

## **FDA Document Suggests Higher Number of Duodenoscope Incidents Than Previously Reported**

On January 13, 2016, Democratic Members of the Senate Committee on Health, Education, Pensions, and Labor (HELP) issued a staff report titled “Preventable Tragedies: Superbugs and How Ineffective Monitoring of Medical Device Safety Fails Patients” on the issue of bacterial transmissions by duodenoscopes.

This report found: “Between 2012 and spring 2015, closed-channel duodenoscopes were linked to at least 25 different incidents of antibiotic-resistant infections that sickened at least 250 patients worldwide.”<sup>1</sup>

The House Committee on Oversight and Government Reform obtained a new document from the Food and Drug Administration (FDA) that indicates that the problem could be significantly greater than previously reported.<sup>2</sup>

This document covers the time period from January 1, 2010, to October 31, 2015, and includes incidents in which duodenoscopes were contaminated, as well as patients that were infected or exposed to bacteria. According to this document, there have been:

- as many as 404 patient infections;
- 44 additional patient exposures to contaminated devices;
- 41 facilities experienced incidents in the U.S. and abroad—30 in the United States and 11 overseas;
- 34 incidents in which patients were infected or exposed to contaminated devices; and
- 319 Medical Device Reports (MDR) on patient infections, exposure, and device contamination.

The document suggests that even these numbers could be underestimated: “In some cases, the MDR mentioned ‘at least XX patients’ in which case there could be additional patients involved.” The document also states: “In 17 reports MDRs [sic], there was mention that the scopes had device contamination after use—which indicates that it was used on at least one patient, even though the patient was not mentioned in the report.”

FDA states that these “reports likely contain duplicate patient reporting,” and “estimate[s] the number of unique patients reported to be 300 to 350 patients.” FDA further clarifies that the “number of patients reflects only numbers mentioned in the MDR reports.” This continues to

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<sup>1</sup> Democratic Staff, Senate Committee on Health, Education, Labor, and Pensions, *Preventable Tragedies: Superbugs and How Ineffective Monitoring of Medical Device Safety Fails Patients* (Jan. 2016) (online at [www.help.senate.gov/imo/media/doc/Duodenoscope%20Investigation%20FINAL%20Report.pdf](http://www.help.senate.gov/imo/media/doc/Duodenoscope%20Investigation%20FINAL%20Report.pdf)).

<sup>2</sup> Food and Drug Administration, *Table: MDR Counts and Patient Counts by User Facility* (Feb. 15, 2016).

raise concerns that the FDA is unaware of the true number of patients affected nationally and is limited to only those reported.

In addition, many infections have been attributed to patients rather than duodenoscopy procedures when their infections were caused by common bacteria. According to the American Society of Microbiology:

Until recently, most infections have been attributed to the patient's own bacterial flora penetrating the normal barriers into the blood stream. For example, a blood stream infection caused by *Escherichia coli* (a normal part of the human bowel flora) would be attributed to that patient's own *E. coli* and no further investigations would be performed. As such, we may be underestimating the incidence of transmission events.<sup>3</sup>

The Senate report agreed, finding:

[B]ecause the hospitals that have reported infections are primarily large, well-resourced research hospitals adept at spotting and addressing antibiotic-resistant infections, it is likely that there have been more incidents of infections linked to these devices that were never identified.<sup>4</sup>

The Senate report also warned:

However, conversations between Senator Murray's HELP Committee staff and hospital staff, state and local health departments, and manufacturers have revealed a disconcerting lack of awareness that these reporting obligations even exist.<sup>5</sup>

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<sup>3</sup> Letter from Susan E. Sharp, President-Elect, American Society for Microbiology, to House Oversight and Government Reform Committee Staff (Oct. 14, 2015).

<sup>4</sup> Democratic Staff, Senate Committee on Health, Education, Labor, and Pensions, *Preventable Tragedies: Superbugs and How Ineffective Monitoring of Medical Device Safety Fails Patients* (Jan. 2016) (online at [www.help.senate.gov/imo/media/doc/Duodenoscopy%20Investigation%20FINAL%20Report.pdf](http://www.help.senate.gov/imo/media/doc/Duodenoscopy%20Investigation%20FINAL%20Report.pdf)).

<sup>5</sup> *Id.*

Food and Drug Administration

*Table: MDR Counts and Patient Counts By User Facility (Feb. 15, 2016).*

**TABLE: MDR COUNTS AND PATIENT COUNTS BY USER FACILITY**

USER FACILITY NAMED IN MDR REPORTS (1/1/2010-10/31/2015)	MDRs mentioning Patient Infections	MDRs mentioning Patient Exposure	MDRs mentioning Device Contamination	TOTAL MDRS	Patients Infected	Patients Exposed	Total Patients
Facility 1	2	8	0	10	2	8	10
Facility 2	10	1	2	13	57	1	58
Facility 3	1	0	0	1	1		1
Facility 4	1	0	0	1	1		1
Facility 5 (International)	0	0	2	2			0
Facility 6	6	0	0	6	6		6
Facility 7	6	0	0	6	8		8
Facility 8	0	4	0	4	0	4	4
Facility 9 (International)	5	0	0	5	5		5
Facility 10 (International)	4	0	0	4	7		7
Facility 11	3	0	0	3	3		3
Facility 12	22	0	0	22	23		23
Facility 13 (International)	4	0	1	5	4		4
Facility 14	0	0	1	1			0
Facility 15	6	0	0	6	7		7
Facility 16	0	0	1	1			0
Facility 17	0	2	0	2		2	2
Facility 18	16	0	0	16	16		16
Facility 19 (International)	0	0	2	2			0
Facility 20 (International)	32	0	0	32	32		32
Facility 21	6	0	0	6	6		6
Facility 22	0	0	1	1			0
Facility 23	4	0	0	4	4		4
Facility 24	0	0	1	1			0
Facility 25	2	0	0	2	2		2
Facility 26 (International)	1	0	0	1	1		1
Facility 27	0	2	0	2		4	4
Facility 28	8	0	3	11	8		8
Facility 29	0	0	1	1			0
Facility 30	16	0	1	17	22	9	31
Facility 31	4	0	0	4	8		8
Facility 32	7	0	0	7	7		7
Facility 33	7	0	0	7	8		8
Facility 34	20	0	0	20	40		40
Facility 35	1	0	0	1	1		1
Facility 36 (International)	12	0	0	12	12		12
Facility 37 (International)	4	0	0	4	4		4
Facility 38	0	2	0	2		2	2
Facility 39	2	12	1	15	2	13	15
Facility 40	39	0	0	39	79		79
Facility not specified	19	1	0	20	28	1	29
<b>Grand Total</b>	<b>270</b>	<b>32</b>	<b>17</b>	<b>319</b>	<b>404</b>	<b>44</b>	<b>448</b>

\* - NOTE: Number of patients reflects only numbers mentioned in the MDR reports. In some cases, the MDR mentioned "at least XX patients" in which case there could be additional patients involved. These reports likely contain duplicate patient reporting (ie, same affected patient, more than once). We estimate the number of unique patients reported to be 300 to 350.

NOTE: There were a total of 448 patients mentioned in the 319 reports. In 17 reports MDRs, there was mention that the scopes had device contamination after use -- which indicates that it was used on at least one patient, even though the patient was not mentioned in the report. Therefore 448 + 17 = 465 patients. The highlighted institutions are foreign hospitals - 88 patients were identified here. There were 6 additional ones that were outside of US, but the hospital was not specifically identified. Therefore, 88 + 6 = 94 patients OUS.

## Summary of Proposed Legislative Provisions

The evidence obtained by the Committee on Oversight and Government Reform during its investigation of duodenoscope-related patient infections identified significant gaps in existing law that contributed to preventable bacterial outbreaks. In addition to the provisions contained in S. 2503, three provisions are needed to ensure that FDA and healthcare providers are equipped to prevent unnecessary bacterial infections by reusable medical devices. These provisions would:

- (1) require manufacturers to notify FDA when they change their designs or reprocessing instructions, regardless of whether their devices are required to be resubmitted for regulatory approval;
- (2) require manufacturers to inform FDA when they alert their foreign customers of problems with the design and cleaning of their devices; and
- (3) require FDA to regulate rapid assessment tests as medical devices.

### I. REPORTING REQUIREMENT FOR DESIGN CHANGES

The evidence obtained by the Committee demonstrates that manufacturers of duodenoscopes failed to report significant changes they made to the design of their devices. As a result, FDA did not evaluate those changes for years after they were introduced into the market.

For example, in 2010 Olympus introduced a major change to its duodenoscope design that closed the elevator channel, making it impossible to clean behind an O-ring seal. The company did not report the change to FDA, and the new model was not evaluated for safety for years.

In November 2010, Olympus made a cursory reference to its new model, the 180V, in a mandatory filing known as a Medical Device Report (MDR) following an adverse event.<sup>1</sup>

FDA responded by asking Olympus for details about its new model and to “list any modifications or enhancements which have been implemented (or are planned)” compared to the previous model.<sup>2</sup>

Olympus responded with a long list of modifications it had made, including:

- “Add directions, warnings, and information about the guidewire locking function (especially about the side lock) to the operation manual.
- Add ancillary devices that can be used with the endoscope to the operation manual.

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<sup>1</sup> Letter from Laura Storms-Tyler, Vice President of Regulatory Affairs and Quality Assurance, Olympus America, Inc., to Deborah Yehia, Center for Devices and Radiological Health, Food and Drug Administration (Feb. 4, 2011).

<sup>2</sup> *Id.*

- Change the maximum diameter of the insertion tube to 15.0 mm.
- Change the material of the L arm; this is a metal piece that is connected to the forceps raiser, and with part# GE678500.”<sup>3</sup>

However, the company omitted reporting the design change to seal the elevator-wire channel. This omission was significant. In March 2014, FDA requested that Olympus submit the 180V for regulatory approval, stating that “we believe that sealing the elevator channel, and consequently, preventing sterilization and high level disinfection of the elevator channel, impacts the safe use of the device.”<sup>4</sup>

Under federal law, medical device manufacturers are required to report modifications that could significantly affect the safety or effectiveness of the device.<sup>5</sup> However, if a manufacturer believes a modification is minor, it may proceed to market without requesting FDA approval.<sup>6</sup>

New legislation is needed to improve FDA awareness of device design or reprocessing changes by requiring that all changes be reported to FDA. The provision would read as follows:

**REPORTING REQUIREMENT FOR DEVICE DESIGN AND REPROCESSING INSTRUCTION CHANGES.**—Before making a change to the design of a device, or the reprocessing instructions of a device, that is marketed in interstate commerce, the manufacturer of the device shall give written notice of the change to the Food and Drug Administration.

## **II. REPORTING REQUIREMENT FOR COMMUNICATIONS TO FOREIGN HEALTH CARE PROVIDERS**

The evidence obtained by the Committee demonstrates that Olympus issued safety warnings and introduced safety enhancements in Europe for its closed-elevator channel duodenoscopes considerably earlier than it did in the United States and did not inform FDA officials about them.

Olympus issued safety warnings in January 2013 instructing European health providers to use a special brush provided by Olympus to clean their 180V closed-elevator channel

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<sup>3</sup> *Id.*

<sup>4</sup> Letter from LaShanda Long, Chief, Center for Devices and Radiological Health, Food and Drug Administration, to Laura Storms-Tyler, Vice President, Olympus Medical Systems Corporation (Mar. 18, 2014) (online at [www.fda.gov/downloads/MedicalDevices/ResourcesforYou/Industry/UCM436587.pdf](http://www.fda.gov/downloads/MedicalDevices/ResourcesforYou/Industry/UCM436587.pdf)).

<sup>5</sup> Memorandum from Congressional Research Service to House Committee on Oversight and Government Reform Staff (Nov. 23, 2015).

<sup>6</sup> *Id.*

duodenoscopes. Olympus distributed these safety notifications in Netherlands and Switzerland, among other places.<sup>7</sup>

Olympus' instructions directed providers: "Use one of the recommended brushes to brush the front and rear side of the forceps elevator."<sup>8</sup> Olympus recommended: "The MAJ-1888 brush can be used for heavy soiling or delayed reprocessing situations and enables deeper access to the forceps elevator."<sup>9</sup>

In July and August 2014, Olympus contacted European customers again, issuing a safety communication entitled, "URGENT: Field Safety Corrective Action" announcing updated cleaning manuals for the company's TJF-Q180V model:

As a result of our complaint investigations, Olympus has determined to revise our reprocessing instructions and recommends the use of an additional cleaning brush. The additional brush is the MAJ-1888. Olympus recommends brushing around the forceps elevator with the MAJ-1888 brush in addition to the existing MH-507 brush in order to adequately clean around the forceps elevator more thoroughly.<sup>10</sup>

Olympus sent these safety notifications in Europe before the majority of major outbreaks in the United States occurred. Olympus did not inform FDA about these safety notices and did not issue similar safety warnings in the United States at the time.<sup>11</sup>

It was not until February 19, 2015, that Olympus distributed its first public safety communication to U.S. healthcare providers, more than two years after the similar communications in Europe.<sup>12</sup> This communication, however, made no mention of the existence of the MAJ-1888 brush, which the company was recommending in Europe.

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<sup>7</sup> Swiss Agency for Therapeutic Products, *Medical Devices—List of Recalls and Other Field Safety Corrective Actions* (Jan. 2013) (accessed on Dec. 25, 2015) (online at [www.swissmedic.ch](http://www.swissmedic.ch)); Dr. Margreet Vos, *The Role of the ERCP Duodenoscope in the Outbreak by VIM Positive P. Aeruginosa at the Erasmus MC* (May 14, 2015) ([www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/Gastroenterology-UrologyDevicesPanel/UCM446944.pdf](http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/Gastroenterology-UrologyDevicesPanel/UCM446944.pdf)).

<sup>8</sup> Olympus Europa Holding GmbH, *Important Safety Advice Safe Reprocessing of TJF-Q180V* (Jan. 2013) (online at [www.swissmedic.ch/recalllists\\_dl/07207/Vk\\_20130123\\_15-e1.pdf](http://www.swissmedic.ch/recalllists_dl/07207/Vk_20130123_15-e1.pdf)).

<sup>9</sup> *Id.*

<sup>10</sup> Olympus, *URGENT: Field Safety Corrective Action* (Aug. 2014) (online at [www.swissmedic.ch/recalllists\\_dl/10220/Vk\\_20140729\\_02-e1.pdf](http://www.swissmedic.ch/recalllists_dl/10220/Vk_20140729_02-e1.pdf)).

<sup>11</sup> Briefing by the Food and Drug Administration to House Committee on Oversight and Government Reform Staff (Jan. 8, 2016).

<sup>12</sup> Olympus America Inc., *URGENT: IMPORTANT SAFETY INFORMATION* (Feb. 19, 2015) (online at [medical.olympusamerica.com/sites/default/files/pdf/TJF-Q180V\\_Customer\\_FINAL\\_English.pdf](http://medical.olympusamerica.com/sites/default/files/pdf/TJF-Q180V_Customer_FINAL_English.pdf)).

On March 26, 2015, Olympus finally announced the introduction of the MAJ-1888 brush in the United States:

The revised cleaning procedure requires brushing of the forceps elevator recess with two different-sized brushes. In addition to that brush that is currently used to clean the elevator recess area, the MAJ-1888 brush (or any Olympus MAJ-1888 equivalent) will be provided for further cleaning of this area. Olympus anticipates shipping the MAJ-1888 brushes no later than May 8, 2015.<sup>13</sup>

When Committee staff asked Olympus why its response in Europe had been so much faster than in the United States, company officials stated:

In December 2012, in the context of ongoing discussions with regulators in the Netherlands regarding infections reported at Erasmus Medical Center, the Dutch Health Care Inspectorate asked Olympus to submit a field safety notice to Dutch customers to remind users of the importance of pre-cleaning and reprocessing. The regulators asked that the notice reference the recent case and indicate that reprocessing instructions must be closely observed, that endoscopes must undergo a thorough visual inspection (and be serviced if damaged), and that training is available. Olympus distributed the notice to European customers.<sup>14</sup>

New legislation is needed to require that communications like those sent by Olympus in 2013 and 2014 in Europe would have to be reported to the FDA. The provision would read as follows:

**REQUIREMENT.**—The manufacturer of a device that is marketed in interstate commerce shall give written notice to the Food and Drug Administration of any communication described in paragraph (2) not more than 5 calendar days after making such communication...described in this paragraph if the communication—

- (A) is made by the manufacturer of the reusable device or an affiliate of the manufacturer;
- (B) relates to a change to the design of the device, a change to the recommended reprocessing protocols, if any, for the device, or a safety concern about the device; and

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<sup>13</sup> Olympus America Inc., *Urgent Safety Notification Important Updated Labeling Information: New Reprocessing Instructions for the Olympus TJF-Q180V Duodenoscope* (Mar. 26, 2015) (online at [medical.olympusamerica.com/sites/default/files/pdf/150326\\_TJF-Q180V\\_Customer\\_letter.pdf](http://medical.olympusamerica.com/sites/default/files/pdf/150326_TJF-Q180V_Customer_letter.pdf)).

<sup>14</sup> Letter from Robert K. Kelner, Covington and Burling LLP, on behalf of Olympus Corporation of the Americas, to House Committee on Oversight and Government Reform Staff (July 2, 2015).

(C) is widely disseminated (including on a voluntary basis) to health care providers in a foreign country.

### III. REGULATION OF RAPID ASSESSMENT TESTS AS MEDICAL DEVICES

Rapid assessment tests of bacterial contamination can detect ATP, a molecule that microorganisms use for energy, as well as carbohydrates and proteins that are indicators that bacteria may be present.

Current law does not regulate rapid assessment tests as medical devices, and experts warn that they have not been subjected to rigorous evaluation. The American Society of Microbiology stated that these rapid tests “have not been well validated” to show that they can detect living bacteria.<sup>15</sup> Dr. Michelle Alfa, a nationally known expert, has stated:

[T]here is no currently available rapid test that has been properly validated that can be used post-HLD on duodenoscopes to show that there are no viable bacteria and that the endoscope is safe to use on the next patient.<sup>16</sup>

Regulating these tests would ensure that they are effective and work as their manufacturers claim. As Dr. Alfa explained:

Regulation could ensure there is validation of the label-claims thereby ensuring the rapid test is appropriate for either cleaning testing or post-HLD testing for viable bacterial residuals. Currently, it is left up to the manufacturer as to what validation is performed and it is often unclear to healthcare providers exactly what the test method can be used for (i.e. cleaning adequacy versus post-HLD levels of viable microorganisms).<sup>17</sup>

New legislation is needed to require the FDA to regulate rapid assessment tests as medical devices. The provision would read as follows:

(a) INCLUSION IN DEVICE DEFINITION.—Section 201 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321) is amended—(1) in paragraph (h)—... (C) by inserting after subparagraph (3) the following:

“(4) a rapid assessment test intended to ensure the proper reprocessing of a reusable device (as defined in paragraph (ss)), and.”

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<sup>15</sup> Email from Dr. Kimberly Walker, Public Affairs Manager, American Society of Microbiology, to House Committee on Oversight and Government Reform Staff (Jan. 15, 2016).

<sup>16</sup> Letter from Dr. Michelle Alfa, Professor of Medical Microbiology, University of Manitoba, to House Committee on Oversight and Government Reform Staff (Jan. 19, 2016).

<sup>17</sup> *Id.*



**MEMORANDUM**

March 14, 2016

**To:** House Oversight & Government Reform Committee

**From:** William Hornbeck,  
Legislative Attorney, American Law Division

**Subject:** **FDA Authority to Require Medical Device Manufacturers to Show That Their Device May Be Effectively Cleaned by Following the Manufacturer's Instructions**

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You asked whether current law requires a manufacturer of a reusable medical device to show proof to the FDA that its device may be effectively cleaned between uses by following the manufacturer's instructions. Current statutes and regulations do not explicitly require medical device manufacturers to demonstrate such proof. However, the FDA's existing authority over certain medical devices could allow the FDA to require a device manufacturer to demonstrate such proof to the FDA as part of any application for clearance of a device as the "substantial equivalent" of a previously approved device. Additionally, the FDA can take certain postmarket enforcement actions against a device manufacturer for failing to show that its device may be effectively cleaned between uses by following the manufacturer's instructions.

## **Background: Concerns About Duodenoscopes**

The FDA has expressed concern that improperly cleaned duodenoscopes may transmit harmful infections.<sup>1</sup> The duodenoscope is a flexible imaging device that doctors insert into a patient's esophagus, stomach, and duodenum in order to see, diagnose, and treat various intestinal ailments.<sup>2</sup> The procedure in which doctors use a duodenoscope is known as endoscopic retrograde cholangiopancreatography (ERCP); doctors perform at least half a million ERCPs each year.<sup>3</sup> After the doctor uses the duodenoscope on one patient, the duodenoscope is to be cleaned and potentially available for use on the next patient.<sup>4</sup>

Recently, germ-laden duodenoscopes have been associated with outbreaks of antibiotic-resistant bacterial infections, particularly in hospitals.<sup>5</sup> After several of these outbreaks, the Centers for Disease Control and

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<sup>1</sup> Food and Drug Administration, *Infections Associated With Reprocessed Duodenoscopes*, available at <http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/ReprocessingofReusableMedicalDevices/ucm454630.htm>.

<sup>2</sup> National Institutes of Health, *Endoscopic Retrograde Cholangiopancreatography*, available at <http://www.niddk.nih.gov/health-information/health-topics/diagnostic-tests/ercp/Pages/diagnostic-test.aspx>.

<sup>3</sup> Food and Drug Administration, *Infections Associated With Reprocessed Duodenoscopes*, available at <http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/ReprocessingofReusableMedicalDevices/ucm454630.htm>.

<sup>4</sup> *Id.*

<sup>5</sup> Chad Terhune and Melody Petersen, *FDA to Require Proof That New Devices Can Be Cleaned Reliably*, L.A. TIMES, Mar. 12, 2015.

Prevention (CDC) alerted the FDA to the danger posed by insufficiently sterilized duodenoscopes.<sup>6</sup> In response, the FDA has issued warning letters to the three companies that manufacture duodenoscopes that are sold in the United States, warning these companies that they had not properly evaluated the effectiveness of their sterilization process.<sup>7</sup> Additionally, the FDA ordered these three manufacturers to conduct postmarket surveillance studies to determine how doctors are actually cleaning duodenoscopes between uses.<sup>8</sup> Finally, the FDA warned two of these manufacturers that the duodenoscopes that they were manufacturing differed significantly from previously approved duodenoscopes to which the new devices were required by law to be “substantially equivalent.”<sup>9</sup>

## Existing Law

In 1976, Congress passed the Medical Device Amendments giving the FDA the authority to regulate medical devices.<sup>10</sup> Pursuant to the Amendments, which amend the Food, Drug, and Cosmetic Act (FDCA), the FDA classifies medical devices as Class I, Class II, or Class III.<sup>11</sup> Class I medical devices are those low-risk devices for which “general controls” (namely, the controls that already exist in other provisions of the FDCA) are sufficient to ensure the device’s safety and effectiveness.<sup>12</sup> Class II medical devices are devices for which the general controls are insufficient to ensure the device’s safety and effectiveness, but for which “special controls” such as “performance standards, postmarket surveillance, patient registries, development and dissemination of guidelines, recommendations, and other appropriate actions as the Secretary deems necessary” would provide sufficient assurance of the device’s safety and effectiveness.<sup>13</sup> Class III medical devices are devices for which neither general controls nor the “special controls” used for Class II devices would be sufficient to ensure the device’s safety and effectiveness, and which are either “represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of public health,” or “present[] a potential unreasonable risk of illness or injury.”<sup>14</sup> Unlike Class I and Class II devices, Class III devices must obtain premarket approval from the FDA as a “new device” before they can be marketed in the United States.<sup>15</sup>

Duodenoscopes are a Class II device, which means that they are subject both to general controls under the FDCA and to “special controls” such as “postmarket surveillance.”<sup>16</sup> However, Class II devices do not require premarket approval as a new device as Class III devices do.<sup>17</sup> Instead of seeking premarket

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<sup>6</sup> Food and Drug Administration, *Infections Associated With Reprocessed Duodenoscopes*, available at <http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/ReprocessingofReusableMedicalDevices/ucm454630.htm>.

<sup>7</sup> FDA Warning Letter to Fujifilm Corporation (Aug. 12, 2015); FDA Warning Letter to Olympus Corporation of the Americas (Aug. 12, 2015); FDA Warning Letter to Hoya Corporation (Aug. 12, 2015) (citing 21 C.F.R. § 820.30).

<sup>8</sup> Food and Drug Administration, *FDA Orders Duodenoscope Manufacturers to Conduct Postmarket Surveillance Studies in Health Care Facilities*, available at <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm465639.htm> (citing 21 U.S.C. § 306*l*, which authorizes the FDA to order Class II and Class III device manufacturers to conduct postmarket surveillance of their devices).

<sup>9</sup> FDA 510k Status Letter to Fujifilm Corp (Aug. 12, 2015); FDA 510k Status Letter to Hoya Corp (Aug. 12, 2015) (citing 21 U.S.C. § 360c.).

<sup>10</sup> Medical Device Amendments of 1976, Pub. L. 94-295, 90 Stat. 539 (1976).

<sup>11</sup> 21 U.S.C. § 360c.

<sup>12</sup> *Id.*

<sup>13</sup> *Id.*

<sup>14</sup> *Id.*

<sup>15</sup> *Id.*

<sup>16</sup> 21 U.S.C. § 360c.

<sup>17</sup> 21 U.S.C. § 360c.

approval as a new device, a Class II device manufacturer must file what is called a “510(k) notification” with the FDA at least 90 days before marketing their device.<sup>18</sup> This 510(k) notification requires the manufacturer to demonstrate that its device is the “substantial equivalent” of a device that the FDA has already cleared.<sup>19</sup> The FDCA defines “substantially equivalent” as having “the same technological characteristics as the predicate device,” or having different technological characteristics if the device “contains information ... that demonstrates that the device is as safe and effective as a legally marketed device, and does not raise different questions of safety and effectiveness than the predicate device.”<sup>20</sup> If a manufacturer files a 510(k) notification but does not provide sufficient information for the FDA to determine that the device is substantially equivalent to the predicate device, the FDA may request any additional information from the manufacturer that would enable the FDA to determine whether the device is “substantially equivalent” to the predicate device.<sup>21</sup>

The FDA therefore has regulatory authority over Class II devices both before they come to market (through 510(k) notifications) and after they are on the market (by using general controls and special controls). The FDA can use and has used all three of these authorities (510(k) notifications, general controls, and special controls) to regulate manufacturers of duodenoscopes and other reusable devices with regard to the cleaning of their devices.

## Premarket Control: 510(k) Notification

As previously stated, the FDA must determine that a Class II device is the “substantial equivalent” of a previously cleared device before the device may be marketed in the United States.<sup>22</sup> When a device manufacturer files a 510(k) notification, it must include sufficient information to allow the FDA to determine that the new device would be “as safe and effective” as the predicate device that the FDA has already cleared.<sup>23</sup> The 510(k) notification must include a proposed label “sufficient to describe the device, its intended use, and the directions for its use.”<sup>24</sup> If the manufacturer does not include sufficient information for the FDA to make this determination about safety and effectiveness, the FDA may “request information” from the manufacturer that would enable the FDA to determine whether the device is as safe and effective as the predicate device.<sup>25</sup>

The FDA interprets these statutory and regulatory requirements to require manufacturers of reusable devices to submit proof that their devices may be effectively cleaned between uses by following the manufacturer’s instructions, as well as the cleaning instructions themselves, as part of the materials submitted with their 510(k) notification.<sup>26</sup> To the FDA, instructions on how to properly clean a reusable device (which the FDA calls “reprocessing instructions”) are the sort of label “sufficient to describe the device, its intended use, and the directions for its use” that federal regulations require for 510(k)

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<sup>18</sup> 21 U.S.C. § 360.

<sup>19</sup> 21 U.S.C. § 360c.

<sup>20</sup> 21 U.S.C. § 360c.

<sup>21</sup> 21 U.S.C. § 360c. For a guide to what the FDA calls its “refuse to accept policy” for 510(k)s, see Food and Drug Administration, “Refuse to Accept Policy for 510(k)s,” August 4, 2015, <http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM315014.pdf>.

<sup>22</sup> 21 U.S.C. § 360c.

<sup>23</sup> 21 U.S.C. § 360c.

<sup>24</sup> 21 C.F.R. § 807.87(e).

<sup>25</sup> 21 U.S.C. § 360c.

<sup>26</sup> Food and Drug Administration, “Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling,” March 17, 2015, <http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm253010.pdf>. at 29.

devices.<sup>27</sup> In the FDA's view, proof that a manufacturer's device may be effectively cleaned between uses by following the manufacturer's instructions (which the FDA calls "validation of reprocessing instructions") is the sort of proof of "safety and effectiveness" that federal law requires for 510(k) devices.<sup>28</sup> If a manufacturer failed to include either the reprocessing instructions or the validation of these reprocessing instructions in its 510(k) submission, the FDA could request this information from the manufacturer as part of the 510(k) review process.<sup>29</sup>

While the FDA has not yet refused to clear any 510(k) clearances for failing to include reprocessing instructions or validation of reprocessing instructions, it has warned duodenoscope manufacturers not to commit potential 510(k) violations. When the FDA discovered that two duodenoscope manufacturers were marketing duodenoscopes that differed significantly from the duodenoscopes described in the manufacturers' pending 510(k) submissions, the FDA ordered the manufacturers to submit new 510(k) notifications.<sup>30</sup> The FDA also ordered the duodenoscope manufacturers to explain to the FDA why they had not filed new 510(k) notifications after making changes to their device.<sup>31</sup>

## Postmarket Controls: General Controls and Special Controls

### General Controls: Adulteration and Misbranding

There are civil and criminal penalties for introducing any device into interstate commerce if the device is "adulterated" or "misbranded."<sup>32</sup> One way in which a device can be "adulterated" is if it fails to comply with "good manufacturing practices."<sup>33</sup> Good manufacturing practices are regulations issued by the Secretary of Health and Human Services to "assure that the device will be safe and effective" by "requiring that the methods used in, and the facilities and controls used for, the manufacture, pre-production design validation, packing, storage and installation of a device conform to current good manufacturing practice."<sup>34</sup>

The FDA has adopted several good manufacturing practice regulations that are relevant to the FDA's view of how to ensure that a reusable device can be effectively cleaned. One of these regulations requires each device manufacturer to "establish and maintain procedures for validating the device design," which "shall ensure that devices conform to defined user needs and intended uses."<sup>35</sup> Another regulation requires each device manufacturer to "establish and maintain procedures for monitoring and control of process

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<sup>27</sup> Food and Drug Administration, "Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling," March 17, 2015, <http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm253010.pdf>. at 29 (citing 21 C.F.R. § 807.87(e)).

<sup>28</sup> Food and Drug Administration, "Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling," March 17, 2015, <http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm253010.pdf>. at 30 (citing 21 U.S.C. § 360c).

<sup>29</sup> 21 U.S.C. § 360c (noting the Secretary's ability to "request information to demonstrate that devices with differing technological characteristics are substantially equivalent").

<sup>30</sup> FDA 510k Status Letter to Fujifilm Corp (Aug. 12, 2015); FDA 510k Status Letter to Hoya Corp (Aug. 12, 2015).

<sup>31</sup> FDA 510k Status Letter to Fujifilm Corp (Aug. 12, 2015); FDA 510k Status Letter to Hoya Corp (Aug. 12, 2015).

<sup>32</sup> 21 U.S.C. § 331.

<sup>33</sup> 21 U.S.C. § 351(h).

<sup>34</sup> 21 U.S.C. § 360j.

<sup>35</sup> 21 C.F.R. § 820.30(g).

parameters for validated processes to ensure that the specified requirements continue to be met.”<sup>36</sup> As the term is used in these regulations, to “establish” a procedure, a device manufacturer must “define, document (in writing or electronically), and implement” that procedure.<sup>37</sup> Therefore, to comply with good manufacturing practice requirements (and thereby avoid distributing an adulterated device), a device manufacturer must establish, document, and implement procedures for ensuring that their device performs as intended throughout the life of the device.

The FDA interprets these regulations to require reusable device manufacturers to validate the design of their reusable devices to ensure that the device can be effectively cleaned and safely reused over the life of the device.<sup>38</sup> To the FDA, this validation of the device must include a validation of the cleaning process for the device, using test conditions that simulate the worst-case scenario for the device.<sup>39</sup> The device’s manufacturer would then be required to document the testing it used to validate its cleaning process, and submit the results of these tests to the FDA.<sup>40</sup>

The FDA has warned duodenoscope manufacturers that their failure to validate their cleaning process violates good manufacturing practices. In warning letters to two duodenoscope manufacturers, the FDA warned the manufacturers that they had failed “to establish and maintain design validation procedures to ensure that devices conform to defined user needs and intended uses” as the good manufacturing practices regulation requires.<sup>41</sup> For both manufacturers, the FDA highlighted the manufacturer’s specific failure to validate the cleaning process for their devices.<sup>42</sup>

As previously stated, the FDCA penalizes distributing both “adulterated” and “misbranded” devices.<sup>43</sup> One way in which a device can be misbranded is if its labeling fails to bear “adequate directions for use.”<sup>44</sup> FDA regulations define “adequate directions for use” as “directions under which the layman can use a device safely and for the purposes for which it is intended,” including the “method of administration or application” and “preparation for use.”<sup>45</sup> To the FDA, for a reusable device to have “adequate directions for use,” the device must have “instructions on how to adequately reprocess [the] reusable device.”<sup>46</sup> In other words, because re-use is part of the “use” of a reusable device, in order to have “adequate directions for use,” a reusable device manufacturer must include adequate directions for

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<sup>36</sup> 21 C.F.R. § 820.75(b).

<sup>37</sup> 21 C.F.R. § 820.3(k).

<sup>38</sup> Food and Drug Administration, “Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling,” March 17, 2015, <http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm253010.pdf>. at 22.

<sup>39</sup> Food and Drug Administration, “Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling,” March 17, 2015, <http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm253010.pdf>. at 23-25.

<sup>40</sup> Food and Drug Administration, “Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling,” March 17, 2015, <http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm253010.pdf>. at 28.

<sup>41</sup> FDA Warning Letter to Fujifilm Corporation (Aug. 12, 2015); FDA Warning Letter to Hoya Corporation (Aug. 12, 2015) (citing 21 C.F.R. § 820.30).

<sup>42</sup> *Id.*

<sup>43</sup> 21 U.S.C. § 331.

<sup>44</sup> 21 U.S.C. § 352(f).

<sup>45</sup> 21 C.F.R. § 801.5.

<sup>46</sup> Food and Drug Administration, “Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling,” March 17, 2015, <http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm253010.pdf>. at 2.

cleaning the device between uses.<sup>47</sup> While the FDA has neither threatened nor taken action to enforce this interpretation of “adequate directions for use,” the FDA guidance document that contains this interpretation is a clear indication of “the FDA’s current thinking on this topic.”<sup>48</sup>

### Special Controls: Postmarket Surveillance

As stated previously, the FDA can use “special controls” such as ordering a manufacturer to conduct “postmarket surveillance” to regulate Class II devices.<sup>49</sup> The requirements for postmarket surveillance are further spelled out in another provision of the FDCA: “within 30 days” of receiving an order from the FDA to conduct a postmarket surveillance study, the manufacturer must submit for FDA approval “a plan for the required surveillance.”<sup>50</sup> The FDA must then determine if the “person designated to conduct the surveillance has appropriate qualifications and experience to undertake such surveillance,” and whether “the plan will result in the collection of useful data that can reveal ... information necessary to protect the public health.”<sup>51</sup>

The FDA has applied this postmarket surveillance authority to duodenoscope manufacturers and other reusable device manufacturers. Recently, the FDA ordered duodenoscope manufacturers to conduct postmarket surveillance of their devices to ensure that doctors were using the device as instructed and the device was cleaned as directed in the user materials.<sup>52</sup> The manufacturers must answer three questions in their study: (1) “are user materials ... sufficient to ensure user adherence to the manufacturers’ reprocessing instructions?”; (2) “after use of the manufacturer’s validated reprocessing instructions, what percentage of clinically used duodenoscopes remain contaminated with viable microorganisms?”; (3) “for devices that remain contaminated after use of the manufacturers’ labeled reprocessing instructions, what factors contribute to microbial contamination and what steps are necessary to adequately decontaminate the device?”<sup>53</sup> This surveillance is still ongoing.<sup>54</sup> The statute requires surveillance to begin within 15 months of the FDA issuing its order to conduct the surveillance, but does not provide an end date.<sup>55</sup>

## The Guidance Document

A guidance document, unlike a legislative rule issued through notice-and-comment agency rulemaking, does not have the force and effect of law. Indeed, in its guidance document the FDA explicitly disclaims any intent to issue an interpretation with the force and effect of law, stating that the guidance document “does not create or confer any rights for or on any person and does not operate to bind FDA or the public.”<sup>56</sup> Parts of the guidance document imply a mandatory obligation on reusable device manufacturers: for example, the guidance document states that “the device design, including its labeling (e.g., reprocessing instructions), *is to be validated* to ensure that the device conforms to defined user

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<sup>47</sup> *Id.*

<sup>48</sup> *Id.* at 1.

<sup>49</sup> 21 U.S.C. § 360c.

<sup>50</sup> 21 U.S.C. § 360l.

<sup>51</sup> 21 U.S.C. § 360l.

<sup>52</sup> Food and Drug Administration, FDA Orders Duodenoscope Manufacturers to Conduct Postmarket Surveillance Studies in Health Care Facilities, available at <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm465639.htm>.

<sup>53</sup> *Id.*

<sup>54</sup> See Chris Newmarker and Brian Buntz, *How Olympus’ Scope Problems Got So Unbelievably Bad*, QMED, Mar. 2, 2016, available at <http://www.qmed.com/news/how-olympus-scope-problems-got-so-unbelievably-bad>.

<sup>55</sup> 21 U.S.C. § 360l.

<sup>56</sup> Guidance at 1.

needs and intended uses.”<sup>57</sup> But the source of this legal obligation is explicitly found in the regulation the FDA cites, not in the guidance document itself.<sup>58</sup> The guidance document does not create the requirement to validate the device design—it merely explains how validating the device design would apply to cleaning instructions of the type that the guidance document recommends.<sup>59</sup>

There are several important differences between legislative rules and guidance documents. Legislative rules are binding on the public and the promulgating agency—they have the force and effect of law.<sup>60</sup> An agency can repeal or amend a legislative rule only by following the same rulemaking procedures required to issue them in the first instance.<sup>61</sup> A legislative rule will often be subject to judicial review even in the absence of any agency action to enforce the rule.<sup>62</sup> When challenged in court, legislative rules typically receive greater deference from a court reviewing the validity of a rule pursuant to *Chevron U.S.A. Inc. v. Natural Resources Defense Council, Inc.*<sup>63</sup>

By contrast, guidance documents do not have the force and effect of law—instead, they inform the public how the agency is going to enforce or apply an already existing statute or legislative rule.<sup>64</sup> An agency, generally, can repeal or amend a guidance document without following notice and comment procedures.<sup>65</sup> Some guidance documents may only be judicially reviewable when an agency acts to enforce the guidance document.<sup>66</sup> And if a court is able to review a guidance document to determine whether the guidance document is consistent with an agency’s organic statute, a court will generally provide a lesser degree of deference to the agency’s position.<sup>67</sup>

This legal status of guidance documents has several important implications for the FDA’s guidance document on reprocessing medical devices. First, the guidance document cannot give the FDA any authority that it does not have under the relevant statutes and regulations—if the statutes and regulations cannot be read to require that duodenoscopes be cleanable, then FDA cannot require duodenoscopes to be cleanable. As the U.S. Court of Appeals for the DC Circuit has stated, “When the agency applies [a guidance document] in a particular situation, it must be prepared to support the policy just as if the policy statement had never been issued.”<sup>68</sup> Second, the FDA’s guidance document likely could not be challenged in court until the FDA had taken an enforcement action against a party using the guidance document. A

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<sup>57</sup> Guidance at 22 (emphasis added).

<sup>58</sup> 21 C.F.R. § 820.30.

<sup>59</sup> Guidance at 22.

<sup>60</sup> See, e.g., *Chrysler Corp. v. Brown*, 441 U.S. 281, 295 (1979); *United States ex rel. Accardi v. Shaughnessy*, 347 U.S. 260 (1954).

<sup>61</sup> 5 U.S.C. §§ 551, 553; *Committee for Effective Cellular Rules v. Federal Communications Commission*, 53 F.3d 1309, 1317 (D.C. Cir. 1995).

<sup>62</sup> 5 U.S.C. § 701 (judicial review is available for agency action “except to the extent that statutes preclude judicial review or agency action is committed to agency discretion by law.”); 5 U.S.C. § 704 (judicial review is available for “final agency action for which there is no other adequate remedy in a court.”); *Sackett v. E.P.A.*, 132 S. Ct. 1367, 1373 (2012) (noting the “presumption favoring judicial review of administrative action.”).

<sup>63</sup> 467 U.S. 837 (1984).

<sup>64</sup> See *Lincoln v. Vigil*, 508 U.S. 182, 197 (1993); *Mada-Luna v. Fitzpatrick*, 813 F.2d 1006, 1013-14 (9th Cir. 1987).

<sup>65</sup> See 5 U.S.C. § 553; *Perez v. Mortgage Bankers Association*, 135 S. Ct. 1199, 1206 (2015) (abrogating the DC Circuit’s case law that had required an agency to use notice-and-comment rulemaking to repeal an earlier guidance document).

<sup>66</sup> E.g. *National Mining Ass’n v. McCarthy*, 758 F.3d 243, 253 (D.C. Cir. 2014) (an EPA finalized guidance document that recommended that states limit the issuance of pollution permits was not a legislative rule or a final agency action subject to pre-enforcement judicial review, as the guidance document “had no legal impact” and the states covered by the regulations could ignore the guidance document “without suffering any legal penalties or disabilities.”)

<sup>67</sup> See *Skidmore v. Swift & Co.*, 323 U.S. 134 (1944).

<sup>68</sup> *National Mining Ass’n v. McCarthy*, 758 F.3d 243, 253 (D.C. Cir. 2014) (quoting *Pacific Gas & Electric Co. v. Federal Power Commission*, 506 F.2d 33, 38 (D.C. Cir. 1974)).

party that was subject to the FDA enforcement action could object to the FDA's interpretation of "instructions for use" to include "instructions for reuse," and other interpretations in the FDA's guidance document, but only after the FDA initiated an enforcement action.<sup>69</sup> Third, the FDA could change the guidance document's interpretations of the relevant statutes and regulations at any time in the future by simply issuing another guidance document with different interpretations of those same rules and regulations.<sup>70</sup> Fourth, courts tend to give greater deference to legislative rules than to guidance documents.<sup>71</sup>

## Conclusion

Current statutes and regulations do not explicitly require that device manufacturers include instructions on how to clean their devices, or test their devices to ensure that they may be properly cleaned. However, the FDA can require device manufacturers who are seeking 510(k) clearance of their device to show that their device may be effectively cleaned between uses by following the manufacturer's instructions. And the FDA can exercise and has exercised certain postmarket enforcement authorities to warn duodenoscope manufacturers not to market duodenoscopes without ensuring that the scopes can be properly cleaned and that doctors and their technicians are properly instructed on how to use and clean the scopes.

FDA has certain indirect ways of achieving their goal of making sure that the manufacturers market cleanable devices without actually taking an enforcement action that says, as the guidance document does, that manufacturers must market only cleanable devices. For example, FDA was within its authority to issue warning letters to duodenoscope manufacturers whose 510(k) clearances did not match the scopes they were actually marketing. The FDA didn't have to tell the manufacturer to make its device cleanable, as it could warn the manufacturer that the scope it was selling differed significantly from the scope that the FDA had approved. These sorts of warnings are an oblique way of solving the problem, are within FDA's authority, and in no way rely on FDA to demand that manufacturers make their devices cleanable.

A law adding cleanability to the FDCA would be extremely helpful. A law would: (a) Preclude any legal challenge to the FDA's authority in case the FDA did take an enforcement action against a manufacturer for making an uncleanable device (b) Prevent any future administration's FDA from changing its mind and moving away from cleanability (c) Signal to the FDA that Congress fully supported any FDA efforts to ensure cleanability. Rather than having to rely on oblique (but legally justified) methods or using an interpretation of the FDCA that cannot be explicitly found anywhere in the statute or regulations, the FDA could straightforwardly hold manufacturers accountable for failing to make their devices cleanable. The regulations requiring validation generally (i.e. does this device perform as intended) have been around since before the guidance document appeared: before the guidance document the Secretary would not and did not ask for cleanability validation. Even now, it is the Secretary's choice whether to ask for cleanability information.

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<sup>69</sup> *National Mining Ass'n v. McCarthy*, 758 F.3d 243, 253 (D.C. Cir. 2014).

<sup>70</sup> *Perez v. Mortgage Bankers Association*, 135 S. Ct. 1199, 1206 (2015) (an agency need not use notice-and-comment rulemaking to reverse an earlier interpretation of a statute or regulation that the agency had given in a guidance document).

<sup>71</sup> See *Skidmore v. Swift & Co.*, 323 U.S. 134 (1944). Legislative rules are generally subject to so-called *Chevron* deference, which determines whether the agency's reading of a statute is a permissible reading of an ambiguous statute. *Chevron U.S.A. Inc. v. Natural Resources Defense Council, Inc.*, 467 U.S. 837 (1984). By contrast, guidance documents are generally subject to so-called *Skidmore* deference, under which a court will determine if the agency's interpretation of a statute is persuasive. *United States v. Mead*, 533 U.S. 218 (2001).