UNITED STATES DISTRICT COURT
MIDDLE DISTRICT OF FLORIDA
TAMPA DIVISION

UNITED STATES OF AMERICA

v.

Case No. 8:15-cr-

GENZYME CORPORATION

21 U.S.C. § 331(k)
21 U.S.C. § 333(a)(1)
21 U.S.C. § 351(f)(1)(B)
21 U.S.C. § 352(a)

INFORMATION

The United States Attorney charges:

At all times material to this Information:

1. Genzyme Corporation (hereinafter, "Genzyme") was a biotechnology company organized under the laws of the Commonwealth of Massachusetts, with its headquarters located in Cambridge, Massachusetts. In April 2011, after the conduct described herein, Genzyme Corporation was acquired by the Sanofi Group. As a result of the acquisition, Genzyme became affiliated with Sanofi US Services, Inc. and Sanofi-Aventis LLC (collectively, "Sanofi US"), which were organized under the laws of the State of Delaware.

2. Genzyme manufactured, marketed, and sold the Seprafilm Adhesion Barrier (hereinafter, "Seprafilm"), a clear piece of thin film that was used during open abdominal and pelvic surgery to reduce the incidence, extent, and severity of

postoperative adhesions. Seprafilm was composed of two chemically modified sugars: hyaluronic acid and carboxymethylcellulose.

3. Genzyme regularly marketed Seprafilm to surgeons and other healthcare providers and shipped Seprafilm to hospitals and other medical institutions located within the Middle District of Florida from facilities located outside of the State of Florida.

FDA's Regulation of Devices

4. The United States Food and Drug Administration ("FDA"), an agency within the United States Department of Health and Human Services, was the agency of the United States government responsible for protecting the health and safety of the American public by assuring, among other things, that medical devices intended for use in human beings were safe and effective for their intended uses. Pursuant to its statutory mandate under the Federal Food, Drug, and Cosmetic Act ("FDCA"), as codified at Title 21, United States Code, Sections 301–399f, FDA regulated the manufacture, processing, packing, labeling, and shipment in interstate commerce of medical devices, including Seprafilm.

5. The FDCA, among other things, governed the manufacture and interstate distribution of medical devices for human use.

6. The FDCA defined a "device" (in relevant part) as an "instrument, apparatus, implement, machine, contrivance, implant … or other similar or related article,

including any component, part, or accessory, which is … intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man … or intended to affect the structure or any function of the body of man … and which does not achieve its primary intended purposes through chemical action … and which is not dependent upon being metabolized for the achievement of its primary intended purposes." 21 U.S.C. § 321(h).

7. Under the FDCA and its implementing regulations, all medical devices were classified into one of three regulatory classes—Class I, II, or III—based on the level of controls necessary to provide reasonable assurance of the device's safety and effectiveness for the general and specific uses for which it was intended. Classification was largely risk-based, that is, the risk the device posed to the patient or the user was a major factor in determining the class assigned to a particular device. In addition, with the exception of certain devices that were exempt from premarket review, "new" devices that came on the market were automatically classified into Class III as a matter of law, and required full premarket approval prior to their being marketed within the United States. 21 U.S.C. §§ 360c(f)(1) and 360e(a).

8. Class III devices generally carried the highest level of risk and were therefore subject to the highest level of regulatory controls in order to provide reasonable assurance of safety and effectiveness for their intended use. Class III

devices included devices that were intended for use in supporting or sustaining life, were of substantial importance in preventing impairment of health, or presented a potential unreasonable risk of illness or injury.

Seprafilm

9. Genzyme's Seprafilm (that is, chemically modified sodium hyaluronate/ carboxymethylcellose absorbable adhesion barrier) was a "device" for purposes of the FDCA.

10. Seprafilm was categorized as a Class III device.

11. Because Seprafilm was a Class III device, Genzyme was required to submit and obtain FDA approval of a Premarket Approval Application ("PMA") before it could lawfully market Seprafilm in the United States. To be approved, a PMA had to provide FDA with sufficient information to demonstrate that there was a reasonable assurance that the device was safe and effective under the conditions of use recommended in the device's proposed labeling.

12. The FDA approved Genzyme's PMA for Seprafilm on or about August 12, 1996.

13. According to its FDA-approved package insert, Seprafilm was "indicated for use in patients undergoing abdominal or pelvic laparotomy as an adjunct intended to reduce the incidence, extent and severity of postoperative adhesions between the abdominal wall and the underlying viscera such as omentum, small bowel, bladder,

and stomach, and between the uterus and surrounding structures such as tubes and ovaries, large bowel, and bladder."

14. According to its FDA-approved package insert, Seprafilm achieved this intended purpose by "serv[ing] as a temporary bioresorbable barrier separating apposing tissue surfaces. The physical presence of the membrane separates adhesiogenic tissue while the normal tissue repair process takes place."

Seprafilm "Slurry"

15. Seprafilm's FDA-approved intended use was for "use in patients undergoing abdominal or pelvic laparotomy." A laparotomy (also known as "open" surgery) was a surgical procedure that involved making an incision into the abdominal wall that allowed the surgeon to gain access to and visualize the internal organs using standard surgical instruments.

16. By contrast, laparoscopy (also known as laparoscopic surgery or minimally invasive surgery) was a surgical technique in which short, narrow tubes (called "trocars") were inserted into the abdomen through smaller incisions. The surgeon would insert long, narrow surgical instruments through these tubes to manipulate, cut, and sew tissue.

17. Seprafilm has never been FDA-approved for use in laparoscopic surgical procedures.

18. To use Seprafilm in laparoscopic surgeries, sheets of Seprafilm were turned into a viscous gel-like fluid that could be introduced into the abdominal cavity through a trocar. Although there were minor variations in the formula and technique, Seprafilm "slurry" was created in the operating room by cutting the Seprafilm into narrow sheets, and hydrating it with saline. The mixture was then agitated until the desired consistency was reached. After drawing the slurry into a large syringe, the surgeon then applied the slurry via a catheter inserted through the trocar onto the affected area within the abdominopelvic cavity.

19. In addition to having an intended use and physical characteristics that were different from FDA-approved Seprafilm, the slurry raised questions of safety and effectiveness that were not evaluated by the FDA. Accordingly, Seprafilm slurry was a different Class III device for which the FDA had not determined its safety and effectiveness.

20. At times between January 1, 2005, and May 18, 2010, certain Genzyme sales representatives, acting within the course and scope of their employment with Genzyme, guided surgical staff regarding, and directly participated in, the preparation of Seprafilm slurry for use in patients undergoing laparoscopic surgical procedures.

Misleading Labeling

21. The FDA-approved package insert for Seprafilm contained the following statement within the "PRECAUTIONS" section: "The safety and effectiveness of

Seprafilm Adhesion Barrier has not been evaluated in clinical studies in the presence of malignancies [*i.e.,* cancer] in the abdominopelvic cavity."

22. The FDCA defined labeling as "all labels and other written, printed, or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article at any time while a device is held for sale after shipment or delivery for shipment in interstate commerce." 21 U.S.C. § 321(m). For purposes of the FDCA, the term "labeling" included written promotional material that "supplements or explains the product" including posters, pamphlets, brochures, and instruction books, regardless of physical accompaniment to the product.

23. Beginning in or about January 2008 and continuing until in or about 2010, Genzyme utilized and disseminated a written and graphic promotional brochure for Seprafilm in its marketing of Seprafilm to healthcare providers. This brochure included statements concerning the potential effects of post-surgical adhesions and described the results of various studies regarding the efficacy and safety of Seprafilm.

24. The brochure was "labeling" for purposes of the FDCA.

25. The third page of the brochure was entitled "No adhesion barrier has been more extensively evaluated/Proven safe and effective in abdominopelvic surgery." A headline on that page touted Genzyme's claim that Seprafilm was "Proven in radical pelvic surgery." Under that headline, the brochure stated in much smaller print that "in

a prospective series of patients receiving Seprafilm at radical oophorectomy (n=14), Seprafilm reduced the severity and extent of pelvic floor adhesions, compared with historical controls. 69% reduction in the extent of pelvic floor adhesions."

26. The "radical oophorectomy" referenced in the brochure referred to the removal of the ovaries and surrounding tissues to treat ovarian cancer.

27. In fact, the study upon which Genzyme based its sweeping claim considered only fourteen patients. As a matter of statistical power and scientific validity, the sample size was far too small to support Genzyme's assertion that Seprafilm had been proven safe and effective in radical pelvic surgery.

28. As a result, the brochure's claim that Seprafilm was "Proven in radical pelvic surgery" was misleading.

COUNT ONE

(Causing a Medical Device to Become Adulterated While Held for Sale)
21 U.S.C. §§ 331(k), 333(a)(1), 351(f)(1)(B)

29. The allegations contained in paragraphs 1 through 20 are hereby realleged and incorporated herein as if set forth in full.

30. Commencing in or about January 2005, and continuing through on or about May 18, 2010, within the Middle District of Florida and elsewhere, the defendant,

GENZYME CORPORATION,

did and caused the doing of acts with regard to Seprafilm Adhesion Barrier, a Class

III medical device, while it was held for sale after shipment in interstate commerce, namely cutting, hydrating, and agitating the Seprafilm to create a "slurry," which resulted in such device becoming adulterated within the meaning of 21 U.S.C. § 351(f)(1)(B), in that the altered, resultant device, that is "Seprafilm slurry," was required to have, but lacked, an approved application for premarket approval in effect.

In violation of Title 21, United States Code, Sections 331(k) and 333(a)(1).

COUNT TWO

(Causing a Medical Device to Become Misbranded While Held for Sale)
21 U.S.C. §§ 331(k), 333(a)(1), 352(a)

31. The allegations contained in paragraphs 1 through 14 and paragraphs 21 through 28 are hereby realleged and incorporated herein as if set forth in full.

32. Commencing in or about January, 2008, and continuing until in or about 2010, the exact dates being unknown to the United States Attorney, within the Middle District of Florida and elsewhere, the defendant,

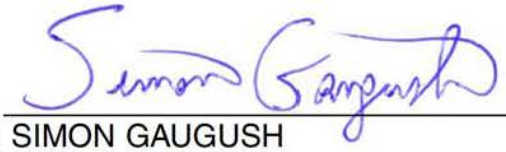
GENZYME CORPORATION,

did and caused the doing of acts with regard to Seprafilm Adhesion Barrier, a Class III medical device, while such article was held for sale after shipment in interstate commerce, that resulted in such article becoming misbranded within the meaning of 21 U.S.C. § 352(a), by disseminating labeling that was misleading in that it

represented that Seprafilm had been proven safe and effective for use in radical pelvic surgery, when in fact it had not been so proven.

In violation of Title 21, United States Code, Sections 331(k) and 333(a)(1).

A. LEE BENTLEY, III
United States Attorney



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