UPDATE

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IN THIS ISSUE

Developments in Medical Device Enforcement

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FDA enforcement against medical device manufacturers in 2015 was characterized by another decrease in the total number of Warning Letters issued over the previous year, but there was continued emphasis on familiar issues, as well as heightened attention on Laboratory Developed Tests (LDTs) and supplier verification. Unsurprisingly, FDA primarily targeted Class II and Class III medical devices, but the agency also scrutinized a number of low-risk Class I devices. The most prevalent violations cited in Warning Letters involved current good manufacturing practice requirements (CGMPs) outlined in the Quality Systems Regulation (QSR), as well as deficiencies in complaint handling and medical device reporting (MDR). Notably missing from medical device Warning Letters in 2015 was any significant enforcement against mobile medical apps, for which FDA finalized guidance in the last years, though the agency did issue several letters concerning medical device software.

In addition to Warning Letters, FDA issued several guidance documents to clarify where the agency will and will not exercise its enforcement authority. Given the enormity of the medical device industry, it is somewhat by necessity that the Center for Devices and Radiological Health (CDRH) must choose its priorities. In the case of LDTs, CDRH is attempting to expand its enforcement, stating the agency has always had authority to regulate such devices, but was previously exercising enforcement discretion. In other cases, FDA is separating categories and classes of lower-risk devices that it will not continue to regulate, either through enforcement discretion or by exempting the medical devices from regulation altogether.

Recent Trends in Medical Device Enforcement

Violations of QSR, MDR, and Supplier Verification

In most Warning Letters, FDA picks and chooses from a laundry list of violations related to quality control that are familiar year-to-year and 2015 was no exception. At the top of that list are violations of the QSR, most commonly failures to establish and maintain procedures for implementing corrective and preventive action (CAPA) and failures to properly verify and validate manufacturing processes and design changes. These types of violations are frequently accompanied by inadequate complaint handling and reporting under the MDR regulations. Manufacturers often do not have adequate written procedures for receiving, reviewing, and evaluating complaints by a formally designated unit, or that those procedures were not followed.

Supplier verification is also receiving more attention, which is in line with FDA's overarching objective of achieving safety up and down supply chains across all product areas. Warning Letters of this nature cited manufacturers for failing to establish standards for suppliers, contractors, and consultants, and failing to evaluate those entities using those standards. Given how often the agency is finding that manufacturers are falling short of compliance in this area, FDA will likely continue

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to closely scrutinize manufacturers' policies and procedures with regard to suppliers.

Premarket Clearance or Approval, Registration, and Listing

FDA continues to enforce premarket compliance, monitoring the marketplace to ensure that medical devices are either cleared through the 510(k) program, have a premarket approval (PMA), or are subject to an exemption from these requirements. Although the agency enforces these requirements against firms who have outright failed to obtain clearance or approval for a marketed product, more often FDA is enforcing these requirements against firms with medical devices that have previously been marketed under a valid 510(k) clearance or PMA, but were since modified, or are now being advertised for new intended uses or a to a new population not included in the device submission. In all of these cases, FDA warned companies that a new submission addressing the safety and effectiveness of the modification, new intended use, or new intended population, is required prior to marketing the medical device at issue in the Warning Letter.

In line with FDA's policy shift toward more strictly regulating LDTs, in 2015, CDRH's Office of In Vitro Diagnostics and Radiological Health issued Untitled Letters to a handful of direct-to-consumer (DTC) genetic screening test manufacturers for failing to obtain 510(k) clearance prior to marketing.

FDA also warned companies for failing to follow the agency's medical device registration and listing requirements, although these violations rarely are the sole subject of a Warning Letter and are more often included with larger violations directly concerning device safety.

Software

Interestingly, FDA did not issue any Warning Letters to mobile medical app manufacturers. However, the agency did issue a small number of letters that concerned other types of medical device software issues, including those used to manufacture or control medical devices and software used in clinical settings to manage patient data. FDA flagged issues relating to failures to validate the device design and failing to adequately establish CAPA procedures, such as Product Change Controls. These violations were also often accompanied by other QSR and MDR deficiencies.

Current Initiatives in Medical Device Enforcement

Laboratory Developed Tests (LDTs) & In Vitro Diagnostics (IVDs)

FDA's efforts to regulate LDTs more strictly is arguably the most controversial issue in current medical device enforcement. In July, 2014, FDA issued a notice to Congress outlining the agency's plan to establish a regulatory framework to oversee LDTs.[1] FDA claimed it already had the authority to do so and had been exercising enforcement discretion while LDTs were largely overseen by Centers for Medicaid and Medicare Services (CMS) under the Clinical Laboratory Improvement Amendments (CLIA). Many members of regulated industry protested, claiming that a policy shift of this magnitude requires notice-and-comment rulemaking and is otherwise illegal. Congress has taken an interest in the issue and may attempt to enact legislation that would effectively undermine FDA's efforts by directing how LDTs should be regulated.

In spite of significant push back, FDA continues to move forward with its agenda to regulated LDTs and has promised a final guidance document by the end of 2016. In the meantime, FDA has taken enforcement action against nearly a dozen LDT or diagnostic test manufacturers, including a handful of direct-to-consumer genetic tests. Nearly all of these letters cited failures to obtain the appropriate premarket clearance, which is precisely what FDA did not require for LDTs prior to the sudden policy shift. The letters often cite additional failures to comply with QSR and MDR regulations.

Looking ahead, if FDA issues a final guidance document by the end of this year, industry members may sue FDA for violations of the Administrative Procedures Act and request that a court order FDA to undertake formal notice-and-comment rulemaking on the subject before changing the rules for industry.

Mobile Medical Apps & Cybersecurity

In an increasingly networked and data-driven world, FDA is attempting to keep pace by issuing draft and final guidance documents on topics that are more relevant to technology, such as mobile medical apps and cybersecurity. In each area, FDA explains how existing regulations provide the framework for enforcement.

In February 2016, FDA issued an amended final guidance for mobile medical apps alongside a final guidance for "Medical Devices Data Systems, Medical Image Storage Devices, and Medical Image Communications

Devices." The latter guidance document finalized FDA's policy of exercising enforcement discretion with regard to the listed devices. Some are exempt from all controls, while others are only exempt from premarket notification requirements, but subject to relevant general controls (e.g. QSR, MDR, etc.).

Last July, FDA issued it's first-ever device-specific safety communication for a cybersecurity vulnerability, encouraging patients to discontinue using a specific computerized infusion pump. While this was not an enforcement action per se, it signifies that FDA considers cybersecurity vulnerabilities an important issue in protecting public health and safety and offers some clues how FDA will handle such vulnerabilities.

In January 2016, FDA released a draft guidance for postmarket management of cybersecurity in medical devices, outlining the agency's recommendations for identifying vulnerabilities and protecting against threats, and describing the circumstances under which a cybersecurity issue would require notifying FDA. The guidance document clarifies that existing medical device regulations (e.g. QSR, MDR, and recall regulations) are sufficient for establishing requirements for identifying, reporting, and remediating cybersecurity vulnerabilities, and illustrates how industry can apply existing regulations to cybersecurity issues to ensure compliance.

Given the relative novelty of mobile medical apps and cybersecurity issues and how fresh FDA regulation is in these areas, it will be important to observe how FDA's enforcement efforts unfold. Cybersecurity issues may prove to be especially challenging considering the rapidly evolving threats and expertise required to identify them.

Categorical Exemption of Certain Low-Risk Medical Devices

In June 2015, FDA announced its intention to exempt 120 product codes of certain low-risk medical devices from premarket notification requirements because they are "sufficiently well understood and do not require premarket notification (510(k)) to assure their safety and effectiveness."[2] This effort makes good on a commitment from FDA during the MDUFA 2012 reauthorization negotiations. FDA plans to conduct notice-and-comment rulemaking by 2018 to formally exempt the product codes from premarket notification, but in the meantime intends to exercise enforcement discretion to the same effect.

Future Outlook for Medical Device Enforcement

Enforcement in 2015 reflected what is likely to remain one of the greatest challenges for CDRH in the coming years: grappling with the rapidly expanding field of technology and devices, deciding which ones are actually medical devices, and selecting for regulation those that have the greatest implications and risks for public health and safety. Though the stream of new devices and software (including apps) is seemingly endless, CDRH's resources are finite and already strained. FDA will need to continue to prioritize enforcement targets to ensure that they can consistently motivate compliance in these areas.

In the coming year, it will be important to monitor developments in CDRH's enforcement in the areas of LDTs, mobile medical apps, and cybersecurity as these are still relatively new and taking shape. In addition to these areas, FDA will almost certainly continue to enforce the most basic requirements for medical device quality and safety: CGMP/QSR, complaint handling, MDR regulations, and proper clearance or approval as required for modifications in devices or their labeling. ⚠

1. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm407321.htm.
2. http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm407292.pdf.