100% of patients receiving chronic therapy. Nexium (esomeprazole), after just 4 weeks of therapy, increased gastrin levels by over 3-fold. These increases reached during the initial period of omeprazole treatment remain constant during long-term therapy.

108. Up to 30% of patients on chronic PPI therapy have been shown to have gastrin blood levels greater than 500 ng/L or more than 6-fold greater than the upper limit of normal.

109. In 1990, Jensen et al[22] published the results of their open multicenter study which looked at 32 patients with chronic reflux esophagitis, initially treated with 40 mg of omeprazole for 1-2 months and subsequently treated with 20 mg. In 6 of the 32 patients, the 20-mg dose of omeprazole had to be increased to 40 mg after a mean of 6 months. Serum gastrin concentration was measured by a sensitive and specific radioimmunoassay using an antibody raised in a rabbit against synthetic unsulphated human gastrin 2-17 covalently coupled to bovine serum albumin.

110. These levels, 50 ng/L (range, 21-186 ng/L), significantly increased ($P \leq 0.01$) after l-2 months of treatment with a single daily dose of 40 mg of omeprazole to values of 172 ng/L (range, 36-378 ng/L)). Subsequent maintenance treatment for 3 months with a lower dose of 20 mg of omeprazole did not significantly reduce these fasting serum gastrin levels, 156 ng/L (range, 31-420), compared with the levels obtained during treatment with the 40-mg dose.

[22] Jan B.M.J. Jansen J.B.M.J, Klinkenberg-Knol EC, S.G.M. Meuwissen, et al. Effect of Long-Term Treatment With Omeprazole on Serum Gastrin and Serum Group A and C Pepsinogensin Patients with Reflux Esophagitis.

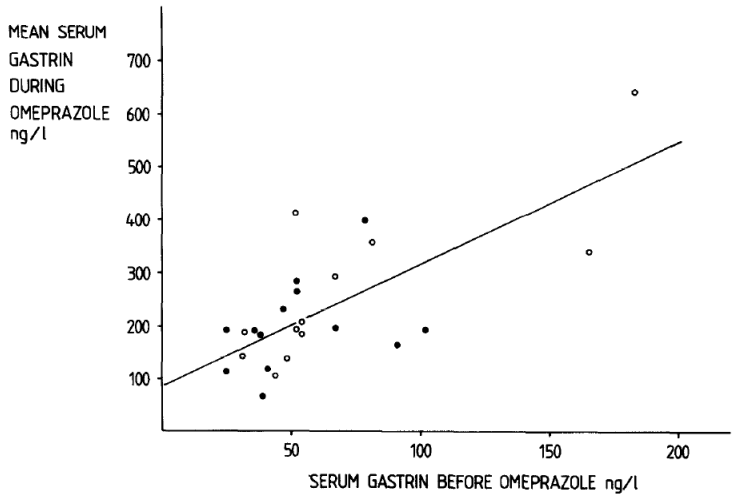


Figure 2. Linear regression analysis between the serum gastrin concentration before omeprazole treatment and the mean of individual serum gastrin levels during treatment. (○) women; (●) men. There was a significant ($P < 0.001$) correlation between these parameters as indicated by the equation of the curve: $y = 2.2x + 89.5$ ($r = 0.7118$, $n = 25$).

111. When gastrin levels in individual patients obtained during different time intervals were analyzed, a strong but slow tendency toward steadily increasing serum gastrin levels with time was observed. In the study by Jensen et al, 8 of the 32 patients achieved basal serum gastrin concentrations over 500 ng/L., i.e., more than 10 times the median level and more than 6 times the upper limit of normal, during omeprazole treatment.

C. Gastric Cancer

112. Gastric cancer is the third leading cause of cancer-related mortality in the world. The large majority (approximately 90%) of gastric cancers are adenocarcinomas, which arise from the glands of the most superficial layer, or the mucosa, of the stomach. The number of new cases of stomach cancer in the U.S. is between 5 - 6 per 100,000 per year.

113. Stomach cancer is most frequently diagnosed among people aged 65-74 and the median age at diagnosis is 68.

114. The overall 5-year relative survival rate of all people with stomach cancer in the United States is about 29%. Those diagnosed early, with stage IA or IB disease, have a 5-year survival rate between 88% and 94% while those unfortunate to develop Stage IV disease have a 0 to 4% 5-year survival rate.

115. The gram-negative bacterium, H. pylori, chronically infects the human gastric mucosa and causes chronic gastritis in virtually all people infected with the bacterium. In many of them, this persistent inflammation ultimately leads to loss of the normal architecture of the gastric mucosa, with disappearance of the gastric glands and specialized cells. This resulting *atrophic mucosa* and *intestinal metaplasia* increase the risk of dysplasia and gastric cancer. In 1994, H. pylori was classified as a Class 1 carcinogen by IRAC.

116. The bacteria, H. pylori, has been shown in multiple studies to result in hypergastrinemia secondary to oxyntic (the secretory cells which produce hydrochloric acid) atrophy; PPIs, as discussed above, have also been shown to result in clinically significant hypergastrinemia.

117. Several types of endocrine cells are found in throughout the gastric mucosa including gastrin-producing cells (G cells), enterochromaffin-like cells (ECLs), and the A cells which produce glucagon. "*It is not unusual that excessive and sustained stimulation of an endocrine cell population results in hyperplasia, and eventually neoplasia*."[23]

D. Proton Pump Inhibitors and Gastric Cancer

118. "*The first compound accepted for use in humans after having induced cancer in its target organ*" – gastroenterologist Kenneth Wormsley's words about the acceptance of omeprazole for clinical use.[1]

119. The gastric cancer risk linked to PPI treatment should have been anticipated by the manufacturers as early as in the late 1980s.[1] Around 1980, it became clear that hypergastrinemia resulted in ECL cell neuroendocrine tumors.

[23] (New Drug Application. Capsules Losec [Omeprazole, MSD]; Volume 1.30; Volume 30 of 105. Merck Sharp & Dohme Research Laboratories. On the Mechanism Behind the Development of Gastric Carcinoids in the Rat with Special Reference to Man. Safety Aspects. 1986-06-24 - Enar Carlsson, PhD and Lennart Solvell, MD. June 24, 1986 at OND00391298.)

120. The interest in such tumors increased dramatically in 1985 when it was reported that the 'insurmountable histamine-2 blocker', loxtidine, caused ECL cell tumors in the rat.[1] Shortly afterwards, similar tumors were found in rats treated long-term with omeprazole.

121. These two compounds, the PPIs and loxtidine, differ chemically as well as pharmacologically, and it was therefore evident that the carcinogenic effect was due to their biological effect: inhibition of gastric acid secretion leading to hypergastrinemia causing proliferation of the target cell of gastrin, the ECL cell.

122. As a result, while Glaxo Wellcome (now GlaxoSmithKline) stopped developing loxtidine; however, AstraZeneca, ignoring the same red flag, continued with omeprazole in clinical trials.

123. Following this discovery, meetings were set up by the PPI manufacturer with gastric pathologists and gastroenterologists and it was concluded, at that time, that the ECL cell did not play any appreciable role in human gastric carcinogenesis.[1] Omeprazole was then accepted for use in patients with severe diseases due to gastric acid hypersecretion.

124. However, researchers soon showed that gastric adenocarcinomas, in fact, originated from the ECL cell. Subsequent research showed that gastric cancers of the *diffuse type*, according to the Lauren classification[24], showed neuroendocrine/ECL cell markers in a high proportion which increased when improving the sensitivity without reducing the specificity of the immunohistochemical method. By this method, virtually all gastric carcinomas in patients with *anacidity*, the absence of hydrochloric acid in the gastric juice, showed ECL cell markers and accordingly were malignant neuroendocrine tumors.

125. Significantly, the cancer cells in the signet ring subgroup of gastric carcinomas of

[24] Lauren P. The two histological main types of gastric carcinoma: diffuse and so-called intestinal-type carcinoma. An attempt at a histoclinical classification. Acta Pathologica Et Microbiologica Scandinavica. 1965;64:31–49.

diffuse type, express neuroendocrine markers abundantly.

126. Recently, in 2018, researchers have also found that an important proportion of human gastric carcinomas, including adenocarcinomas, express the gastrin receptor confirming previously published research.

127. The role of gastrin in gastric carcinogenesis is also supported by the recent work by researchers, including those from the Division of Cancer Epidemiology and Genetics of the National Cancer Institute, supported in part by the Intramural Research Program of the NIH and the National Cancer Institute and by the U.S. Public Health Service and National Cancer Institute, Department of Health and Human Services.

128. Murphy et al[2] reported that those with high gastrin had an increased risk of gastric non-cardia adenocarcinomas (fully adjusted OR: 1.92; 95% CI: 1.21, 3.05) and gastric carcinoids.

129. Moreover, the claim that the ECL cell was insignificant in gastric carcinogenesis was flawed; ECL-derived gastric carcinomas had been described already in the late 1970s.

130. Various medical and scientific groups around the world, for 30 years and more, have investigated, and published, on the role of gastrin and the risk of PPI treatment with respect to gastric cancer. The medical literature is replete with publications reporting on this association.

131. While researchers concluded, and published, that PPI treatment in the long term would cause gastric cancer, the manufacturers of PPIs have not done studies to dismiss the published results. "*However, the gastric cancer risk linked to PPI treatment should have been anticipated as early as in the late 1980s*."[1] In 2017, a study from Finland found that patients with high gastrin values in samples from the 1980s had increased risk of gastric cancer. For every unit increase in gastrin, the OR for gastric cancer was 1.23 (adjusted model; 95% CI: 1.04, 1.45).[2] Those with higher gastrin had a significantly increased risk of gastric non-cardia adenocarcinomas

(fully adjusted OR: 1.92; 95% CI: 1.21, 3.05) and this trend was statistically significant (P=0.002). Serum gastrin was also significantly associated with risk of gastric carcinoids, (age-adjusted continuous model OR: 4.67; 95% CI: 2.67, 8.15), though the small number of carcinoid cases meant the fully adjusted model was unstable.

132. Waldum et al have long proposed that the carcinogenic effect of H. pylori infection is best explained by the hypergastrinemia secondary to oxynticatrophy and have concluded that the carcinogenic effect by PPI treatment is due to hypergastrinemia, "*which should have been realized decades ago before exposing so many patients to a risk of a serious disease*."[2]

i. Epidemiology of the Link Between PPI Ingestion and Gastric Cancer

133. In 2006, Garcia Rodriguez et al conducted a case–control study, based on the General Practice Research Database and reported that current PPI users with more than 3-years of use experienced a threefold increased risk (OR 3.0, 95% CI: 1.0–9.0) of non-cardia gastric cancer, whereas current long-term users of histamine-2 antagonists (H_2RA), such as Zantac and Tagamet, had no excess risk (OR 0.9, 95% CI: 0.5–1.8).[25]

134. In 2008, Tamim et al conducted a nested case-control study among people registered in the Quebec, Canada health insurance plan.[26] The exposure definition in the 5 years preceding the index date was based on the defined daily doses of acid-suppressive drugs and categorized into quartiles.

135. The adjusted odds ratios (ORs) for the association between exposure to acid-suppressive drugs and risk of gastric cancer were 1.47 (95% CI 1.23, 1.76), 1.32 (95% CI 1.10, 1.58), 1.48 (95% CI 1.24, 1.77) and 1.18 (95% CI 0.97, 1.44) for the first, second, third and fourth

[25] Garcia Rodriguez LA, Lagergren J, Lindblad M (2006) Gastric acid suppression and risk of oesophageal and gastric adenocarcinoma: a nested case control study in the UK. Gut 55: 1538 – 1544).
[26] Tamim H, Duranceau A, Chen LQ, et al. Association between use of acid-suppressive drugs and risk of gastric cancer: A nested case-control study. Drug Saf 2008;31:675–684.

exposure quartiles, respectively.

136. In 2009, Poulsen et al published the results of their population-based cohort study within North Jutland County, Denmark with its approximately 500,000 inhabitants.[27] Using the Danish Civil Registration System that has provided information on vital status and residence for the entire population since 1968, they identified all individuals aged 40–84 years during the study period and resident in North Jutland County on January 1, 1989.

137. They observed 109 cases of gastric cancer among PPI users and 52 cases among H2RA users. The overall incidence rate ratios (IRR) of gastric cancer was 9.0 (95% CI: 6.9–11.7) among PPI users without taking into consideration the lag time. However, after incorporating the 1-year lag time, they observed IRRs for gastric cancer of 1.2 (95% CI: 0.8–2.0) among PPI users and 1.2 (95% CI: 0.8–1.8) among H2RA users compared with non-users.

138. They concluded that the increased incidence of gastric cancer associated with PPI use observed in their study, along with earlier studies, was "*likely to result from confounding by indication*"; nevertheless, they also stated that "*we cannot not rule out the possibility of a causal association* between long-term PPI use and risk of gastric cancer and suggested, "*more studies be conducted*".

139. In 2009, Duan et al conducted a population-based case-control study and recruited patients with incident esophageal adenocarcinoma (n = 220), gastric cardiac adenocarcinoma (n = 277), or distal gastric adenocarcinoma (n = 441) diagnosed between 1992 and 1997, and 1,356 control participants in Los Angeles County.[28]

140. They found that, amongst participants who took nonprescription acid neutralizing

[27] Poulsen AH, Christensen S. McLaughlin JK, et al. Proton pump inhibitors and risk of gastric cancer: a population-based cohort study. Br J Cancer. 2009 May 5; 100(9): 1503–1507.
[28] Duan L, Wu AH, Sullivan-Halley J, Bernstein L. Antacid drug use and risk of esophageal and gastric adenocarcinomas in Los Angeles County. Cancer Epidemiol Biomarkers Prev 2009; 18: 526-533.

agents for >3 years, the odds ratio for *esophageal adenocarcinoma* was 6.32 compared with never users. However, the regular use of nonprescription acid neutralizing agents was not associated with risk of adenocarcinomas of the gastric cardia or distal stomach. Furthermore, regular use of prescription acid suppressive drugs was also not associated with risk for any of these cancers.

141. In 2013, Ahn et al conducted a meta-analysis of both case-control and cohort studies to date looking at the association between PPIs, H2Ras and gastric cancer.[29] Just 4 of the 11 studies Ahn et al included within their analysis included PPIs; the remaining 7 involved H2-receptor antagonists alone. An increased risk of gastric cancer was found with PPI use [adjusted OR = 1.39; 95%CI: 1.19-1.64] leading the authors to conclude,

> "[*T]here is biological evidence of the effect of acid suppressive drug use on the risk of gastric cancer. First, PPIs and H_2Ras (H_2-receptor antagonists) can reduce gastric acidity by modulating H(+)-K(+) ATPase or competitive inhibitors of histamine binding sites in gastric parietal cells. Decreased gastric acidity, whether caused by gastric atrophy or acid suppressive drug-induced hypochlorhydria, may result in increased bacterial colonization and a greater number of bacteria that can produce nitrosamines [Refs], which are compounds that are associated with an increased risk of gastric adenocarcinoma[Ref]*.
>
> *"Second, the reduction of gastric acid secretion by acid-suppressive drugs switches on the positive feedback of a gastric acid-producing cascade, which leads to hypergastrinemia [Ref]. This condition is a possible cause of carcinoids, gastric polyps, and gastric and colonic carcinomas because elevated serum gastrin could have a trophic effect on neoplastic growth in the gastrointestinal tract [Ref]. The use of long-term PPIs can cause hyperplasia in enterochromaffin-like cells and increase the incidence of*

[29] Ahn JS, Eom CS, Jeon CY, et al. Acid suppressive drugs and gastric cancer: A meta-analysis of observational studies. World J Gastroenterol 2013;19:2560–2568.

> *atrophic gastritis and gastric polyps, which are a precursor to gastric cancer*."

142. In 2016, Tran-Duy et al, performed a systematic review with a meta-analysis of randomized controlled trials and observational studies that assessed the risks of PPI therapy of fundic gland polyps (FGPs) and gastric cancer.[30] They calculated a pooled odds ratio for FGPs and the risk ratio for gastric cancer in PPI users compared with PPI nonusers from data from 12 studies, comprising more than 87,324 patients. The pooled risk ratio for gastric cancer was 1.43 (95% CI, 1.23–1.66) from each model.

143. For cases with exposure of less than 12 months, the pooled effect was 1.76 (1.24, 2.52) under the fixed-effect model and 1.76 (1.24, 2.52) under the random-effect model. For PPI usage > 36 months, the pooled effect relative risk was a statistically significant 2.45 (1.41, 4.25) under both statistical methods.

144. In 2017, Cheung et al[31] performed a population-based case-control study designed to determine the risk of gastric cancer development among individuals who had received treatment for H. pylori with focus on the role of long-term PPIs, which was published on October 31, 2017.

145. To remove the potential confounding effects of symptoms from gastric cancer leading to the use of PPIs or H2RA (i.e., protopathic bias), prescriptions of these agents started within 6 months prior to the gastric cancer diagnosis were excluded. Since gastric cancer can masquerade as non-healing ulcer, all patients with gastric ulcer diagnosed at the time of or any time after receiving triple therapy were excluded. Because previous studies have not revealed any association between gastric cancer development and exposure to H_2RA medication, e.g., Tagamet,

[30] Tran-Duy A, Spaetgens B, Hoes AW, et al. Use of proton pump inhibitors and risks of fundic gland polyps and gastric cancer: systematic review and meta-analysis. Clin Gastroenterol Hepatol 2016;14:1706–19.
[31] Cheung KS, Chan EW, Wong AYS, et al. Long-term proton pump inhibitors and risk of gastric cancer development after treatment for Helicobacter pylori: a population-based study. Gut 2018;67:28–35.

H_2RA was selected as a negative control exposure in this study.

146. PPIs users (at least weekly use) were found to have a higher risk of gastric cancer (HR 2.44, 95% CI 1.42 to 4.20) after adjustment. After stratification by the site of tumor, PPIs use was found to be significantly associated with an increased risk of non-cardia gastric cancer (HR 2.59, 95% CI 1.42 to 4.72) but not cardia cancer (HR 1.97, 95% CI 0.57 to 6.82). However, while the increase in HR was limited to non-cardia cancer, they noted that this result should be interpreted with caution as this subgroup analysis has a relatively small number of cardia cancers.

147. Cheung et al found a statistically significant hazard ratio (HR) of 2.43 with weekly < daily use; HR 4.55 with daily use; and an impressive HR of 5.04 in weekly to < daily users with ≥ 1-year exposure, HR of 6.65 with ≥ 2 years and HR 8.34 with ≥ 3 years exposure, supporting The Bradford Hill viewpoints of both 'consistency' and a 'biological gradient'.

148. Over-all, their results showed that, even after apparent successful H. pylori eradication therapy, those who used long-term PPIs had a 2.4-fold increase in the risk of gastric cancer development than non-users. Further analysis demonstrated a dose-dependent and time-dependent increase in the HRs of gastric cancer with PPIs use, with the highest risk observed in daily users of PPIs (HR 4.55). Patients who took PPIs daily for ≥3 years were at the highest risk (HR 8.34).

149. On the same day that the above-mentioned Cheung et al epidemiological study was published, Brusselaers et al's "nationwide population-based cohort study which included virtually all adults residing in Sweden exposed to maintenance therapy with PPIs" was also published.[32]

150. Maintenance use of PPI was defined as at least 180 days during the study period and maintenance use of H_2 receptor antagonist was evaluated for comparison reasons.

[32] Brusselaers N, Wahlin K, Engstrand L, Lagergren J. Maintenance therapy with proton pump inhibitors and risk of gastric cancer: a nationwide population-based cohort study in Sweden. BMJ Open. 2017 Oct 30;7(10):e017739.

151. Among 797,067 individuals on maintenance PPI therapy, the standardized incidence ratios (SIR) of gastric cancer was over three-fold increased (SIR=3.38, 95% CI 3.23 to 3.53) to a statistically significant degree. Increased SIRs were found in both sexes and all age groups but were especially increased among PPI users younger than 40 years with a massive SIR of 22.76 (95% CI 15.94 to 31.52). The association was similar for cardia and non-cardia gastric cancer. Long-term users of H_2 receptor antagonists, which have the same indications as PPIs, again, were not at any increased risk.

152. In December 2017, Niikura et al[33], as a result of having…

> "…*concerns about the limitations of (the Cheung) study, in particular the lack of endoscopic and histological examinations, the results of which could influence the association between PPI use and gastric cancer…in particular the lack of endoscopic and histological examinations, the results of which could influence the association between PPI use and gastric cancer*," (performed a) "…*retrospective cohort analysis with intensive microscopic and pathological examinations to confirm the impact of acid-suppressing drugs on the incidence of gastric cancer in patients who received eradication therapy*."

153. They noted that *"[T]he presence of gastric atrophy and intestinal metaplasia (IM) in H. pylori-infected patients is an independent risk factor for gastric cancer*" and, that in a previous study which they had conducted they had noted a 7.6-fold increase in the risk of gastric cancer in patients who have intestinal metaplasia throughout the stomach compared with patients who have no intestinal metaplasia even after eradication; thus, gastric atrophy and intestinal metaplasia may be major confounders in estimating the risk of gastric cancer.

[33] Niikura R, Hayakawa Y, Hirata Y, et al. Long-term proton pump inhibitor use is a risk factor of gastric cancer after treatment for Helicobacter pylori: a retrospective cohort analysis. Gut. 2017 Dec 22.

154. Specifically, in the subgroup of patients with mild IM (antrum only), PPI was associated with a markedly increased risk of gastric cancer (aHR 16.0), while in the subgroups of patients with no and severe IM (including the corpus), no significant association between drug use and risk of gastric cancer was observed.

155. They concluded,

> "*Our past and current studies confirmed a distinct risk of gastric cancer in patients with IM. A greater risk in patients with IM in PPI users may suggest that strong acid suppression by PPI and IM synergistically increase the risk of gastric cancer, perhaps due to subsequent hypergastrinemia, gastric dysbiosis or other mechanism(s).*"

156. In April 2018, Lai et al used the 2000–2013 database of Taiwan National Health Insurance Program to conduct a population-based case–control study.[34] Only those subjects whose first-time prescriptions for proton pump inhibitors were noted >12 months before the index date could be included in order to adjust for 'confounding by indication'.

157. The odds ratios of gastric cancer were 1.59 (95% CI 1.24 to 2.05) for subjects with cumulative duration of proton pump inhibitors use ≤6 months; however, the OR was 2.00 (95% CI 1.36 to 2.95) for subjects with cumulative duration of proton pump inhibitors use >6 months compared with never use.

158. They concluded that after excluding immortal time bias and latency bias, proton pump inhibitors use is associated with increased odds of gastric cancer, which appeared to be duration dependent.

159. In April 2018, Wan et al[35] published the results of their meta-analysis looking at

[34] Lai SW, Lai HC, Lin CL, Liao KF. Proton pump inhibitors and risk of gastric cancer in a case-control study. Gut. 2018 Apr 16. pii: gutjnl-2018-316371. doi: 10.1136/gutjnl-2018-316371. [Epub ahead of print])

[35] Wan QY, Wu XT, Li N, Du L, Zhou Y. Long-term proton pump inhibitors use and risk of gastric cancer: a meta-analysis of 926,386 participants.

the associations between long-term PPIs use and risk of gastric cancer. Wan et al evaluated the Peng, Cheung, Brusselaers, Niikura, Poulsen, Tamim, Rodriguez studies in their meta-analysis and found that participants with long-term PPIs use had over twofold risk of gastric cancer (OR 2.10; 95% CI 1.10 to 3.09; I^2=97.3%; $P_{heterogeneity}$ <0.001), and this result was similar to the studies by Cheung et al and Peng et al.

160. Also, in 2018 Peng et al[36] published the results of their performed a case–control study to investigate the association of PPIs use and risk of gastric cancer using data from a nationwide population database, the National Health Insurance Research Database (NHIRD) in Taiwan in addition to using sub dataset of the NHIRD, which comprises one million randomly sampled beneficiaries enrolled in the NHI program in 2000 (Longitudinal Health Insurance Database 2000).

161. Patients aged ≥20 years with newly diagnosed gastric cancer were selected for the case group. Patients were excluded if they had taken a PPI within 1 year before the index date, again, to adjust for 'confounding by indication'.

162. The adjusted OR for gastric cancer risk in patients who received a PPI compared with that in patients without PPI use was 2.48 (95% CI 1.92 to 3.20). Compared with controls, PPI users had risk for proximal gastric cancer (adjusted OR=2.58, 95% CI 1.38 to 4.83), distal gastric cancer (adjusted OR=3.33, 95% CI 1.97 to 7.45), unspecified gastric cancer (adjusted OR=2.64, 95% CI 1.92 to 3.63) and others (adjusted OR=2.66, 95% CI 1.95 to 3.63), respectively.

163. Also, in 2018 Lai et al[34], "*(I)n order to clarify the relationship between proton pump inhibitors use and gastric cancer…used the 2000–2013 database of Taiwan National Health Insurance Program to conduct a population-based case–control study*".

[36] Peng Y-C, Huang L-R, Lin C-L, et al. Gut Epub ahead of print: doi:10.1136/gutjnl-2018-316057

164. Importantly, these researchers stated that, "*In order to reduce the latency bias, subjects whose first-time prescriptions for proton pump inhibitors were noted ≤12 months before the index date were excluded from the study. Therefore, only those subjects whose first-time prescriptions for proton pump inhibitors were noted >12 months before the index date could be included. In addition, subjects with other cancers before the index date were excluded*".

165. Lai et al found ORs of gastric cancer were 1.59 (95% CI 1.24 to 2.05) for subjects with cumulative duration of proton pump inhibitors use ≤6 months and 2.00 (95% CI 1.36 to 2.95) for subjects with cumulative duration of proton pump inhibitors use >6 months compared with never use.[34]

166. Lai et al also noted that, "*Misclassifications of proton pump inhibitors exposure is not likely in the case and the control groups. Thus, immortal time bias is less likely to happen". They concluded that, after excluding immortal time bias and latency bias, proton pump inhibitors use is associated with increased odds of gastric cancer, which seems to be duration-dependent*."

167. The epidemiological confounders of 'protopathic bias' and 'confounding by indication' are frequently used interchangeably and have to do with the potential in some observational epidemiological studies for the condition under study, e.g., gastric cancer, to, itself, cause the symptoms, e.g., 'heartburn', leading to the subsequent use of PPIs and *then* a diagnosis of gastric cancer. In such a case, the PPIs would not have 'caused' the gastric cancer (though they may have significantly contributed to the progression of the cancer by elevating gastrin levels). More specifically, "…*in pharmacoepidemiological studies, protopathic bias occurs when a pharmaceutical agent is prescribed for an early manifestation of a disease that has not yet been diagnostically detected, which then appears to be the cause of the disease when it is eventually*

diagnosed".[37]

168. There are several steps researchers, including epidemiologists, can employ to minimize, if not eradicate, the potential confounder of protopathic bias (or confounding by indication).

169. To control for protopathic bias, some studies have incorporated the concept of lag-time into their exposure definition (time period before the index date that was not considered in assessing exposure).

170. Tamim et al[38], in 2007, introduced "…*a procedure to identify the best lag-time to be applied in studies where control for protopathic bias is required*". Serendipitously, they used "…*data from a case-control study carried out to assess the association between exposure to proton pump inhibitors (PPIs) and risk of gastric cancer, using RAMQ databases*".

171. Exposure was defined as "…*the number of defined daily doses of PPIs dispensed during the 5-year period prior to the index date (divided into four quartiles)*". Thirty-one different lag-times were applied (0–30 months) based on 1-month intervals. Logistic regression was used to estimate the matched odds ratio for each lag-time.

172. They found that a "…*trend of decreasing ORs was found with the application of an increasing lag-time. As an illustration, the ORs for the 1st quartile of defined daily doses, when applying the 31 different lag-times, ranged between 3.52 when applying a 0 lag-time and 0.97 when applying a 30 months lag-time. Applying the two methods for the different lag-times showed that the ORs stabilized at around 6 months*" leading them to conclude that, "*(F)or the purpose of controlling for protopathic bias in pharmacoepidemiological studies, we have provided a method to assess the most appropriate lag-time that should be applied for the assessment of drug*

[37] Tamim H, Monfared AAT and J. LeLorier. Application of lag-time into exposure definitions to control for protopathic bias. Pharmacoepi Drug Safety 2007; 16: 250–258.

exposure."

173. The study by Murphy et al[2], discussed *supra*, noted that *"(T)he temporal nature of the association between serum gastrin and CCK and risk of gastric cancer was explored in a series of lag analyses…Cases were divided into those occurring with 5 years of serum collection/baseline, between 5 and 10 years of baseline, and more than 10 years after baseline serum collection. For those with high serum gastrin, risk of (non-cardia gastric adenocarcinoma) was highest for those diagnosed more than 10 years after baseline blood draw compared with those with normal gastrin concentrations. In this group, each unit increase in gastrin (log-scale) was associated with a 55% increase in risk of GNCA (OR:1.55; 95% CI: 1.24, 1.95)".*

174. Each study since October 31, 2017 has considered and taken appropriate steps to minimize protopathic bias.

175. Cheung et al[31], *"(T)o remove the confounding effects of symptoms from gastric cancer leading to the use of PPIs or histamine 2-receptor antagonist (H2RA) (ie, protopathic bias), prescriptions of these agents started within 6 months prior to the gastric cancer diagnosis were excluded"*, consistent with the mathematical model published by Tamim et al.[38]

176. Brusselaers et al[32], *"(T)o assess reverse causality (protopathic bias)"* conducted a sensitivity analysis excluding all cancer cases occurring within 1 year of the start of the study; six months more than that deemed necessary by Tamim et al.[39]

177. Peng et al[38] excluded patients if they had taken a PPI within 1 year before the index date.

178. Lai et al[34], to reduce the latency bias, excluded subjects whose first-time prescriptions for proton pump inhibitors were noted ≤12 months before the index date.

[38] Peng Y-C, Huang L-R, Lin C-L, et al. Gut Epub ahead of print: doi:10.1136/gutjnl-2018-316057

179. To date, Defendants' esomeprazole products lack detailed risk information for stomach adenocarcinomas, carcinoid tumors and gastric neuroendocrine tumors, despite science stating otherwise. The June 2018 product insert for omeprazole magnesium merely advises prescribers (and patients) that "…*the symptomatic response to therapy does not preclude the presence of gastric malignancy. Consider additional follow-up and diagnostic testing in adult patients who have suboptimal response or an early symptomatic relapse after completing treatment with a PPI. In older patients also consider an endoscopy*."[39] In other words, a 'pre-existing malignancy'.

180. In addition, the June 2018 'HIGHLIGHTS OF PRESCRIBING INFORMATION' product insert adds, "*Interactions with Diagnostic Investigations for Neuroendocrine Tumors: Increased chromogranin A (CgA) levels may interfere with diagnostic investigations for neuroendocrine tumors, temporarily stop NEXIUM at least 14 days before assessing CgA levels*."[40]

181. Once again, this language does not *warn* healthcare practitioners, nor patients, of the association between the long-term ingestion of the PPIs and the *development* of gastric malignancies including adenocarcinomas, carcinoid tumors and signet-ring carcinomas; instead, merely of the possibility of PPIs interfering with the diagnosis of these gastric malignancies.

182. Defendants knew or should have known of the risk of stomach cancer based on the data available to them or that could have been generated by them, including but not limited to animal studies, mechanisms of action, pharmacodynamics, pharmacokinetics, pre-clinical studies, clinical studies, animal models, genetic models, analogous compounds, analogous conditions, adverse event reports, case reports, post-marketing reports and regulatory authority investigations.

[39] https://www.drugs.com/pro/nexium.html
[40] https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/021153s053,022101s017,021957s020lbl.pdf

183. Despite their knowledge of the risks of stomach cancer associated with esomeprazole, Defendants took no action to inform Plaintiff or Plaintiff's physicians of this known risk. Instead, Defendants continued to represent that esomeprazole did not pose any risks of stomach cancer in humans. They promoted and marketed esomeprazole as safe and effective for persons such as Plaintiff throughout the United States, including the State of Georgia.

184. Defendants knew of the significant risk of stomach cancer that could result from esomeprazole use, but Defendants did not adequately and sufficiently warn consumers, including Plaintiff's physician or the medical community in a timely manner.

185. Even if used as directed, Defendants failed to adequately warn against the negative effects and risks associated with this esomeprazole including, but not necessarily limited to, long term usage and the cumulative effects of long-term usage.

186. In omitting, concealing, and inadequately providing critical safety information regarding the use of esomeprazole to induce its purchase and use, Defendants engaged in, and continue to engage in, conduct likely to mislead consumers including Plaintiff. This conduct is fraudulent, unfair, and unlawful.

187. Despite clear knowledge that long-term usage of esomeprazole products cause a significantly increased risk of stomach cancer, acute and kidney injuries, Defendants continued to market and sell esomeprazole products without warning consumers or healthcare providers of these significant risks.

188. Even if used as directed, persons who ingested esomeprazole, such as Plaintiff, have been exposed to significant risks stemming from unindicated and/or long-term usage.

189. The June 2018 'HIGHLIGHTS OF PRESCRIBING INFORMATION' advises that the use of 20 mg or 40 mg Nexium, in adults be for "Once daily for 4 to 8 weeks" while, for young

adults, ages 12-17 the duration of treatment is "Once daily for up to 8 weeks" and, in patients aged 1 to 11, the duration of treatment is, also, "Once daily for up to 8 weeks".[41]

190. However, the Product Inserts, both the 'Fulling Prescribing' insert and the 'Highlights' version on the FDA's website fail to warn both the prescribers and the consumers of the well-recognized propensity of the PPIs to cause '*rebound acid hypersecretion*'; in other words, the cessation of proton-pump inhibitor therapy induces the very symptoms it is used to treat, often to an even worse degree.

191. Rebound acid hypersecretion is defined by the FDA as an increase in gastric acid secretion above pretreatment levels after antisecretory therapy.[42]

192. This phenomenon was reported as early as 1988 when Larsson et al[43] reported that female rats treated orally for 3 months with omeprazole experienced total inhibition of gastric acid secretion and resultant hyperplasia of the gastric oxyntic, or acid producing, mucosa. The results suggested that hypergastrinemia, induced in the rat by pharmacological inhibition of gastric acid secretion, caused a hyperplasia of oxyntic mucosal cells.

193. This phenomenon was then observed in humans by many

[41] https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/021153s053,022101s017,021957s020lbl.pdf
[42] US Food and Drug Administration. Rebound of gastric acid secretion. 2000. http://www.fda.gov/ohrms/dockets/ac/00/backgrd/3650b1a_11.pdf.
[43] Larsson H, Carlsson E, Ryberg B, Fryklund J, Wallmark B. Rat parietal cell function after prolonged inhibition of gastric acid secretion. Am J Physiol 1988; 254: G33–9.

researchers[44,45,46,47,48,49,50,51,52,53,54] and has been observed within 2 weeks after withdrawal of treatment.[55]

194. Reimer et al, in 2009, published the results of their randomized, double-blind, placebo-controlled trial (RCT) which was conducted between September 2007 and March 2008.[56] Healthy volunteers, without acid-related disease or symptoms, were chosen as the study population to establish that the symptoms observed were actually symptoms caused by the acid rebound phenomenon and not relapse of symptoms of underlying disease after discontinuation of treatment.

195. The results of this RCT by Reimer et al established that rebound acid hypersecretion caused by ingestion of PPIs was clinically significant, inducing acid-related symptoms like heartburn, acid regurgitation, and dyspepsia.

196. The duration of rebound acid hypersecretion continued 4 weeks after

[44] Waldum HL, Arnestad JS, Brenna E, et al. Marked increase in gastric acid secretory capacity after omeprazole treatment. Gut 1996; 39: 649–53.
[45] Gillen D, McColl KE. Problems related to acid rebound and tachyphylaxis. Baillieres Best Pract Res Clin Gastroenterol. 2001; 15: 487–95.
[46] Gillen D, Wirz AA, Ardill JE, McColl KE. Rebound hypersecretion after omeprazole and its relation to on treatment acid suppression and Helicobacter pylori status. Gastroenterology 1999; 116: 239–47.
[47] Reimer C, Søndergaard B, Hilsted L, Bytzer P. Gastroenterology. Proton-pump inhibitor therapy induces acid-related symptoms in healthy volunteers after withdrawal of therapy. 2009 Jul;137(1):80-7, 87.e1. doi: 10.1053/j.gastro.2009.03.058. Epub 2009 Apr 10.
[48] Laine L, Ahnen D, McClain C, et al. Review article: potential gastrointestinal effects of long-term acid suppression with proton pump inhibitors. Aliment Pharmacol Ther 2000;14:651–668.
[49] Sanduleanu S, Stridsberg M, Jonkers D, et al. Serum gastrin and chromogranin A during medium- and long-term acid suppressive therapy: a case-control study. Aliment Pharmacol Ther 1999;13: 145–153.
[50] Waldum HL, Sandvik AK, Syversen U, et al. The enterochromaffin-like (ECL) cell. Physiological and pathophysiological role. Acta Oncol 1993;32:141–147.
[51] Pezeshkian S, Conway SE. Proton Pump Inhibitor Use in Older Adults: Long-Term Risks and Steps for Deprescribing. Consult Pharm. 2018 Sep 1;33(9):497-503. doi: 10.4140/TCP.n.2018.497.
[52] Singh A, Cresci GA, Kirby DF. Proton Pump Inhibitors: Risks and Rewards and Emerging Consequences to the Gut Microbiome. Nutr Clin Pract. 2018 Oct;33(5):614-624. doi: 10.1002/ncp.10181. Epub 2018 Aug 2.
[53] Kim J1, Blackett JW1, Jodorkovsky D2. Strategies for Effective Discontinuation of Proton Pump Inhibitors. Curr Gastroenterol Rep. 2018 May 16;20(6):27. doi: 10.1007/s11894-018-0632-y.
[54] McColl KE, Gillen D. Evidence that proton-pump inhibitor therapy induces the symptoms it is used to treat. Gastroenterology. 2009 Jul;137(1):20-2.
[55] Reimer C, Søndergaard B, Hilsted L, Bytzer P. Gastroenterology. Proton-pump inhibitor therapy induces acid-related symptoms in healthy volunteers after withdrawal of therapy. 2009 Jul;137(1):80-7, 87.e1. doi: 10.1053/j.gastro.2009.03.058. Epub 2009 Apr 10.
[56] Id

discontinuation of PPIs in the RCT, consistent with the findings from two other studies showing increased acid secretory capacity ≥ 8 weeks after discontinuation of therapy.[57,58]

197. An editorial also published in 2009, stated that "*The current finding that these drugs induce symptoms means that such liberal prescribing is likely to be creating the disease the drugs are designed to treat and causing patients with no previous need for such therapy to require intermittent or long-term treatment*."[59]

198. The practical, 'real-world' effect of this PPI-induced rebound acid hypersecretion is the inability of many users of PPIs for the recommended length of time (4 to 8 weeks) to be able to 'quit' the PPIs, creating, in fact, a class of patients 'dependent' upon PPIs and having to utilize them for years at a time.

199. Consumers, including Plaintiff and Plaintiff's physicians relied on the Defendants' false representations and were misled as to esomeprazole's safety.

200. Had the Plaintiff known of the risks of hypergastrinemia, rebound acid hypersecretion and stomach cancer associated with esomeprazole, Plaintiff would not have begun using the drug.

201. At all relevant times, Plaintiff had alternative safer methods for treating peptic disorders that provided the same benefits but acted through a different mechanism and were not associated with stomach cancer.

202. One safer alternative is the class of drugs collectively known as the H_2 antagonists, also called H_2 blockers, a class of medications that block the action of histamine at the histamine

[57] Gillen D, Wirz AA, Ardill JE, et al. Rebound hypersecretion after omeprazole and its relation to on-treatment acid suppression and Helicobacter pylori status. Gastroenterology 1999;116:239-247.
[58] Fossmark R, Johnsen G, Johanessen E, et al. Rebound acid hypersecretion after long-term inhibition of gastric acid secretion. Aliment Pharmacol Ther 2005;21:149–154.
[59] McColl KEL and Gillen D. Evidence That Proton-Pump Inhibitor Therapy Induces the Symptoms it Is Used to Treat

H2 receptors of the parietal cells in the stomach. This class of medication includes Tagamet, and Tagamet HB (cimetidine), Pepcid and Pepcid AC (famotidine), Axid (nizatidine) and Zantac (ranitidine). The H_2 receptor antagonists, which are prescribed for the same indications as the PPIs, are not associated with stomach cancer. The PPIs are much more potent than H2RA in terms of gastric acid suppression,[60] and many epidemiological studies have not revealed any association between gastric cancer development and H_2Ras[32,33,61,62,63,64,65]

203. Because of Defendants' action and inactions as outlined herein, Plaintiff was injured due to Plaintiff's ingestion of esomeprazole, which caused Plaintiff and continues to cause Plaintiff to suffer from stomach cancer and all its sequelae and co-morbidities.

204. Safer Alternatives to PPIs

205. Even though PPI Products lead to an increased risk of such severe injuries as outlined herein, several safer alternatives have been and are available, including but not limited to:

a) The use of over-the-counter calcium carbonate tablets that have been available since the 1930s, such as Maalox and Tums; and/or

b) The use of histamine H2-receptor antagonists (also known as "H2 Blockers") that were developed in the late 1960s. H2 Blockers act to prevent the production of stomach acid, work more quickly than PPI Products and are prescribed for the same indications as PPI

[60] Howden CW, Hunt RH. The relationship between suppression of acidity and gastric ulcer healing rates. Aliment Pharmacol Ther 1990;4:25–33.
[61] Tamim H, Duranceau A, Chen LQ, et al. Association between use of acid suppressive drugs and risk of gastric cancer. A nested case-control study. Drug Saf 2008;31:675–84.
[62] Poulsen AH, Christensen S, McLaughlin JK, et al. Proton pump inhibitors and risk of gastric cancer: a population-based cohort study. Br J Cancer 2009;100:1503–7.
[63] García Rodríguez LA, Lagergren J, Lindblad M. Gastric acid suppression and risk of oesophageal and gastric adenocarcinoma: a nested case control study in the UK. Gut 2006;55:1538–44.
[64] Chan EW, Wong AYS, et al.
[65] Peng Y-C, Huang L-R, Lin C-L, et al. Gut Epub ahead of print: doi:10.1136/gutjnl-2018-316057

Products. Examples of H2 Blockers include Zantac, Pepcid and Tagamet. H2 Blockers are not associated with an increased risk of gastric cancer.

206. Despite their commercial success and global popularity, up to 70% of PPI Products may be used inappropriately for indications or durations that were never tested or approved.[66]

207. Consumers, including Plaintiff, who have used Defendants' esomeprazole products for the treatment of increased gastric acid have and had several alternative safer treatments available and have not been adequately warned about the significant risks and lack of benefits associated with use of esomeprazole products.

TOLLING OF THE STATUTE OF LIMITATIONS

208. Defendants negligently represented to the medical and healthcare community, the FDA, to Plaintiff and the public that esomeprazole had been tested and was found to be safe and/or effective for its indicated use.

209. Defendants, at all relevant times, knew or should have known of the risks and defects with esomeprazole products, however Defendants concealed their knowledge of esomeprazole's risks and defects and failed to notify Plaintiff, the FDA, the public and the medical community including Plaintiff's prescribing physicians of the risks of gastric adenocarcinoma.

210. Defendant concealed and continue to conceal their knowledge of esomeprazole's unreasonably dangerous risks from Plaintiff, the FDA, the public and the medical community including Plaintiff's prescribing physicians. Specifically, Defendants failed to adequately inform consumers and the prescribing medical community about the magnified risk of gastric cancer related to the use of esomeprazole.

[66] D. Marks, Time to Halt the Overprescribing of Proton Pump Inhibitors, THE PHARMACEUTICAL JOURNAL (Aug. 8, 2016).

211. Defendants concealed and continue to conceal their knowledge that esomeprazole can cause gastric cancer from Plaintiff, the FDA, the public and the medical community including Plaintiff's prescribing physicians. Specifically, Defendants have failed to adequately inform consumers and the prescribing medical community against the serious risks associated with esomeprazole and completely failed to warn about the risk of gastric cancer.

212. To this day, Defendants continue to conceal their knowledge that esomeprazole can cause gastric cancer and still do not warn consumers and the prescribing medical community of the serious and potentially fatal risks of gastric cancer associated with the use of esomeprazole.

213. To this day, Defendants deny that esomeprazole can cause gastric cancer and actively conceal their knowledge relating to the true risks of gastric cancer and other injury related to the use of esomeprazole.

214. Defendants, through their affirmative misrepresentations and omissions, actively concealed from Plaintiff and Plaintiff's prescribing physicians the true and significant risks associated with the use of esomeprazole.

215. Defendants undertook such action with the intent of defrauding and deceiving the public and the medical community at large, including Plaintiff and Plaintiff's prescribing physicians, with the intent of inducing the prescription, dispensing, and/or purchasing of esomeprazole for the treatment of GERD, all of which evidenced a callous, reckless, willful indifference to the health, safety and welfare of Plaintiff herein.

216. As a result of Defendants' actions, Plaintiff and Plaintiff's prescribing physicians were unaware, and could not have reasonably known or learned through reasonable diligence, that Plaintiff had been exposed to the risks alleged herein, and that those risks were the direct and proximate result of Defendants' action, omissions, and misrepresentations.

217. Defendants are estopped from relying on any statute of limitations defense because of their concealment of the truth, quality and nature of esomeprazole. Defendants were under a duty to disclose the true character, quality and nature of esomeprazole because this was non-public information that Defendants had and continue to have exclusive control, and because the Defendants knew that this information was not available to the Plaintiff, the FDA, the public and the medical community including Plaintiff's prescribing physicians.

218. Defendants had the ability to and did spend enormous amounts of money in furtherance of their purpose of marketing and promoting a profitable drug, notwithstanding the known or reasonably known risks. Plaintiff and Plaintiff's prescribing physicians could not have afforded and could not have possibly conducted studies to determine the nature, extent and identity of related health risks and were forced to rely on Defendants' representations.

219. Plaintiff could not have discovered the still unlabeled risks of gastric cancer from using esomeprazole through the exercise of reasonable care.

220. Plaintiff did not have the same knowledge as Defendants and no adequate warning or other clinically relevant information and data was communicated to Plaintiff or Plaintiff's physicians.

221. Any applicable statute of limitations has therefore been tolled by Defendants' knowledge, active concealment and denial of the facts alleged herein, which behavior is still ongoing.

222. Plaintiffs only recently discovered that Plaintiff's injuries could have been caused by the use of esomeprazole.

CAUSES OF ACTION

COUNT I

STRICT PRODUCT LIABILITY

223. Plaintiffs repeat, reiterate, and reallege each and every allegation of this Complaint contained in each of the foregoing paragraphs inclusive, with the same force and effect as if more fully set forth herein.

224. At the time of Plaintiff's injuries, esomeprazole was defective and unreasonably dangerous to foreseeable consumers, including the Plaintiff.

225. At the time of Plaintiff's injuries, Defendants placed esomeprazole into the stream of commerce that were defective and in an unreasonably dangerous condition to foreseeable users, including the Plaintiff.

226. At all times herein mentioned, the Defendants designed, researched, manufactured, tested, advertised, promoted, marketed, sold, distributed, and/or have recently acquired the Defendants who have designed, researched, manufactured, tested, advertised, promoted, marketed, sold and distributed esomeprazole as hereinabove described that was used by the Plaintiff.

227. Esomeprazole was expected to and did reach consumers, handlers and persons coming into contact with said products without substantial change in the condition in which they were produced, manufactured, sold, distributed and marketed by the Defendants.

228. Esomeprazole was manufactured in an unsafe, defective and inherently dangerous condition, which was dangerous to users, including the Plaintiff.

229. The esomeprazole designed, researched, manufactured, tested, advertised, promoted, marketed, sold and distributed by Defendants were defective in design or formulation

in that, when they left the hands of the manufacturers and/or suppliers, the foreseeable risks exceeded the benefits associated with the design or formulation of esomeprazole.

230. At all times herein mentioned, the esomeprazole was in a defective condition and unsafe, and Defendants knew or had reason to know that esomeprazole was defective and unsafe, including when used in the formulation and manner recommended by the Defendants.

231. The esomeprazole designed, researched, manufactured, tested, advertised, promoted, marketed, sold and distributed by Defendants were defective in design and/or formulation, in that, when they left the hands of the Defendants, manufacturers and/or suppliers, esomeprazole was unreasonably dangerous, and was more dangerous than an ordinary consumer would expect, and more dangerous than other medications on the market designed to treat peptic disorders, including gastroesophageal reflux disease (GERD), peptic ulcer disease and nonsteroidal anti-inflammatory drug induced gastropathy.

232. Defendants knew or should have known that at all times herein mentioned esomeprazole was in a defective condition and were and are inherently dangerous and unsafe.

233. At the time Plaintiff used esomeprazole, the esomeprazole was being used for the purposes and in a manner normally intended and foreseeable, namely to treat peptic disorders, including gastroesophageal reflux disease (GERD), peptic ulcer disease and nonsteroidal anti-inflammatory drug induced gastropathy.

234. Defendants, with this knowledge, voluntarily designed esomeprazole in a dangerous condition for use by the public and the Plaintiff.

235. Defendants had a duty to create a product that was not unreasonably dangerous for its normal, intended and foreseeable use.

236. Defendants created a product unreasonably dangerous for its intended and foreseeable use.

237. The esomeprazole designed, researched, manufactured, tested, advertised, promoted, marketed, sold and distributed by Defendants were manufactured defectively in that esomeprazole left the hands of Defendants in a defective condition and were unreasonably dangerous to its intended users.

238. The esomeprazole designed, researched, manufactured, tested, advertised, promoted, marketed, sold and distributed by Defendants reached their intended users in the same defective and unreasonably dangerous condition in which they were manufactured.

239. Defendants designed, researched, manufactured, tested, advertised, promoted, marketed, sold and distributed a defective product which created an unreasonable risk to the health of consumers, and Defendants are therefore strictly liable for the injuries sustained by the Plaintiff.

240. The Plaintiff could not, by the exercise of reasonable care, have discovered esomeprazole's defects herein mentioned and perceived their danger.

241. The esomeprazole designed, researched, manufactured, tested, advertised, promoted, marketed, sold and distributed by Defendants were defective due to inadequate warnings or instructions, as the Defendants knew or should have known that esomeprazole created a risk of serious and dangerous side effects, including stomach cancer, kidney injuries and other severe and personal injuries which are permanent and lasting in nature, and the Defendants failed to adequately warn of said risk.

242. The esomeprazole designed, researched, manufactured, tested, advertised, promoted, marketed, sold and distributed by Defendants were defective due to inadequate warnings or instructions, as the Defendants knew or should have known that esomeprazole created

a risk of serious and dangerous side effects, including rebound acid hypersecretion, and the Defendants failed to adequately warn of said risk.

243. The esomeprazole designed, researched, manufactured, tested, advertised, promoted, marketed, sold and distributed by Defendants was defective due to inadequate warnings or instructions, as the Defendants knew or should have known that esomeprazole was ineffective for their intended use of treating peptic disorders, including gastroesophageal reflux disease (GERD), peptic ulcer disease and nonsteroidal anti-inflammatory drug induced gastropathy, and that there were less dangerous alternatives on the market to treat peptic disorders.

244. The esomeprazole designed, researched, manufactured, tested, advertised, promoted, marketed, sold and distributed by Defendants were defective due to inadequate warnings and/or inadequate testing.

245. Esomeprazole as designed, researched, manufactured, tested, advertised, promoted, marketed, sold and distributed by Defendants is defective due to inadequate post-marketing surveillance and/or warnings because, after Defendants knew or should have known of the risks of serious side effects including, stomach cancer and kidney injuries, as well as other severe and permanent health consequences from esomeprazole, they failed to provide adequate warnings to users or consumers of the product, and continued to improperly advertise, market and/or promote esomeprazole.

246. The esomeprazole ingested by Plaintiff was in the same or substantially similar condition as it was when it left the possession of Defendants.

247. Plaintiffs did not misuse or materially alter esomeprazole.

248. Defendants are strictly liable for Plaintiffs' injuries in the following ways:

a. The esomeprazole as designed, manufactured, sold and supplied by the Defendants, were defectively designed and placed into the stream of commerce by Defendants in a defective and unreasonably dangerous condition;

b. Defendants failed to properly market, design, manufacture, distribute, supply and sell esomeprazole;

c. Defendants failed to warn and place adequate warnings and instructions on esomeprazole;

d. Defendants failed to adequately test esomeprazole;

e. Defendants failed to provide timely and adequate post-marketing warnings and instructions after they knew of the risk of injury associated with the use of esomeprazole; and

f. Feasible alternative designs, including but not limited to those used of H2 Blockers and other available treatments, existed that were capable of treating Plaintiff's conditions, while decreasing the risk of gastric cancer.

249. By reason of the foregoing, Defendants are strictly liable in tort to the Plaintiff for the manufacturing, marketing, promoting, distribution, and selling of a defective product, esomeprazole.

250. Defendants' defective design, manufacturing defect and inadequate warnings on esomeprazole were acts that amount to willful, wanton and/or reckless conduct by Defendants.

251. These defects in esomeprazole were a substantial factor in causing Plaintiffs' injuries.

252. As a result of the foregoing acts and omissions, the Plaintiff was caused to suffer serious and dangerous side effects, including stomach cancer, and other severe and personal injuries, which are permanent and lasting in nature, physical pain and mental anguish, diminished enjoyment of life and financial expenses for hospitalization and medical care.

253. Defendants' conduct, as described herein, was extreme and outrageous. Defendants risked the lives of the consumers and users of esomeprazole, including the Plaintiff, with

knowledge of the safety and efficacy problems with esomeprazole and suppressed this knowledge from the general public, the Plaintiff, and/or the Plaintiff's healthcare providers. Defendants made conscious decisions not to redesign, re-label, warn or inform the unsuspecting consuming public. Defendants' outrageous conduct warrants an award of punitive damages.

WHEREFORE, the Plaintiffs respectfully request that this Court enter judgment in Plaintiffs' favor for compensatory and punitive damages, together with interest, cost herein incurred, attorneys' fees, and all such other and further relief as this Court deems just and proper. Plaintiffs also demands that the issues contained herein be tried by a jury.

COUNT II

STRICT PRODUCT LIABILITY –DESIGN DEFECT

254. Plaintiffs incorporate by reference each preceding and succeeding paragraph as though set forth fully at length herein.

255. At all times relevant, esomeprazole was designed, developed, manufactured, tested, packaged, promoted, marketed, distributed, labeled and/or sold by Defendants in a defective and unreasonably dangerous condition at the time they were placed in the stream of commerce.

256. Esomeprazole is defective in design or formulation in that it is not merchantable, reasonably suitable and/or safe for their intended and foreseeable use, and its condition when sold was the proximate cause and/or a substantial factor of the injuries sustained by Plaintiff.

257. Esomeprazole did not perform safely or as Plaintiff or an ordinary consumer would have expected.

258. At all times relevant, esomeprazole was used as intended or in a way reasonably foreseeable to the Defendants.

259. Defendants placed esomeprazole into the stream of commerce with wanton and reckless disregard for public safety.

260. At all times relevant hereto, esomeprazole was expected to reach, and did reach, consumer's in Plaintiff's home state, the State of New Jersey, and throughout the United States, including receipt by Plaintiff, without substantial change in the condition in which it was sold.

261. Esomeprazole was sold in an unsafe, defective and inherently dangerous condition.

262. Esomeprazole contains defects in its design which render the drug dangerous to consumers, including Plaintiff, when used as intended or as reasonably foreseeable to Defendants. The design defects render esomeprazole more dangerous than other drugs designed to treat peptic disorders, including gastroesophageal reflux disease (GERD), peptic ulcer disease and nonsteroidal anti-inflammatory drug induced gastropathy, and cause an unreasonable increased risk of injury, including but not limited to gastric cancer, kidney disease, and other life-threatening injuries.

263. Esomeprazole was in a defective condition and unsafe, and Defendants knew, had reason to know or should have known that esomeprazole was defective and unsafe, even when used as instructed.

264. The nature and magnitude of the risk of harm associated with the design of esomeprazole, including the risk of gastric cancer that may be irreversible, permanently disabling and life-threatening, is high in light of the intended and reasonably foreseeable use of esomeprazole.

265. The risks of harm associated with the design of esomeprazole are higher than necessary.

266. Esomeprazole was not accompanied by adequate instructions and/or warnings to fully apprise consumers, including Plaintiff, of the full nature and extent of the risks and side effects associated with its use, thereby rendering Defendants liable to Plaintiff.

267. It is unlikely that users would be aware of the risks associated with Defendants' esomeprazole, and Plaintiff specifically was not aware of these risks, nor would Plaintiff expect such risks.

268. The design of esomeprazole did not conform to any applicable public or private product standard that was in effect when esomeprazole left the Defendants' control.

269. Esomeprazole's designs are more dangerous than a reasonably prudent consumer would expect when used in their intended or reasonably foreseeable manner. Esomeprazole is more dangerous than Plaintiff expected.

270. Esomeprazole was insufficiently and inadequately tested;

271. The intended or actual utility of esomeprazole is not of such benefit to justify the risk of gastric cancer that may be irreversible, permanently disabling and life-threatening.

272. In addition, at the time esomeprazole left the control of Defendants, there were practical and feasible alternative designs that would have prevented and/or significantly reduced the risk of Plaintiff's injuries without impairing the reasonably anticipated or intended function of the product. These safer alternative designs were economically and technologically feasible – indeed they were already on the market – and would have prevented or significantly reduced the risk of Plaintiff's injuries without substantially impairing the product's utility.

273. Defendants' conduct was extreme and outrageous. Defendants risked the lives of consumers and users of esomeprazole, including Plaintiff, with the knowledge of the safety and efficacy problems and suppressed this knowledge from Plaintiff, the medical community and the

general public. Defendants made conscious decisions not to warn or inform the unsuspecting consuming public. Defendants' outrageous conduct warrants an award of punitive damages.

274. The unreasonably dangerous nature of esomeprazole caused serious harm to Plaintiff.

275. Esomeprazole is defective in its design which renders esomeprazole dangerous to consumers, including Plaintiff, when used as intended or as reasonably foreseeable to Defendants.

276. The design defects render esomeprazole more dangerous than other products used for the same intended purpose and cause an unreasonable increased risk of harm.

277. Esomeprazole's design is defective and unsafe, and Defendants knew or had reason to know that esomeprazole was defective and unsafe in their design when used as instructed and in a foreseeable manner for the treatment of peptic disorders by consumers, including the Plaintiff.

278. The nature and magnitude of the risk of harm associated with the design of esomeprazole, including the risk of gastric cancer that may lead to permanently disabling and life-threatening or life-ending conditions, was high in light of the intended and reasonably foreseeable use of esomeprazole by patients for treatment of peptic disorders.

279. Users of esomeprazole would not be aware of the risks of gastric cancer associated with either the defective design or warnings associated with esomeprazole through warnings, general knowledge or otherwise, and the Plaintiff was specifically unaware of these risks, and would not be expected to be aware of these risks.

280. The intended or actual utility and benefit of esomeprazole does not justify the risk of gastric cancer that may be irreversible, permanently disabling, life-threatening or life- ending.

281. The design of esomeprazole was negligently formulated by the Defendants in disregard of the known risk of gastric cancer.

282. The warnings and instructions for use accompanying esomeprazole was negligently formulated by the Defendants in disregard of the known risk of gastric cancer.

283. The warnings and instructions for use accompanying esomeprazole was negligently formulated by the Defendants in disregard of the known risk of rebound acid hypersecretion.

284. The defects in design and warnings caused and/or increased the risk of harm of Plaintiff's injuries and damages.

285. The defective nature of esomeprazole was a substantial factor in causing Plaintiff's injuries.

286. As a result of the foregoing acts and omissions, Plaintiff was caused to suffer serious and dangerous side effects, including gastric cancer and other severe and personal injuries, which are permanent and lasting in nature, physical pain and mental anguish, diminished enjoyment of life and financial expenses for hospitalization and medical care.

287. Defendants' conduct, as described herein, was extreme and outrageous. Defendants risked the lives of the consumers and users of esomeprazole, including Plaintiff, with knowledge of the safety and efficacy problems with esomeprazole and suppressed this knowledge from the general public, Plaintiff, and/or Plaintiff's healthcare providers. Defendants made conscious decisions not to redesign, re-label, warn or inform the unsuspecting consuming public. Defendants' outrageous conduct warrants an award of punitive damages.

WHEREFORE, the Plaintiffs respectfully request that this Court enter judgment in Plaintiffs' favor for compensatory and punitive damages, together with interest, cost herein incurred, attorneys' fees, and all such other and further relief as this Court deems just and proper. Plaintiffs also demands that the issues contained herein be tried by a jury.

COUNT III

STRICT PRODUCT LIABILITY – FAILURE TO WARN

288. Plaintiffs repeat, reiterate, and reallege each and every allegation of this Complaint contained in each of the foregoing paragraphs inclusive, with the same force and effect as if more fully set forth herein.

289. Defendants have engaged in the business of designing, developing, researching, testing, licensing, manufacturing, packaging, labeling, promoting, marketing, selling, and/or distributing esomeprazole. Through that conduct, Defendants knowingly and intentionally placed esomeprazole into the stream of commerce with full knowledge that it reaches consumers, such as Plaintiff, who ingested it.

290. Defendants researched, developed, designed, tested, manufactured, inspected, labeled, distributed, marketed, promoted, sold, and otherwise released esomeprazole into the stream of commerce. In the course of same, Defendants directly advertised, marketed, and promoted esomeprazole to the FDA, health care professionals, Plaintiff, and other consumers, and therefore had a duty to warn of the risks associated with the use of esomeprazole.

291. Defendants expected esomeprazole to reach, and it did in fact reach, prescribing health care professionals and consumers, including Plaintiff and Plaintiff's prescribing health care professionals, without any substantial change in the condition of the product from when it was initially distributed by Defendants

292. Defendants failed to provide adequate warnings or instructions that a manufacturer exercising reasonable care would have provided concerning the risk of gastric cancer that may be irreversible, permanently disabling and life-threatening in light of the likelihood that esomeprazole would cause these injuries.

293. Defendants failed to update warnings based on information received from surveillance and research conducted after esomeprazole were first approved by the FDA and marketed, sold and used in the United States and throughout the world.

294. A manufacturer exercising reasonable care would have updated its warnings on the basis of reports of injuries to individuals using esomeprazole after FDA approval.

295. Esomeprazole, as manufactured and/or supplied by Defendants, was defective due to inadequate warnings or instructions. Defendants knew or should have known that the product created significant risks of serious bodily harm to consumers, as alleged herein, and they failed to adequately warn consumers and/or their health care professionals of such risks.

296. Esomeprazole was defective and unsafe such that it was unreasonably dangerous when it left Defendants' possession and/or control, was distributed by Defendants, and ingested by Plaintiff. Esomeprazole contained warnings insufficient to alert consumers, including Plaintiff, to the dangerous risks and reactions associated with esomeprazole, including the development of Plaintiff's injuries

297. This defect caused serious injury to Plaintiff, who used esomeprazole for its intended purpose and in a reasonably anticipated manner.

298. Plaintiff and/or Plaintiff's healthcare providers could not, by the exercise of reasonable care, have discovered the defects or perceived the danger of esomeprazole because the risks were not open or obvious.

299. Defendants, as the manufacturers and distributors of esomeprazole, are held to the level of knowledge of an expert in the field.

300. The warnings that were given by Defendants were not accurate or clear, and were false and ambiguous.

301. The warnings that were given by the Defendants failed to properly warn Plaintiff and/or Plaintiff's healthcare providers of the risks associated with the esomeprazole, subjecting Plaintiff to risks that exceeded the benefits to the Plaintiff. Plaintiff, individually and/or Plaintiff through their healthcare providers, reasonably relied upon the skill, superior knowledge and judgment of the Defendants.

302. Defendants had a continuing duty to warn Plaintiff and/or Plaintiff's healthcare providers of the dangers associated with esomeprazole.

303. Had Plaintiff and/or Plaintiff's healthcare providers received adequate warnings regarding the risks associated with the use of esomeprazole, they would not have used it, or they would have altered the frequency or duration of use.

304. Defendants failed to update warnings based on information received after esomeprazole entered the market, and continued to market, promote, detail, distribute and sell esomeprazole without appropriately updated and amended warnings.

305. A manufacturer exercising reasonable and prudent care would have updated warnings on esomeprazole on the basis of epidemiology studies and/or reports of injuries to individuals using esomeprazole after FDA approval.

306. Plaintiff and Plaintiff's healthcare providers were led to believe, through Defendants' use of aggressive and pervasive marketing, promotion and detailing, that Defendants' esomeprazole was safe and effective for treatment of peptic disorders, including gastroesophageal reflux disease (GERD), peptic ulcer disease and nonsteroidal anti-inflammatory drug induced gastropathy.

307. The warnings and instructions that were given by Defendants to healthcare providers were not accurate or clear, and were, in fact, false and misleading.

308. The warnings that were given by the Defendants failed to properly warn physicians and/or other healthcare providers, including those of the Plaintiff, of the risks associated with Defendants' esomeprazole, thereby subjecting patients, including the Plaintiff, to unreasonable and foreseeable risks that exceeded the purported and marketed benefits of Defendants' esomeprazole.

309. Plaintiff's healthcare providers reasonably relied upon the representations, warning and instructions provided by Defendants for use and administration of esomeprazole.

310. Had the Plaintiff and/or Plaintiff's healthcare providers received adequate, appropriate and correct warnings regarding the risks associated with the use of Defendants' esomeprazole, these healthcare providers would not have prescribed, recommended, continued to prescribe or continued the recommendation of esomeprazole, or would have altered the duration and frequency of use.

311. Defendants' conduct as described herein was a substantial factor in causing Plaintiff's injuries.

312. The Plaintiff's injuries were the direct and proximate result of Defendants' failure to warn of the dangers of Defendants' esomeprazole.

313. As a result of the foregoing acts and omissions, Plaintiff was caused to suffer serious and dangerous side effects, including gastric cancer and other severe and personal injuries, which are permanent and lasting in nature, physical pain and mental anguish, diminished enjoyment of life and financial expenses for hospitalization and medical care.

314. Defendants' conduct, as described herein, was extreme and outrageous. Defendants risked the lives of the consumers and users of esomeprazole, including Plaintiff, with knowledge of the safety and efficacy problems with esomeprazole and suppressed this knowledge

from the general public, Plaintiff, and/or Plaintiff's healthcare providers. Defendants made conscious decisions not to redesign, re-label, warn or inform the unsuspecting consuming public. Defendants' outrageous conduct warrants an award of punitive damages.

WHEREFORE, the Plaintiffs respectfully request that this Court enter judgment in Plaintiffs' favor for compensatory and punitive damages, together with interest, cost herein incurred, attorneys' fees, and all such other and further relief as this Court deems just and proper. Plaintiffs also demands that the issues contained herein be tried by a jury.

COUNT IV

NEGLIGENCE

315. Plaintiffs repeat, reiterate and reallege each and every allegation of this Complaint contained in each of the foregoing paragraphs inclusive, with the same force and effect as if more fully set forth herein.

316. Defendants had a duty to exercise reasonable care in designing, researching, manufacturing, marketing, supplying, promoting, packaging, selling and/or distributing esomeprazole into the stream of commerce, including a duty to assure that esomeprazole would not cause users to suffer unreasonable, dangerous side effects.

317. Defendants failed to exercise ordinary care in the design, research, manufacture, labeling, warnings, marketing, promotion, quality assurance, quality control, sale and/or distribution of esomeprazole in that Defendants knew or should have known that the drugs could proximately cause Plaintiff's injuries and/or presented an unreasonably high risk of injury.

318. Defendants, acting by and through their authorized divisions, subsidiaries, agents, servants and/or employees, acted with carelessness, recklessness, negligence, gross negligence

and/or willful, wanton, outrageous and reckless disregard for human life and safety in manufacturing, designing, labeling, marketing, distributing, supplying, selling and/or placing esomeprazole into the stream of commerce, including but not limited to the following particular respects:

a) Failing to use due care in design and/or manufacture of esomeprazole so as to avoid the aforementioned risks to individuals;

b) Failing to conduct adequate testing, including pre-clinical and clinical testing and post-marketing surveillance to determine the safety of esomeprazole;

c) Failing to use reasonable and prudent care so as to conduct sufficient post marketing, pharmacovigilance and pharmacosurveillance;

d) Failing to recognize the significance of their own and other testing, and information regarding esomeprazole, which testing and information evidenced such products are dangerous and potentially harmful to humans;

e) Failing to respond promptly and appropriately to their own and other testing, and information regarding esomeprazole, and failing to promptly and adequately warn of the potential for gastric cancer, kidney disease, and other serious injuries, when using esomeprazole;

f) Failing to promptly, adequately and appropriately recommend testing and monitoring of patients upon whom esomeprazole was used in light of esomeprazole's dangers and potential harm to humans;

g) Failing to properly, appropriately and adequately monitor the post-market performance of esomeprazole and such products effects on patients;

h) Aggressively promoting, marketing, advertising and/or selling esomeprazole given their knowledge and experience of esomeprazole's potential harmful effects;

i) Failing to use reasonable and prudent care in their statements of the efficacy, safety and risks of using esomeprazole, which were knowingly false and misleading, in order to influence patients, such as the Plaintiff, to use esomeprazole in excess and/or in preference to safer and effective alternative treatments;

j) Failing to accompany esomeprazole with proper and/or accurate warnings regarding all possible adverse side effects and risk of gastric cancer associated with the use of esomeprazole;

k) Failing to accompany esomeprazole with proper and/or accurate warnings regarding all possible adverse side effects and risk of rebound acid hypersecretion associated with the use of esomeprazole.

l) Failing to disclose to Plaintiff and/or the medical community their full knowledge and experience regarding the potential dangers and harm associated with use of esomeprazole;

m) Failing to disclose to Plaintiff and/or the medical community in an appropriate and timely manner, facts relative to the potential dangers and harm associated with use of esomeprazole;

n) Failing to warn Plaintiff and/or Plaintiff's healthcare providers of the severity and duration of such adverse effects;

o) Failing to warn Plaintiff and/or Plaintiff's healthcare providers prior to actively encouraging the sale of esomeprazole, either directly or indirectly, orally or in writing, about the increased risk of gastric cancer;

p) Placing and/or permitting the placement of esomeprazole into the stream of commerce without adequate warnings that they are harmful to humans and/or without properly warning of esomeprazole's dangerousness;

q) Failing to withdraw esomeprazole from the market and stream of commerce, or restrict their use and/or warn of esomeprazole's potential dangers, given their knowledge of the dangers and harms associated with use of esomeprazole;

r) Failing to respond or react promptly and appropriately to reports of esomeprazole causing harm to patients;

s) Disregarding government and/or industry studies, information, documentation and recommendations, consumer complaints and reports and/or other information regarding the hazards of esomeprazole and its potential harm to humans;

t) Under-reporting, underestimating and/or downplaying the serious dangers of esomeprazole;

u) Failing to exercise reasonable care in informing physicians and healthcare providers using esomeprazole about their own knowledge regarding the potential dangers and harm associate with use of esomeprazole;

v) Failing to adequately warn Plaintiff and/or Plaintiff's healthcare providers of the known or reasonably foreseeable danger that Plaintiff would suffer serious injuries or death by ingesting esomeprazole;

w) Promoting esomeprazole in advertisements, websites and other modes of communication aimed at creating and/or increasing user and consumer demand without regard to the dangers and risks associated using esomeprazole;

x) Failing to conduct and/or respond to post-marketing surveillance of complications and injuries associated with esomeprazole;

y) Failing to use due care under the circumstances; and

z) Other such acts or omissions constituting negligence and carelessness as may appear during the course of discovery or at the trial of this matter.

319. Despite the fact that Defendants knew or should have known that esomeprazole caused unreasonable, dangerous risk of gastric cancer, Defendants continued to market esomeprazole to consumers, including the medical community and Plaintiff.

320. Defendants knew or should have known that consumers such as the Plaintiff would foreseeably suffer injury as a result of Defendants' failure to exercise ordinary care a described herein, including the failure to comply with federal requirements.

321. It was foreseeable to Defendants that esomeprazole, as designed and marketed, would cause serious injury to consumers, including Plaintiff.

322. Despite the fact that Defendants knew or should have known that esomeprazole caused unreasonable risks of harm when used as intended by the Defendants, the Defendants continued to advertise, market and sell esomeprazole to patients, including the Plaintiff and healthcare providers.

323. As a direct and proximate result of Defendants' negligence, Plaintiff suffered serious physical injury, harm, damages and economic loss and will continue to suffer such harm, damages and economic loss in the future.

324. Defendants' knowingly and intentionally defectively designed and provided inadequate warnings relating to the design of esomeprazole in willful, wanton and reckless

disregard for the safety and well-being of all patients and consumers, including the Plaintiff, for the purpose of achieving profits and market share over safety.

325. Defendants acted in reckless disregard to public safety and well-being, including Plaintiff's safety and well-being, and with actual knowledge that esomeprazole was unsafe for their recommended use for the treatment of peptic disorders, including gastroesophageal reflux disease (GERD), peptic ulcer disease and nonsteroidal anti-inflammatory drug induced gastropathy.

326. Defendants made conscious decisions not to redesign, re-label, warn or inform the unsuspecting consuming public, Plaintiff, and/or Plaintiff's healthcare providers concerning the dangers of esomeprazole, and consciously decided to aggressively market and sell esomeprazole, putting economic, financial and market share advantage over safety and efficacy considerations.

327. As a result of the foregoing acts and omissions, Plaintiff was caused to suffer serious and dangerous side effects, including gastric cancer and other severe and personal injuries which are permanent and lasting in nature, physical pain and mental anguish, diminished enjoyment of life and financial expenses for hospitalization and medical care.

328. Defendants' conduct, as described herein, was extreme and outrageous. Defendants risked the lives of the consumers and users of esomeprazole, including Plaintiff, with knowledge of the safety and efficacy problems with esomeprazole and suppressed this knowledge from the general public, Plaintiff, and/or Plaintiff's healthcare providers. Defendants made conscious decisions not to redesign, re-label, warn or inform the unsuspecting consuming public. Defendants' outrageous conduct warrants an award of punitive damages.

WHEREFORE, the Plaintiffs respectfully request that this Court enter judgment in Plaintiffs' favor for compensatory and punitive damages, together with interest, cost herein

incurred, attorneys' fees, and all such other and further relief as this Court deems just and proper. Plaintiffs also demands that the issues contained herein be tried by a jury.

COUNT V

NEGLIGENCE PER SE

329. Plaintiffs repeat, reiterate and reallege each and every allegation of this Complaint contained in each of the foregoing paragraphs inclusive, with the same force and effect as if more fully set forth herein.

330. Defendants violated the Federal Food, Drug and Cosmetic Act 21 U.S.C. §301, et seq., and regulations as described herein, including but not limited to 21 U.S.C. §352, 21, CFR §201.5, 21 CFR § 201.56, 21 CFR § 201.57, 21 CFR § 201.66, 21 CFR § 210.1, 21 CFR § 210.122, 21 CFR § 211.165, 21 CFR § 211.198, 21 CFR § 310.303, 21 CFR §310.305, 21 CFR § 314.80, and 21 CFR § 312.32.

331. These statutes and regulations are aimed at preserving the health and safety of Plaintiff and the general public.

332. Defendants' acts were the proximate cause and/or a substantial factor in bringing about the harm to the Plaintiff as alleged herein.

333. Plaintiff is among the class of individuals that these statutes and regulations were designed to protect.

334. Plaintiff's injuries are the type that these federal statutes and regulations were intended to prevent.

335. As a result of the foregoing acts and omissions, Plaintiff was caused to suffer serious and dangerous side effects, including gastric cancer and other severe and personal injuries

which are permanent and lasting in nature, physical pain and mental anguish, diminished enjoyment of life and financial expenses for hospitalization and medical care.

336. Defendants' conduct, as described herein, was extreme and outrageous. Defendants risked the lives of the consumers and users of esomeprazole, including Plaintiff, with knowledge of the safety and efficacy problems with esomeprazole and suppressed this knowledge from the general public, Plaintiff, and/or Plaintiff's healthcare providers. Defendants made conscious decisions not to redesign, re-label, warn or inform the unsuspecting consuming public. Defendants' outrageous conduct warrants an award of punitive damages.

WHEREFORE, the Plaintiffs respectfully request that this Court enter judgment in Plaintiffs' favor for compensatory and punitive damages, together with interest, cost herein incurred, attorneys' fees, and all such other and further relief as this Court deems just and proper. Plaintiffs also demands that the issues contained herein be tried by a jury.

COUNT VI

BREACH OF EXPRESS WARRANTY

337. Plaintiffs repeat, reiterate and reallege each and every allegation of this Complaint contained in each of the foregoing paragraphs inclusive, with the same force and effect as if more fully set forth herein.

338. Defendants expressly warranted that esomeprazole was safe and effective to members of the consuming public, including Plaintiff.

339. Defendants expressly warranted that esomeprazole was safe and effective for use by members of the consuming public, including the Plaintiff, for the treatment of peptic disorders and did not disclose the material risks that esomeprazole could cause gastric cancer that may be

irreversible, permanently disabling and life-threatening. The representations were not justified by the performance of esomeprazole.

340. Defendants expressly warranted that esomeprazole was safe and effective to use.

341. Defendants expressly represented to Plaintiff, Plaintiff's physicians, healthcare providers and/or the FDA that esomeprazole was safe and fit for use for the intended purpose, that they were of merchantable quality, that they did not produce any dangerous side effects in excess of those risks associated with other forms of treatment for peptic disorders, including gastroesophageal reflux disease (GERD), peptic ulcer disease and nonsteroidal anti-inflammatory drug induced gastropathy, that the side effects they did produce were accurately reflected in the warnings, and that they were adequately tested and fit for its intended use.

342. Defendants knew or should have known that, in fact, said representations and warranties were false, misleading and untrue in that esomeprazole was not safe and fit for the use intended, and, in fact, produced serious injuries to the users that were not accurately identified and represented by Defendants.

343. Plaintiff and/or Plaintiff's healthcare providers reasonably relied on Defendants' express representations.

344. Esomeprazole does not conform to these express representations because they are not safe and have serious side effects, including gastric cancer and in some cases, death.

345. Defendants breached their express warranty in one or more of the following ways:

a) Esomeprazole, as designed, manufactured, sold and/or supplied by the Defendants, were defectively designed and placed in to the stream of commerce by Defendants in a defective and unreasonably dangerous condition;

b) Defendants failed to warn and/or place adequate warnings and instructions on esomeprazole;

c) Defendants failed to adequately test esomeprazole; and,

d) Defendants failed to provide timely and adequate post-marketing warnings and instructions after they knew the risk of injury from esomeprazole.

346. Defendants made statements, affirmations and representations of fact concerning esomeprazole through their advertisements, educational campaigns and multi-platform marketing and promotional initiatives directed at consumers, patients and healthcare providers promoting unnecessary and dangerous use and overuse of esomeprazole.

347. Defendants' statements, affirmations and representations of fact did reach the Plaintiff, and formed a "basis of the bargain" for the Plaintiff's decision to purchase or accept the prescription of esomeprazole.

348. Defendants did not disclose material risk of gastric cancer alleged herein that esomeprazole caused.

349. Defendants' representations concerning the safety and efficacy of esomeprazole were not justified by its performance or benefits.

350. Defendants expressly warranted that esomeprazole was safe and effective for treatment of peptic disorders, including gastroesophageal reflux disease (GERD), peptic ulcer disease and nonsteroidal anti-inflammatory drug induced gastropathy. In fact, Defendants, through their advertisements, promoted use of esomeprazole for ongoing and daily use. Esomeprazole did not conform to Defendants' representations, statements and/or affirmations of fact in terms of the express warranties made to consumers and patients concerning the drugs' safety and efficacy as formulated for use.

351. The Plaintiff reasonably and justifiably relied upon Defendants' representations, statements and/or affirmations of fact that esomeprazole was safe and effective when the Plaintiff chose to purchase, use and continue to use them.

352. The Plaintiff was unskilled in the research, design and manufacture of medical drugs and pharmaceutical products, including esomeprazole, and reasonably and justifiably relied entirely on the skill, judgment and express warranty of the Defendants in the choosing to use Defendants' esomeprazole.

353. Defendants herein breached the aforesaid express warranties as esomeprazole is defective.

354. Plaintiff's injuries were the direct and proximate result of Defendants' breach of their express warranty.

355. As a result of the foregoing acts and omissions, Plaintiff was caused to suffer serious and dangerous side effects, including gastric cancer and other severe and personal injuries which are permanent and lasting in nature, physical pain and mental anguish, diminished enjoyment of life and financial expenses for hospitalization and medical care.

356. Defendants' conduct, as described herein, was extreme and outrageous. Defendants risked the lives of the consumers and users of esomeprazole, including Plaintiff, with knowledge of the safety and efficacy problems with esomeprazole and suppressed this knowledge from the general public, Plaintiff, and/or Plaintiff's healthcare providers. Defendants made conscious decisions not to redesign, re-label, warn or inform the unsuspecting consuming public. Defendants' outrageous conduct warrants an award of punitive damages.

WHEREFORE, the Plaintiffs respectfully request that this Court enter judgment in Plaintiffs' favor for compensatory and punitive damages, together with interest, cost herein incurred, attorneys' fees, and all such other and further relief as this Court deems just and proper. Plaintiffs also demands that the issues contained herein be tried by a jury.

COUNT VII

BREACH OF IMPLIED WARRANTY

357. Plaintiffs repeat, reiterate and reallege each and every allegation of this Complaint contained in each of the foregoing paragraphs inclusive, with the same force and effect as if more fully set forth herein.

358. At all times herein mentioned, the Defendants manufactured, compounded, portrayed, distributed, recommended, merchandized, advertised, promoted and sold esomeprazole and/or have recently acquired the Defendants who have manufactured, compounded, portrayed, distributed, recommended, merchandized, advertised, promoted and sold esomeprazole for the treatment of peptic disorders which include gastroesophageal reflux disease (GERD), peptic ulcer disease, and nonsteroidal anti-inflammatory drug induced gastropathy.

359. At the time Defendants marketed, sold, and distributed esomeprazole for use by Plaintiff, Defendants knew of the uses for which esomeprazole was intended and impliedly warranted the product to be of merchantable quality and safe and fit for such use.

360. The Defendants impliedly represented and warranted to the users of esomeprazole and their physicians, healthcare providers, and/or the FDA that esomeprazole was safe and of merchantable quality and fit for the ordinary purpose for which said products were to be used.

361. That said representations and warranties aforementioned were false, misleading, and inaccurate in that esomeprazole is unsafe, unreasonably dangerous, improper, not of merchantable quality, and defective.

362. Plaintiff reasonably relied on Defendants' representations that esomeprazole was safe and free of defects and was a safe means of managing and treating symptoms associated with

peptic disorders, including gastroesophageal reflux disease (GERD), peptic ulcer disease and nonsteroidal anti-inflammatory drug induced gastropathy.

363. At all relevant times hereto, Defendants knew or had reason to know of the purpose for and manner in which users of esomeprazole, including Plaintiff, were using esomeprazole, and that those users were relying on Defendants' promotional and advertising materials in their selection of the product for that particular use.

364. Through aggressive healthcare provider promotion and patient advertising, educational, informational and marketing campaigns, Defendants participated in the selection of esomeprazole by healthcare providers, patients and consumers.

365. At all relevant times hereto, Defendants' esomeprazole did not have the requisite clinical safety or efficacy profiles to be deemed fit for the particular purpose of treating peptic disorders, including gastroesophageal reflux disease (GERD), peptic ulcer disease and nonsteroidal anti-inflammatory drug induced gastropathy.

366. Defendants' esomeprazole did not conform to this implied warranty of fitness for the use in treating peptic disorders, including gastroesophageal reflux disease (GERD), peptic ulcer disease and nonsteroidal anti-inflammatory drug induced gastropathy.

367. The Plaintiff was unskilled in the research, design and manufacture of medical drugs and pharmaceutical products, including esomeprazole, and reasonably and justifiably relied entirely on the skill, judgment and warranty of the Defendants in the choice to use Defendants' esomeprazole.

368. Esomeprazole was neither safe nor fit for its intended use nor of merchantable quality, as warranted by Defendants to the Plaintiff, in that esomeprazole poses a dangerous risk when used as intended to cause gastric cancer.

369. Defendants' breach of the implied warranty of merchantability was the direct and proximate cause of Plaintiff's injuries.

370. As a result of the foregoing acts and omissions, Plaintiff was caused to suffer serious and dangerous side effects, including gastric cancer and other severe and personal injuries which are permanent and lasting in nature, physical pain and mental anguish, diminished enjoyment of life and financial expenses for hospitalization and medical care.

371. Defendants' conduct, as described herein, was extreme and outrageous. Defendants risked the lives of the consumers and users of esomeprazole, including Plaintiff, with knowledge of the safety and efficacy problems with esomeprazole and suppressed this knowledge from the general public, Plaintiff, and/or Plaintiff's healthcare providers. Defendants made conscious decisions not to redesign, re-label, warn or inform the unsuspecting consuming public. Defendants' outrageous conduct warrants an award of punitive damages.

WHEREFORE, the Plaintiffs respectfully request that this Court enter judgment in Plaintiffs' favor for compensatory and punitive damages, together with interest, cost herein incurred, attorneys' fees, and all such other and further relief as this Court deems just and proper. Plaintiffs also demands that the issues contained herein be tried by a jury.

COUNT VIII

NEGLIGENT MISREPRESENTATION

372. Plaintiffs repeat, reiterate and reallege each and every allegation of this Complaint contained in each of the foregoing paragraphs inclusive, with the same force and effect as if more fully set forth herein.

373. From the time Defendants' esomeprazole was first tested, studied, researched, evaluated, endorsed, manufactured, marketed and distributed, and up to the present, Defendants made misrepresentations to Plaintiff, Plaintiff's physicians and the general public, including but not limited to the misrepresentation that esomeprazole was safe and effective for the treatment of peptic disorders, including gastroesophageal reflux disease (GERD), peptic ulcer disease and nonsteroidal anti-inflammatory drug induced gastropathy. At all times mentioned, Defendants conducted sales and marketing campaigns to promote the sale, use and overuse of esomeprazole and willfully deceived Plaintiff, Plaintiff's physicians and the general public as to the health risks and consequences of the use of esomeprazole.

374. Defendants had a duty to ensure that the representations they made about esomeprazole was true and complete when made. Defendants made the foregoing representation without any reasonable ground for believing them to be true.

375. At all relevant times hereto, Defendants conducted sales and marketing campaigns to promote the sale of esomeprazole and deceived patients, consumers, physicians and healthcare providers, including the Plaintiff and Plaintiff's healthcare providers, as to the health risks and consequences of the use of esomeprazole.

376. The Defendants made these false and misleading representations without any reasonable ground for believing them to be true concerning the safety and efficacy of esomeprazole for treatment of peptic disorders, including gastroesophageal reflux disease (GERD), peptic ulcer disease and nonsteroidal anti-inflammatory drug induced gastropathy.

377. These representations were made directly by Defendants, their sales representatives and other authorized agents of the Defendants to physicians and other healthcare providers; in television media directed towards the general public; in publications, the popular

press, and other written materials which were directed to physicians, patients, consumers and the general public; and on Internet websites and applications directed to consumers and physicians, including the Plaintiff, with the intention of inducing and influencing the demand for, the ultimate prescription, purchase and use of esomeprazole.

378. The representations by the Defendants were in fact false, in that esomeprazole is not safe, fit and/or effective for human consumption as labeled, using esomeprazole is hazardous to consumers' health, and esomeprazole has a serious propensity to cause serious injuries to users, including but not limited to gastric cancer and related personal injuries suffered by Plaintiff.

379. The foregoing representations by Defendants, and each of them, were made with the intention of inducing reliance and the prescription, purchase and use of esomeprazole.

380. In reliance on the misrepresentations by the Defendants, Plaintiff was induced to purchase and use esomeprazole. If Plaintiff had known the truth and the facts concealed by the Defendants, Plaintiff would not have used esomeprazole or would have used far less esomeprazole. The reliance of Plaintiff upon Defendants' misrepresentations was justified because such misrepresentations were made and conducted by individuals and entities that were in a position to know all of the facts.

381. Defendants breached their duty in representing esomeprazole 's serious side effects to the medical and healthcare community, to the Plaintiff, the FDA and the public in general.

382. As a result of the foregoing acts and omissions, Plaintiff was caused to suffer serious and dangerous side effects, including gastric cancer and other severe and personal injuries which are permanent and lasting in nature, physical pain and mental anguish, diminished enjoyment of life and financial expenses for hospitalization and medical care.

383. Defendants' conduct, as described herein, was extreme and outrageous. Defendants risked the lives of the consumers and users of esomeprazole, including Plaintiff, with knowledge of the safety and efficacy problems with esomeprazole and suppressed this knowledge from the general public, Plaintiff, and/or Plaintiff's healthcare providers. Defendants made conscious decisions not to redesign, re-label, warn or inform the unsuspecting consuming public. Defendants' outrageous conduct warrants an award of punitive damages.

WHEREFORE, the Plaintiffs respectfully request that this Court enter judgment in Plaintiffs' favor for compensatory and punitive damages, together with interest, cost herein incurred, attorneys' fees, and all such other and further relief as this Court deems just and proper. Plaintiffs also demands that the issues contained herein be tried by a jury.

COUNT IX

FRAUD AND FRAUDULENT MISREPRESENTATION

384. Plaintiffs repeat, reiterate, and reallege each and every allegation of this Complaint contained in each of the foregoing paragraphs inclusive, with the same force and effect as if more fully set forth herein.

385. The Defendants falsely and fraudulently represented to the medical and healthcare community, and to the Plaintiff, and/or the FDA, and the public in general, that said product, esomeprazole, had been tested and were found to be safe and/or effective for treatment of peptic disorders which include gastroesophageal reflux disease (GERD), peptic ulcer disease, and nonsteroidal anti-inflammatory drug induced gastropathy.

386. Defendants widely advertised, marketed and promoted esomeprazole as safe and effective medications for the treatment of peptic disorders, including gastroesophageal reflux

disease (GERD), peptic ulcer disease and nonsteroidal anti-inflammatory drug induced gastropathy, and widely advertised, marketed and promoted esomeprazole as a safe for daily and extended use.

387. These representations were made by the Defendants with the intent of deceiving the medical and healthcare community, patients, consumers, the general public and the Plaintiff, with the intent of inducing the prescription and use of esomeprazole in circumstances that the Defendants knew were dangerous, unsafe and created a high risk of harm.

388. These representations made by Defendants were false and misleading.

389. Defendants knew these representations to be false when made and willfully, wantonly and recklessly disregarded whether the representations were true.

390. These representations were made by said Defendants with the intent of defrauding and deceiving the Plaintiff, the public in general, and the medical and healthcare community in particular, and were made with the intent of inducing the public in general, and the medical and healthcare community in particular, to recommend, prescribe, dispense and/or purchase esomeprazole for treatment of peptic disorders which include gastroesophageal reflux disease (GERD), peptic ulcer disease, and nonsteroidal anti-inflammatory drug induced gastropathy, all of which evinced a callous, reckless, willful, depraved indifference to the health, safety and welfare of the Plaintiff herein.

391. At the time the Defendants made aforesaid representations, Plaintiff used esomeprazole and was unaware of the falsity of the representations and reasonably believed them to be true.

392. In reliance on Defendants' misrepresentations, the Plaintiff was induced to and did use esomeprazole, thereby sustaining severe and permanent personal injuries, and/or being at an increased risk of sustaining severe and permanent personal injuries in the future.

393. Defendants knew or should have known that esomeprazole had not been sufficiently tested, were defective in nature and/or that lacked adequate and/or sufficient warnings.

394. Defendants knew or should have known that esomeprazole had a potential to, could and would cause severe and grievous injury to the users of said product, and that they were inherently dangerous in a manner that exceeded any purported, inaccurate and/or down-played warnings.

395. Defendants brought esomeprazole to the market and acted fraudulently, wantonly and maliciously to the detriment of the Plaintiff.

396. As a result of the foregoing acts and omissions, Plaintiff was caused to suffer serious and dangerous side effects, including gastric cancer and other severe and personal injuries which are permanent and lasting in nature, physical pain and mental anguish, diminished enjoyment of life and financial expenses for hospitalization and medical care.

397. Defendants' conduct, as described herein, was extreme and outrageous. Defendants risked the lives of the consumers and users of esomeprazole, including Plaintiff, with knowledge of the safety and efficacy problems with esomeprazole and suppressed this knowledge from the general public, Plaintiff, and/or Plaintiff's healthcare providers. Defendants made conscious decisions not to redesign, re-label, warn or inform the unsuspecting consuming public. Defendants' outrageous conduct warrants an award of punitive damages.

WHEREFORE the Plaintiffs respectfully request that this Court enter judgment in Plaintiffs' favor for compensatory and punitive damages, together with interest, cost herein

incurred, attorneys' fees, and all such other and further relief as this Court deems just and proper. Plaintiffs also demands that the issues contained herein be tried by a jury.

COUNT X

FRAUDULENT CONCEALMENT

398. Plaintiffs repeat, reiterate and reallege each and every allegation of this Complaint contained in each of the foregoing paragraphs inclusive, with the same force and effect as if more fully set forth herein.

399. Prior to Plaintiff's use of esomeprazole and, during the period in which Plaintiff actually used esomeprazole, Defendants fraudulently suppressed material information regarding the safety and efficacy of esomeprazole, including information regarding adverse events, pre and post marketing injuries, and epidemiological studies indicating unreasonable risks associated with using esomeprazole.

400. Furthermore, Defendants fraudulently concealed the safety information about the use of esomeprazole. As described herein, esomeprazole presents high risk of gastric cancer, kidney disease and other serious and dangerous side effects not present in other methods and drugs for the treatment of peptic disorders.

401. At all times during the course of dealing between Defendants and Plaintiff, and/or Plaintiff's healthcare providers, and/or the FDA, Defendants misrepresented the safety of es esomeprazole for its intended use.

402. These representations and omissions were made by said Defendants with the intent of defrauding and deceiving the Plaintiff, the public in general, and the medical and healthcare community in particular, and were made with the intent of inducing the public in general, and the medical and healthcare community in particular, to recommend, prescribe, dispense and/or

purchase esomeprazole, all of which evinced a callous, reckless, willful, depraved indifference to the health, safety and welfare of the Plaintiff herein.

403. At the time the aforesaid representations and omissions were made by the Defendants, and at the time the Plaintiff used esomeprazole, the Plaintiff was unaware of the falsity of said representations and reasonably believed them to be true.

404. Defendants fraudulently concealed the safety issues associated with esomeprazole use to induce Plaintiff to purchase and use, and physicians to prescribe and/or esomeprazole.

405. Plaintiff and/or Plaintiff's healthcare providers reasonably relied on Defendants' omissions and representations in using or prescribing esomeprazole, thereby causing Plaintiff to sustain severe and permanent personal injuries. Defendants knew, were aware or should have been aware that esomeprazole had not been sufficiently tested, were defective in nature and/or that esomeprazole lacked adequate and/or sufficient warnings.

406. Defendants knew or were reckless in not knowing that its representations were false.

407. Defendants knew or should have known that esomeprazole had a potential to, could and would cause severe and grievous injury to the users of said product, and that they were inherently dangerous in a manner that exceeded any purported, inaccurate and/or down-played warnings.

408. Defendants had a duty to provide consumers, patients and healthcare providers with full, complete, accurate and truthful information concerning esomeprazole, including the appropriate use of the product.

409. Defendants were also under a duty to disclose to Plaintiff, and Plaintiff's physicians, hospitals, healthcare providers, and/or the FDA the defective nature of esomeprazole, including but not limited to the heightened risks of stomach cancer.

410. By virtue of Defendants' omissions and partial disclosures about the medications, in which Defendants touted esomeprazole as a safe and effective medication, Defendants had a duty to disclose all facts about the risks associated with use of the medication, including the risk of gastric cancer, kidney disease and other serious and dangerous side effects.

411. Plaintiff and/or Plaintiff's healthcare providers reasonably relied on these material misrepresentations and omissions when deciding to prescribe, recommend, purchase and/or consume esomeprazole.

412. Plaintiff's healthcare providers were not provided the necessary information by the Defendants to provide an adequate warning to the Plaintiff.

413. Plaintiff was not provided the necessary information by Defendants to provide an adequate warning to the Plaintiff.

414. Esomeprazole was improperly marketed to the Plaintiff and/or their healthcare providers as the Defendants did not provide proper instructions about how to use the medication and did not adequately warn about the risks associated with esomeprazole use.

415. Plaintiff would not know, in the exercise of reasonable diligence, that Defendants' statements concerning esomeprazole were knowingly and intentionally false and misleading, or that Defendants had not disclosed material facts and information to the Plaintiff and/or the Plaintiff's healthcare providers that would have been material to the choice of treatment.

416. As a direct and proximate result of Defendants' malicious and intentional concealment of material information from Plaintiff and Plaintiff's healthcare providers, Defendants caused or contributed to Plaintiff's injuries.

417. Prior to the Plaintiff's use of esomeprazole and during the period in which Plaintiff used esomeprazole, Defendants fraudulently suppressed material information regarding the safety and efficacy of the drugs, including information regarding increased risk of gastric cancer.

418. Had Plaintiff been aware of the hazards associated with esomeprazole, Plaintiff would have used a safer alternative treatment for peptic disorders, including gastroesophageal reflux disease (GERD), peptic ulcer disease and nonsteroidal anti-inflammatory drug induced gastropathy, would not have consumed esomeprazole and/or would have reduced the duration or quantity of use.

419. Defendants' conduct was reckless, willful, wanton, and outrageous, and manifested a reckless indifference for the safety and well-being of patients and consumers, including the Plaintiff.

420. As a direct and proximate result of Defendants' intentional and willful fraudulent concealment of material facts and information from the Plaintiff and Plaintiff's healthcare providers, Defendants caused, and increased the risk of harm of, the injuries and damages suffered by the Plaintiff from the use of esomeprazole.

421. Had Plaintiff been aware of the hazards associated with esomeprazole use as concealed by Defendants, Plaintiff would not have accepted esomeprazole treatment and would have accepted a safer and more effective alternative.

422. Defendants actively and fraudulently concealed information in Defendants' exclusive possession regarding the hazards associated with esomeprazole for the purpose of preventing consumers, such as Plaintiff, from discovering these hazards.

423. Defendants conduct is outrageous and shocks the conscience, and knowingly and intentionally placed considerations of financial gain, revenues and profits, market share and marketing advantage over patient safety and well-being.

424. As a result of the foregoing acts and omissions, Plaintiff was caused to suffer serious and dangerous side effects, including gastric cancer and other severe and personal injuries which are permanent and lasting in nature, physical pain and mental anguish, diminished enjoyment of life and financial expenses for hospitalization and medical care.

425. Defendants' conduct, as described herein, was extreme and outrageous. Defendants risked the lives of the consumers and users of esomeprazole, including Plaintiff, with knowledge of the safety and efficacy problems with esomeprazole and suppressed this knowledge from the general public, Plaintiff, and/or Plaintiff's healthcare providers. Defendants made conscious decisions not to redesign, re-label, warn or inform the unsuspecting consuming public. Defendants' outrageous conduct warrants an award of punitive damages.

WHEREFORE, the Plaintiffs respectfully request that this Court enter judgment in Plaintiffs' favor for compensatory and punitive damages, together with interest, cost herein incurred, attorneys' fees, and all such other and further relief as this Court deems just and proper. Plaintiffs also demands that the issues contained herein be tried by a jury.

COUNT XI

VIOLATION OF CONSUMER PROTECTION LAWS

AND DECEPTIVE TRADE PRACTICES

426. Plaintiffs repeat, reiterate, and reallege each and every allegation of this Complaint contained in each of the foregoing paragraphs inclusive, with the same force and effect as if more fully set forth herein.

427. Plaintiff used esomeprazole and suffered ascertainable losses as a result of Defendants' actions in violation of the consumer protection laws.

428. Defendants have engaged in unfair competition or unfair or deceptive acts or trade practices or have made false representations in violation of the following consumer protection laws:

a) Ala. Code§§ 8-19-1 et seq.;

b) Alaska Stat. § 45.50.561 et seq.;

c) A.R.S. § 44-1521 et seq.;

d) A.C.A. § 4-88-101 et seq.;

e) Cal Bus & Prof Code § 17000 et seq. and § 17500 et seq.;

f) C.R.S. 6-1-101 et seq.;

g) Conn. Gen. Stat. § 42-110a et seq.;

h) Del. Code Ann. tit. 6, §§ 2511 et seq. and §§ 2531 et seq.

i) D.C. Code Ann.§§ 28-3901 et seq.;

j) Fla. Stat. Ann. §§ 501.201 et seq.;

k) O.C.G.A. §§ 10-1-372 et seq.;

l) Haw. Rev. Stat. §§ 480-1 et seq.;

m) Id. Code Ann.§§ 48-601 et seq.;

n) 815 ILCS 505/1 et seq.;

o) Ind. Code Ann. §§ 24-5-0.5-1 et seq.;

p) Iowa Code Ann. §§ 714.16 et seq.;

q) Kan. Stat. Ann. §§ 50-623 et seq.;

r) Ky. Rev. Stat. Ann.§§ 367.170 et seq.;

s) La. Rev. Stat. Ann.§§ 51:1401 et seq.;

t) Me. Rev. Stat. Ann. tit. 5, §§ 205-A et seq.;

u) Md. Code Ann., Com. Law§§ 13-101 et seq.;

v) Mass. Gen. Laws Ann. Ch. 93A et seq.;

w) Mich. Comp. Laws§§ 445.901 et seq.;

x) Minn. Stat. § 325F.68 et seq.;

y) Miss. Code Ann. § 75-24-5 et seq.;

z) § 407.020 R.S.Mo. et seq.;

aa) 30-14-101, MCA et seq.;

bb) R.R.S. Neb. § 59-1601 et seq.;

cc) Nev. Rev. Stat. Ann. § 598.0903 et seq.; and § 598A.010 et seq.;

dd) N. H. RSA 358-A:1 et seq.;

ee) N.J. Stat. § 56:8-1 et seq.;

ff) N.M. Stat. Ann.§§ 57-12-1 et seq.;

gg) N.Y. Gen. Bus. Law§§ 349 et seq. and §§ 350-e et seq.;

hh) N.C. Gen. Stat.§§ 75-1.1 et seq.;

ii) N.D. Cent. Code§§ 51-12-01 et seq. and §§ 51-15-01 et seq.;

jj) Ohio Rev. Code Ann. §§ 1345.01 et seq.;

kk) Okla. Stat. tit. 15 §§ 751 et seq.;

ll) Or. Rev. Stat. §§ 646.605 et seq.;

mm) 73 Pa. Stat.§§ 201-1 et seq.;

nn) 10 L.P.R.A. § 258 et seq.;

oo) R.I. Gen. Laws. §§ 6-13.1-1 et seq.;

pp) S.C. Code Ann. §§ 39-5-10 et seq.;

qq) S.D. Codified Laws§§ 37-24-1 et seq.;

rr) Tenn. Code Ann.§§ 47-18-101 et seq.;

ss) Tex. Bus. & Com. Code §§17.41 et seq.;

tt) Utah Code Ann.§§ 13-11-1 et seq.;

uu) Vt. Stat. Ann. tit. 9, §§ 2451 et seq.;

vv) Va. Code Ann.§§ 59.1-196 et seq.;

ww) Rev. Code Wash. (ARCW) § 15.04.410 et seq.;

xx) W. Va. Code § 46A-6-101 et seq.

yy) Wis. Stat. § 421.101 et seq.;

zz) Wyo. Stat. § 40-12-101 et seq.

429. As a result of the foregoing acts and omissions, Plaintiff was caused to suffer serious and dangerous side effects, including gastric cancer and other severe and personal injuries which are permanent and lasting in nature, physical pain and mental anguish, diminished enjoyment of life and financial expenses for hospitalization and medical care.

430. Defendants' conduct, as described herein, was extreme and outrageous. Defendants risked the lives of the consumers and users of esomeprazole, including Plaintiff, with knowledge of the safety and efficacy problems with esomeprazole and suppressed this knowledge from the general public, Plaintiff, and/or Plaintiff's healthcare providers. Defendants made

conscious decisions not to redesign, re-label, warn or inform the unsuspecting consuming public. Defendants' outrageous conduct warrants an award of punitive damages.

WHEREFORE, the Plaintiffs respectfully request that this Court enter judgment in Plaintiffs' favor for compensatory and punitive damages, together with interest, cost herein incurred, attorneys' fees, and all such other and further relief as this Court deems just and proper. Plaintiffs also demands that the issues contained herein be tried by a jury.

COUNT XII

LOSS OF CONSORTIUM

431. Plaintiffs repeat, reiterate, and reallege each and every allegation of this Complaint contained in each of the foregoing paragraphs inclusive, with the same force and effect as if more fully set forth herein.

432. Plaintiff, Stephanie Hudson, was at all times relevant hereto the spouse of Plaintiff, Daniel Hudson, and as such lives and cohabites with said Plaintiff.

433. For the reasons set forth herein, Plaintiff have necessarily paid and have become liable to pay for medical aid, treatment and for medications, and will necessarily incur further expenses of a similar nature in the future.

434. For the reasons set forth herein, Plaintiff have been caused, presently and in the future, to suffer the loss of their spouse's companionship, services, society and the ability of the Plaintiff's spouse has in those respects been impaired and depreciated, and the martial association between husband and wife has been altered, and, accordingly, the Plaintiff has been caused great mental anguish.

435. Defendants misled both the medical community and the public at large, including Plaintiff, by making false representations about the safety of esomeprazole. Defendants downplayed, understated and disregarded their knowledge of the serious and permanent injuries associated with esomeprazole use despite available information demonstrating that the product was likely to cause serious side-effects to its users.

436. Defendants were or should have been in possession of evidence demonstrating that esomeprazole caused serious side effects. Nevertheless, they continued to market the products by providing false and misleading information with regard to the safety and efficacy of esomeprazole.

437. Defendants' actions, as described herein, were performed willfully, intentionally and with reckless disregard for the rights of the Plaintiff and the public.

438. As a result of the foregoing acts and omissions, Plaintiff's spouse and/or significant others were caused to suffer serious and dangerous side effects, including gastric cancer and other severe and personal injuries which are permanent and lasting in nature, physical pain and mental anguish, diminished enjoyment of life and financial expenses for hospitalization and medical care.

439. Defendants' conduct, as described herein, was extreme and outrageous. Defendants risked the lives of the consumers and users of esomeprazole, including Plaintiff, with knowledge of the safety and efficacy problems with esomeprazole and suppressed this knowledge from the general public, Plaintiff, and/or Plaintiff's healthcare providers. Defendants made conscious decisions not to redesign, re-label, warn or inform the unsuspecting consuming public. Defendants' outrageous conduct warrants an award of punitive damages.

WHEREFORE, the Plaintiffs respectfully request that this Court enter judgment in Plaintiffs' favor for compensatory and punitive damages, together with interest, cost herein

incurred, attorneys' fees, and all such other and further relief as this Court deems just and proper.

Plaintiffs also demands that the issues contained herein be tried by a jury.

PRAYER FOR RELIEF

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

1. Awarding compensatory damages in excess of $75,000, including, but not limited to pain, suffering, discomfort, physical impairment, emotional distress, loss of enjoyment of life, loss of consortium, and other noneconomic damages in an amount to be determined at trial of this action;

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

3. Punitive and/or exemplary damages for the wanton, willful, fraudulent, reckless acts of the Defendants who demonstrated a complete disregard and reckless indifference for the safety and welfare of the general public and Plaintiffs in an amount sufficient to punish Defendants and deter future similar conduct;

4. Prejudgment interest;

5. Post-judgment interest;

6. Awarding reasonable attorneys' fees;

7. Awarding the costs of these proceedings; and

8. For such other and further relief as this Court may deem just and proper.

DEMAND FOR JURY TRIAL

Plaintiff hereby demands trial by jury as to all issues.

Dated: _____

RESPECTFULLY SUBMITTED,

JOHN M. RESTAINO, JR
(CA -138268)
RESTAINO LAW, LLC.
130 Forest St
Denver, CO 80220
Ph: (303) 838-8000
Fax: (720) 221-0449

GREGORY D. RUEB, ESQ.
(CA- 154589)
DALIMONTE RUEB, LLP
1990 N. California Blvd. 8th Floor Walnut Creek, CA 94596
Ph: (833) 827-5150
Fax: (925) 932-7001

ATTORNEYS FOR PLAINTIFF

JS 44 (Rev. 06/17)

CIVIL COVER SHEET

The JS 44 civil cover sheet and the information contained herein neither replace nor supplement the filing and service of pleadings or other papers as required by law, except as provided by local rules of court. This form, approved by the Judicial Conference of the United States in September 1974, is required for the use of the Clerk of Court for the purpose of initiating the civil docket sheet. *(SEE INSTRUCTIONS ON NEXT PAGE OF THIS FORM.)*

I. (a) PLAINTIFFS

Daniel Hudson and Stephanie Hudson

(b) County of Residence of First Listed Plaintiff _____
(EXCEPT IN U.S. PLAINTIFF CASES)

(c) Attorneys *(Firm Name, Address, and Telephone Number)*

John M Restaino, Jr.
Restaino Law, LLC
130 Forest St.
Denver, CO 80220
(303) 839-8000

Gregory D Rueb, Esq.
Dalimonte Rueb, LLP
1990 N California Blvd, 8th Floor
Walnut Creek, CA 94596
(833) 827-5150

DEFENDANTS

AstraZeneca Pharmaceuticals LP, AstraZeneca LP, and Merck & Co. Inc. d/b/a/ Merck, Sharpe & Dohme Corporation

County of Residence of First Listed Defendant _____
(IN U.S. PLAINTIFF CASES ONLY)

NOTE: IN LAND CONDEMNATION CASES, USE THE LOCATION OF THE TRACT OF LAND INVOLVED.

Attorneys *(If Known)*

II. BASIS OF JURISDICTION *(Place an "X" in One Box Only)*

- ☐ 1 U.S. Government Plaintiff
- ☐ 3 Federal Question *(U.S. Government Not a Party)*
- ☐ 2 U.S. Government Defendant
- ☒ 4 Diversity *(Indicate Citizenship of Parties in Item III)*

III. CITIZENSHIP OF PRINCIPAL PARTIES *(Place an "X" in One Box for Plaintiff and One Box for Defendant)*
(For Diversity Cases Only)

	PTF	DEF		PTF	DEF
Citizen of This State	☐ 1	☐ 1	Incorporated *or* Principal Place of Business In This State	☐ 4	☐ 4
Citizen of Another State	☐ 2	☐ 2	Incorporated *and* Principal Place of Business In Another State	☐ 5	☒ 5
Citizen or Subject of a Foreign Country	☐ 3	☐ 3	Foreign Nation	☐ 6	☐ 6

IV. NATURE OF SUIT *(Place an "X" in One Box Only)*

Click here for: Nature of Suit Code Descriptions.

CONTRACT
- ☐ 110 Insurance
- ☐ 120 Marine
- ☐ 130 Miller Act
- ☐ 140 Negotiable Instrument
- ☐ 150 Recovery of Overpayment & Enforcement of Judgment
- ☐ 151 Medicare Act
- ☐ 152 Recovery of Defaulted Student Loans (Excludes Veterans)
- ☐ 153 Recovery of Overpayment of Veteran's Benefits
- ☐ 160 Stockholders' Suits
- ☐ 190 Other Contract
- ☐ 195 Contract Product Liability
- ☐ 196 Franchise

REAL PROPERTY
- ☐ 210 Land Condemnation
- ☐ 220 Foreclosure
- ☐ 230 Rent Lease & Ejectment
- ☐ 240 Torts to Land
- ☐ 245 Tort Product Liability
- ☐ 290 All Other Real Property

TORTS

PERSONAL INJURY
- ☐ 310 Airplane
- ☐ 315 Airplane Product Liability
- ☐ 320 Assault, Libel & Slander
- ☐ 330 Federal Employers' Liability
- ☐ 340 Marine
- ☐ 345 Marine Product Liability
- ☐ 350 Motor Vehicle
- ☐ 355 Motor Vehicle Product Liability
- ☐ 360 Other Personal Injury
- ☐ 362 Personal Injury - Medical Malpractice

PERSONAL INJURY
- ☐ 365 Personal Injury - Product Liability
- ☒ 367 Health Care/ Pharmaceutical Personal Injury Product Liability
- ☐ 368 Asbestos Personal Injury Product Liability

PERSONAL PROPERTY
- ☐ 370 Other Fraud
- ☐ 371 Truth in Lending
- ☐ 380 Other Personal Property Damage
- ☐ 385 Property Damage Product Liability

CIVIL RIGHTS
- ☐ 440 Other Civil Rights
- ☐ 441 Voting
- ☐ 442 Employment
- ☐ 443 Housing/ Accommodations
- ☐ 445 Amer. w/Disabilities - Employment
- ☐ 446 Amer. w/Disabilities - Other
- ☐ 448 Education

PRISONER PETITIONS

Habeas Corpus:
- ☐ 463 Alien Detainee
- ☐ 510 Motions to Vacate Sentence
- ☐ 530 General
- ☐ 535 Death Penalty

Other:
- ☐ 540 Mandamus & Other
- ☐ 550 Civil Rights
- ☐ 555 Prison Condition
- ☐ 560 Civil Detainee - Conditions of Confinement

FORFEITURE/PENALTY
- ☐ 625 Drug Related Seizure of Property 21 USC 881
- ☐ 690 Other

LABOR
- ☐ 710 Fair Labor Standards Act
- ☐ 720 Labor/Management Relations
- ☐ 740 Railway Labor Act
- ☐ 751 Family and Medical Leave Act
- ☐ 790 Other Labor Litigation
- ☐ 791 Employee Retirement Income Security Act

IMMIGRATION
- ☐ 462 Naturalization Application
- ☐ 465 Other Immigration Actions

BANKRUPTCY
- ☐ 422 Appeal 28 USC 158
- ☐ 423 Withdrawal 28 USC 157

PROPERTY RIGHTS
- ☐ 820 Copyrights
- ☐ 830 Patent
- ☐ 835 Patent - Abbreviated New Drug Application
- ☐ 840 Trademark

SOCIAL SECURITY
- ☐ 861 HIA (1395ff)
- ☐ 862 Black Lung (923)
- ☐ 863 DIWC/DIWW (405(g))
- ☐ 864 SSID Title XVI
- ☐ 865 RSI (405(g))

FEDERAL TAX SUITS
- ☐ 870 Taxes (U.S. Plaintiff or Defendant)
- ☐ 871 IRS—Third Party 26 USC 7609

OTHER STATUTES
- ☐ 375 False Claims Act
- ☐ 376 Qui Tam (31 USC 3729(a))
- ☐ 400 State Reapportionment
- ☐ 410 Antitrust
- ☐ 430 Banks and Banking
- ☐ 450 Commerce
- ☐ 460 Deportation
- ☐ 470 Racketeer Influenced and Corrupt Organizations
- ☐ 480 Consumer Credit
- ☐ 490 Cable/Sat TV
- ☐ 850 Securities/Commodities/ Exchange
- ☐ 890 Other Statutory Actions
- ☐ 891 Agricultural Acts
- ☐ 893 Environmental Matters
- ☐ 895 Freedom of Information Act
- ☐ 896 Arbitration
- ☐ 899 Administrative Procedure Act/Review or Appeal of Agency Decision
- ☐ 950 Constitutionality of State Statutes

V. ORIGIN *(Place an "X" in One Box Only)*

☐ 1 Original Proceeding ☐ 2 Removed from State Court ☐ 3 Remanded from Appellate Court ☐ 4 Reinstated or Reopened ☐ 5 Transferred from Another District *(specify)* ☐ 6 Multidistrict Litigation - Transfer ☒ 8 Multidistrict Litigation - Direct File

VI. CAUSE OF ACTION

Cite the U.S. Civil Statute under which you are filing ***(Do not cite jurisdictional statutes unless diversity)***:
28:1332pl Diversity- Product Liability

Brief description of cause:
367 Personal Injury: Health Care/Pharmaceutical Personal Injury Product Liability

VII. REQUESTED IN COMPLAINT:

☐ CHECK IF THIS IS A **CLASS ACTION** UNDER RULE 23, F.R.Cv.P.

DEMAND $

CHECK YES only if demanded in complaint:

JURY DEMAND: ☒ Yes ☐ No

VIII. RELATED CASE(S) IF ANY

(See instructions): JUDGE Claire C. Cecchi DOCKET NUMBER MDL No. 2789

DATE 04/30/2019

SIGNATURE OF ATTORNEY OF RECORD /s/ John M Restaino, Jr. /s/ Gregory D. Rueb, Esq.

FOR OFFICE USE ONLY

RECEIPT # _____ AMOUNT _____ APPLYING IFP _____ JUDGE _____ MAG. JUDGE _____