2011R00796/JTE/RDW/PJ

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

UNITED STATES OF AMERICA	:	Hon.
	:	Crim. No. 18-
v.	:	
HISAO YABE	:	21 U.S.C. §§ 331(a) and 333(a)(1)

I N F O R M A T I O N

The Acting United States Attorney for the District of New Jersey charges:

BACKGROUND

At all times relevant to this Information, unless otherwise alleged:

Defendant Hisao Yabe, Olympus Medical Systems Corporation, and the TJF-Q180V Duodenoscope

1. Olympus Corporation is a multinational manufacturer of optical imaging, laboratory, and medical equipment. Olympus Corporation is headquartered in Tokyo, Japan, is listed on the Tokyo Stock Exchange, and has subsidiaries throughout the world, including in the United States.

2. Olympus Medical Systems Corporation ("OMSC") is a wholly owned subsidiary of Olympus Corporation, and is located

in Tokyo, Japan. OMSC developed and manufactured endoscopes, including duodenoscopes, for direct internal observations of the human body.

3. HISAO YABE was the Division Manager for the Quality Assurance and Environment Division of OMSC. YABE was the top-ranking person at OMSC for regulatory matters, including having responsibility for adverse event reporting to the U.S. Food and Drug Administration ("FDA").

4. Duodenoscopes are flexible, lighted tubes that are threaded through the mouth, throat, and stomach into the top of the small intestine (duodenum). The end of the tube has a light, camera, and forceps elevator, which is controlled by an elevator wire that passes through a channel in the tube.

5. Duodenoscopes are used during endoscopic retrograde cholangiopancreatography ("ERCP"), a potentially life-saving procedure to diagnose and treat problems in the pancreas and bile ducts. Duodenoscopes are used throughout the world, including within the United States, where duodenoscopes are used in more than 500,000 ERCP procedures each year.

6. Because duodenoscopes are reusable devices, duodenoscopes must be reprocessed (cleaned) after each use by a procedure established by the manufacturer. If a reprocessing is unsuccessful, infectious material may remain on or in the duodenoscope, and subsequent patients treated with the

duodenoscope may become infected, which may lead to serious illness or death.

7. Reprocessing a duodenoscope involves an initial "pre-cleaning" step in which a technician manually washes the duodenoscope with fluids and a brush and a second step that can also be done manually but that most commonly is done automatically by placing the scope in a dishwasher-type machine, called an automated endoscope reprocessor.

8. Between August 2012 and October 2014, Olympus Corporation and its subsidiaries had approximately 85% of the United States market for duodenoscopes.

9. In 2010, Olympus America Inc. ("OAI"), another wholly owned, indirect subsidiary of Olympus Corporation, began marketing and distributing the TJF-Q180V duodenoscope ("Q180V") in the United States. OMSC manufactured the Q180V.

10. Unlike previous Olympus duodenoscopes, the Q180V had a closed elevator wire channel. The Q180V's sealed channel was intended to prevent bodily fluids from entering the elevator wire channel, thus, according to OMSC, eliminating the need to clean the elevator wire channel.

FDA and the FDCA

11. FDA is responsible for protecting the health and safety of the American public by assuring, among other things, that medical devices intended for use in the treatment of human beings are safe and effective for their intended uses. Pursuant to its statutory mandate, FDA regulates the manufacture, processing, packing, labeling, and shipment in interstate commerce of medical devices.

12. The Federal Food, Drug, and Cosmetic Act ("FDCA"), among other things, governs the manufacture and interstate distribution of medical devices for human use, as codified at Title 21, United States Code, Sections 301-399f.

Medical Device Reporting

13. The FDCA and its implementing regulations provide a mechanism that allows FDA, and others, to identify and monitor adverse events (deaths and serious injuries) and certain malfunctions involving medical devices.

14. Pursuant to 21 U.S.C. § 360i(a) and 21 CFR Part 803, medical device manufacturers must (1) develop, maintain, and implement written procedures for the identification and evaluation of all malfunctions, serious injuries, and deaths to determine whether a Medical Device Report ("MDR") is required for an event; (2) submit MDR reportable events involving their medical devices to FDA; and (3) establish and maintain complete

files for all MDR events. These requirements apply to all manufacturers of medical devices in the United States, including foreign manufacturers who export devices to the United States, such as OMSC.

15. Manufacturers must file an MDR with FDA within thirty (30) days of receiving or becoming aware of information that reasonably suggests that a device the manufacturer markets (a) may have caused or contributed to a death or serious injury or (b) has malfunctioned and the device or a similar device the manufacturer markets would be likely to cause or contribute to a death or serious injury if the malfunction were to recur. Such reports are referred to as "initial reports." Manufacturers who subsequently obtain information about the event that was not known or was not available when the initial report was submitted, but which would have been required to be submitted as part of the initial report had that additional information been known or available, must file a supplemental report or "supplemental MDR" with FDA within thirty (30) days of receiving the additional information.

16. MDRs are one of the post-market surveillance tools FDA uses to monitor device performance, detect potential device-related safety issues, and contribute to benefit-risk assessments of devices.

17. A device is deemed to be "misbranded" under 21 U.S.C. § 352(t)(2) if a manufacturer fails or refuses to furnish any material information required by or under 21 U.S.C. § 360i respecting the device. The FDCA prohibits the introduction of misbranded medical devices into interstate commerce, pursuant to 21 U.S.C. § 331(a).

The Q180V and OMSC's MDR Reporting

18. As the manufacturer of the Q180V, OMSC bore ultimate responsibility for the filing of MDRs to FDA for adverse events involving the Q180V anywhere in the world. Prior to April 2012, OAI personnel filed MDRs for OMSC for adverse events occurring anywhere in the world. In early 2012, HISAO YABE approved shifting responsibility for preparing and filing MDRs for adverse events occurring outside of North and South America from OAI personnel in the United States to OMSC personnel in Japan.

19. OMSC employees received minimal training to prepare for this transfer of responsibilities, which left them uncertain about what information must be included in an MDR and in what circumstances a supplemental MDR must be filed. Some OMSC employees believed that they had inadequate resources to take over the responsibility, and informed HISAO YABE that they needed additional training and resources to meet the MDR

reporting requirements. HISAO YABE denied their requests for assistance.

Erasmus Medical Center (Netherlands) Infections

20. Between January and April 2012, approximately 22 patients at the Erasmus Medical Center in the Netherlands were infected with *Pseudomonas aeruginosa* after the same TJF-Q180V duodenoscope was used on them. *Pseudomonas aeruginosa* was detected in a sample collected from the device.

21. In March 2012, officials from Erasmus Medical Center notified an Olympus Corporation subsidiary in the Netherlands of the infections. In April 2012, employees of OMSC learned of the infections.

22. On or about May 25, 2012, OMSC filed an MDR concerning the infections at Erasmus Medical Center. The MDR stated, "OMSC can not [sic] conclusively determine the cause [sic] this event. However, it can be considered as a possible cause of this phenomenon that the patient infected from other than the endoscope and procedure such as environmental factor in the facility." HISAO YABE was aware of the filing of this MDR.

23. As OMSC was preparing the MDR, an independent expert, Dr. Arjo Loeve of Delft University of Technology in the Netherlands, disassembled the Erasmus duodenoscope in the presence of representatives from Olympus Europe and Erasmus. He took samples from various points on the scope, analyzed the

scope itself, and prepared a detailed report –- “Investigation Report on Scope G-206” –- commonly referred to as “the Delft Report.”

24. The Olympus subsidiary in the Netherlands received a draft of the Delft Report in Dutch on or about May 22, 2012, and a final version of the Delft Report in Dutch on or about June 30, 2012. OMSC, including HISAO YABE, received an English translation of the Delft Report on or about August 6, 2012.

25. The Delft Report stated that *Pseudomonas aeruginosa* was found on the cap of the scope and that brownish deposits were found at several places, including in the closed elevator channel (referred to in the Delft Report as the propulsion cavity). The Delft Report observed that the tip of the scope had cracks, corners, and cavities that were very difficult to reach with a brush. The Delft Report further stated that the O-ring –- which was designed to seal the closed elevator wire channel -- likely failed to function properly and that it was “likely that moisture and/or biological material from the shaft or the tip of the endoscope entered the propulsion cavity and has remained and/or grown there.” The Delft Report’s conclusions included that the scope’s tip had various cracks, corners, and crevices that could harbor bacteria and could be cleaned only with great difficulty; that deposits

were found at various places, including in an area that should have been sealed from liquids; and that the O-ring did not guarantee a reliable seal. The Delft Report recommended immediate further investigation of all such scopes, updating the cleaning instructions, and improving the quality of the seals.

26. OMSC was required to supplement the initial MDR regarding the Erasmus adverse events upon receiving the Delft Report, but did not do so.

27. HISAO YABE did not implement the Delft Report's recommendations. Instead, HISAO YABE was involved in writing and approved a submission to the Dutch Health Inspectorate ("IGZ") –- a Dutch government agency akin to FDA –- on or about September 12, 2012, that dismissed the Delft Report's methodology and conclusions, insisted that Olympus's existing reprocessing instructions -– if followed properly –- were sufficient to clean the TJF-Q180V duodenoscope, and pointed to other potential causes of infections, including "hands of doctor/nurse and etc. which are used around the procedure."

28. FDA considered the Delft Report's findings significant when it first learned of the report more than two years later. Upon learning of the Delft Report independently of OMSC, FDA contacted OAI, asked if Olympus was aware of the report, and encouraged the company to obtain and read the report -- a report that, unbeknownst to FDA, OMSC and HISAO YABE had

received more than two years earlier. FDA communicated concerns regarding information included in the Delft Report and asked OAI for additional information.

29. In January 2013, an Olympus Corporation subsidiary in Europe, at the request of the IGZ, sent a Field Safety Corrective Action ("FSCA") to customers in the Netherlands. A subsidiary of Olympus Corporation in Europe prepared the notice and sent it to all European customers in or around January 2013. The January 2013 FSCA reminded customers to pay close attention to the Q180V's reprocessing instructions. An accompanying "Quick Reference Guide" suggested use of a small brush –- the MAJ-1888, which was an optional accessory available only in Europe –- to obtain deeper access to the forceps elevator during reprocessing.

30. On or about September 17, 2013, as part of an FDA effort to review information regarding risks associated with the transmission of infections by all major duodenoscopes being marketed in the United States, FDA sent OMSC a request for additional information ("AIR"), seeking more information about certain MDRs OMSC had filed relating to the Q180V and other scopes. The letter reminded OMSC of its obligation to file initial MDRs or supplemental MDRs if required. HISAO YABE received a copy of this letter.

31. On or about October 9, 2013, HISAO YABE and OMSC employees he supervised had a meeting in which they discussed, among other things, whether to file a supplemental MDR regarding the Erasmus adverse events. Prior to the meeting, HISAO YABE instructed the employees that if a supplemental MDR were required, it should be filed. An internal OMSC document circulated to HISAO YABE around the time of the meeting stated that a supplemental MDR was required. However, OMSC did not file a supplemental MDR at that time.

32. On or about March 13, 2015, over two years and seven months after receiving an English translation of the final Delft Report, OMSC filed supplemental MDRs concerning each of the 22 Erasmus patients who were infected with *Pseudomonas aeruginosa* after the same Olympus TJF-Q180V duodenoscope was used on them. The supplemental MDRs stated that Delft University had disassembled the duodenoscope and found brownish deposits on both sides of the O-ring.

Additional Infections and FDA's Response

33. From 2012 until at least early 2015, OMSC and HISAO YABE learned of additional infection outbreaks at multiple hospitals in Europe and the United States. In each instance, multiple patients on which the same Q180V duodenoscope was used were infected with the same type of infection.

34. In July 2014, Olympus Europe, at the request of the French Agence Nationale de Sécurité du Médicament et des Produits de Santé ("ANSM") –- a French government agency akin to FDA –- sent a Field Safety Corrective Action ("FSCA") to its customers in Europe. The FSCA recommended that European customers use the MAJ-1888 brush while cleaning the Q180V.

35. On or about February 19, 2015, FDA issued a Safety Communication –- Design of Endoscopic Retrograde Cholangiopancreatography (ERCP) Duodenoscopes May Impede Effective Cleaning –- informing users that the complex design of duodenoscopes may impede effective cleaning. The Safety Communication stemmed from the FDA's effort to assess the safety of all duodenoscopes -- not just OMSC's Q180V duodenoscope -- and applied to all duodenoscopes. The FDA Safety Communication noted that the design of duodenoscopes "causes challenges for cleaning and high-level disinfection . . . part of the scopes may be extremely difficult to access and effective cleaning of all areas of the duodenoscope may not be possible." The FDA Safety Communication recommended that users "[f]ollow closely all manufacturer instructions for cleaning and processing," and noted that "[e]ven though duodenoscopes are inherently difficult to reprocess, strict adherence to the manufacturer's reprocessing instructions will minimize the risk of infection."

36. On or about March 4, 2015, FDA released Updated Information for Healthcare Providers Regarding Duodenoscopes. FDA recommended that healthcare professionals inform patients of the potential risks of infection accompanying the use of duodenoscopes, and stated that FDA would continue evaluating "alternative cleaning protocols . . . and explore additional strategies to reduce the risk of infections. . . ." The FDA Updated Information noted that "FDA's analysis indicates that the reported duodenoscope-associated infections have occurred in patients who have had procedures with duodenoscopes from all three manufacturers." FDA noted that it was "not recommending that healthcare providers cancel ERCP procedures for their patients who need them."

37. On or about March 26, 2015, FDA issued a Safety Communication –- New Reprocessing Instructions Validated for Model TJF-Q180V Duodenoscopes –- which announced new and validated reprocessing instructions for the Q180V. The new instructions included changes to processing procedures on precleaning, manual cleaning, and manual high-level disinfection and required use of the MAJ-1888 brush.

Count One

(Introduction of Misbranded Medical Devices into Interstate Commerce, 21 U.S.C. §§ 331(a) and 333(a)(1))

38. The allegations contained in paragraphs 1 through 37 are realleged and incorporated herein as if set forth in full.

39. On or about April 10, 2014, in the District of New Jersey and elsewhere, defendant

HISAO YABE

did introduce and deliver for introduction, and cause the introduction or delivery for introduction, into interstate commerce, misbranded (pursuant to 21 U.S.C. § 352(t)(2)) medical devices, including a device shipped to a hospital in New Jersey, which were misbranded due to HISAO YABE's failure by that time to cause OMSC to file with FDA a supplemental MDR relating to infections at Erasmus Medical Center.

All in violation of 21 U.S.C. §§ 331(a) and 333(a)(1).

RACHAEL A. HONIG
ATTORNEY FOR THE
UNITED STATES ACTING UNDER
AUTHORITY CONFERRED BY
28 U.S.C. § 515