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Editor's Note: Due to summer breaks, *International Devices & Diagnostics Monitor* will not be published July 24. The next issue will be published July 31.

Full House Passes User Fee Reauthorization Package Including MDUFA

The House passed by voice vote its version of the FDA user fee reauthorization package Wednesday, which includes an updated version of MDUFA expected to bring in \$183 million in fiscal 2018.

The reauthorization package, H.R. 2430, saw strong, bipartisan support on the House floor leading up to its passage. The Senate's version of the user fee bill is currently awaiting a vote. Afterwards, both houses must reconcile any differences between their texts before sending the bill for the president's signature. In early June, the House Energy & Commerce Committee unanimously voted to advance the user fee package to the floor.

The next generation of user fees is expected to bring in a total of \$1.42 billion in fiscal 2018, including a 45.2 percent increase over the \$126 million expected from MDUFA this fiscal year.

(See **User Fee**, Page 2)

Taiwan FDA Drafts First Medical Devices Act

The Taiwan Food and Drug Administration is beginning the process of drafting separate medical device regulations for the first time.

Medical devices are currently regulated in Taiwan under the Pharmaceutical Affairs Act, which was enacted in 1993.

The Taiwan FDA said that as other countries have developed laws and regulations specifically for regulating medical devices, it was time the country separated out regulations covering the management of medical devices.

TFDA classifies medical devices into three risk-based categories similar to those used by the U.S. FDA: Class I is low risk; Class II is medium risk and Class III is high risk. TFDA also conducts pre-market assessments of devicemakers' facilities, audits their quality management systems and conducts post-market surveillance.

(See **Act**, Page 2)

User Fee, from Page 1

FDA Commissioner Scott Gottlieb said he was grateful for the House's passage of the bill and specifically thanked the leaders of the House Energy and Commerce Committee, Reps. Greg Walden (R-Ore.) and Frank Pallone (D-N.J.).

The Senate's version is expected to be delayed until after movement on Republicans' efforts to repeal the Affordable Care Act, which is anticipated over the next two weeks.

Last week, Senate Majority Leader Mitch McConnell (R-Ky.) delayed the start of the Senate's August recess period by two weeks, to provide extra time to complete the work. Senate HELP committee chairman Lamar Alexander (R-Tenn.) said he is urging his colleagues to pass the bill as soon as possible.

But Sen. Ron Johnson (R-Wis.), chairman of the Senate homeland security committee, has threatened to slow passage of the user fee bill unless it contains language on "right to try" measures, which can prohibit the FDA from considering adverse event reports from investigational drugs administered under expanded access or compassionate use requests. Johnson has supported multiple pieces of right-to-try legislation over the past year.

In a statement, the White House reiterated its position that the pharmaceutical industry should finance 100 percent of the FDA's premarket review, eliminating the need for taxpayer dollars. However, leaders in Congress said the Trump administration's requests came "too late" as the amounts in the must-pass bill had been negotiated between the FDA and industry over the past two years.

If the agreements are not reauthorized by Aug. 1, 60 days before the current agreements expire at the end of September, the FDA will be required to begin sending layoff notices to more than 5,000 employees, potentially crippling the agency's ability to review applications and complete inspections.

The text of H.R. 2430, the FDA Reauthorization Act of 2017, is available here: www.fdanews.com/07-12-17-HR2430.pdf. — Conor Hale

Act, from Page 1

The proposed Medical Devices Act will further define the device classification system and will include electronic listing and reporting. The new act will also require devicemakers to annually declare their licensed devices.

Importantly, the new regulations will strengthen the oversight of medical devicemakers and their manufacturing processes. For example, manufacturers will need to establish track and trace mechanisms for their products, and the TFDA will require manufacturers to comply with good manufacturing and good distribution practices.

Manufacturers that design and place devices on the market will be incorporated as device manufacturers. Legal entities that lease devices and service or repair them will be incorporated under medical device distributors.

The new regulations are expected to boost the country's medical device industry, particularly in the area of life cycle management, TFDA said.

TFDA said it expects a draft of the new regulations to be available for review by the end of this year.

Read the Taiwan FDA notice here: www.fdanews.com/07-11-17-TaiwanFDA.pdf.

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Medical Device Risk Management

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What Device Manufacturers Can Learn From FDA’s Inspection Data

Medical device quality managers that don’t want to wind up a statistic in a future FDA report on quality deviations should dig deeply into the agency’s recently released report on inspections, Form 483s and warning letters, says Michael Gaba, a partner in the law firm Polsinelli.

The agency released *CY2016 Annual FDA Medical Device Quality System Data Inspections, FDA Form 483 Observations, and Warning Letter Citations*, says Gaba, to give companies a peek into data collected by the FDA during inspections so they can see what’s happening across the regulated industry.

The report “lets you see trends, which can show you potential problems that you should be focusing on because the odds are that you too will find yourself in the same bucket of deviations,” says Gaba, who will present an FDAnews webinar on lessons from the FDA report August 9.

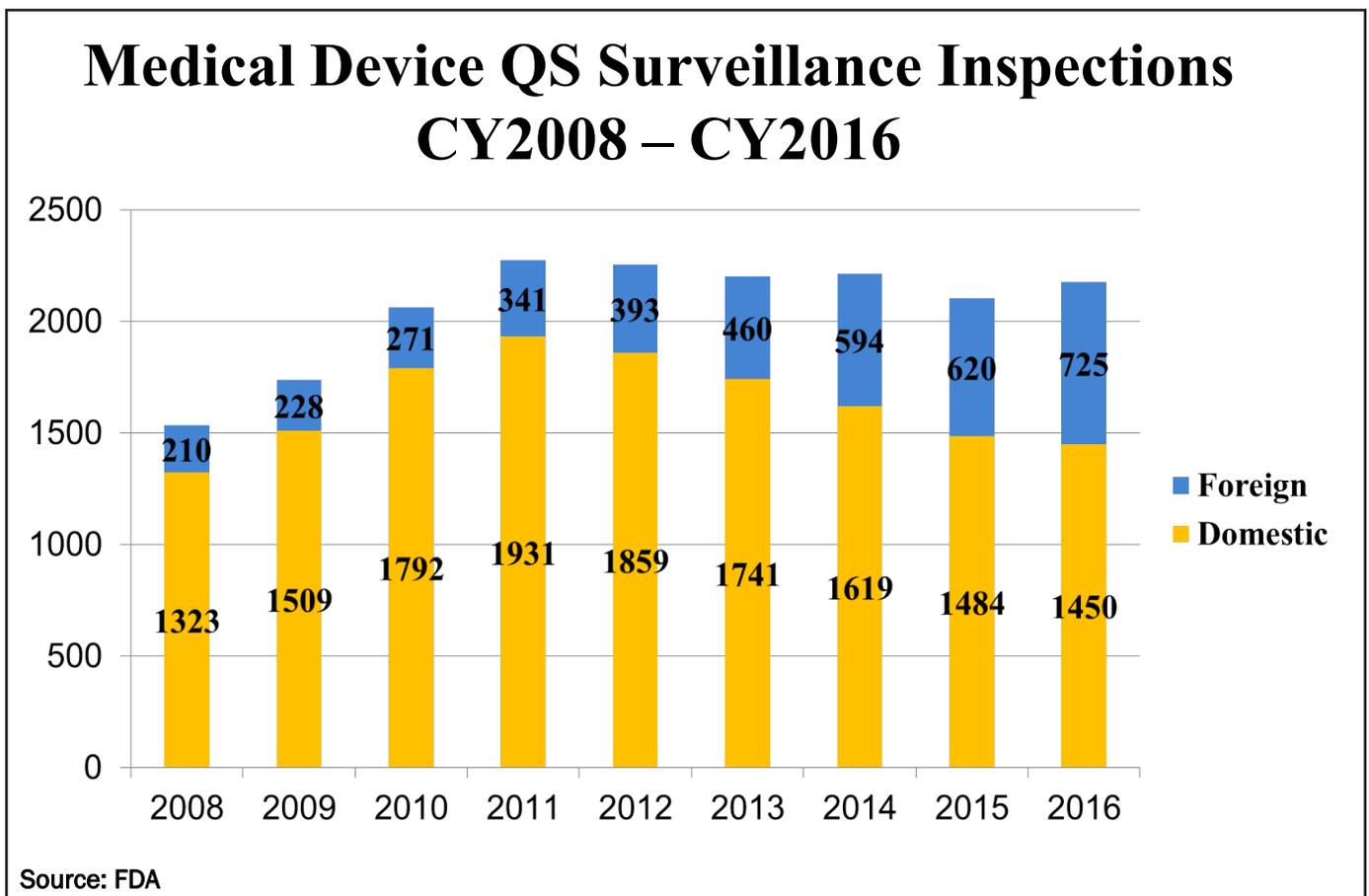
For example, he says, it’s helpful for foreign companies to know foreign inspections increased while domestic inspections decreased. It’s also helpful to know that foreign companies got slapped with an Official Action Indicated (OAI) after an inspection 12 percent of the time, when domestic companies got OAIs 7 percent of the time.

“U.S. companies seem to be doing a better job getting it right,” says Gaba, which he added may be a function of their having been in the market and subjected to FDA regulations for longer.

Companies in China, Germany and the United Kingdom should take heed, as they are the companies most often getting OAIs.

In 2016, FDA issued 854 Form 483s, and 3,027 Form 483 observations were cited for 21 CFR 820 (Quality System regulation)

(See **Data**, Page 4)



Data, from Page 3

deficiencies. Two thirds of those observations fell into the categories of Corrective and Preventive Action (CAPA) and Production and Process Controls (P&PC). CAPA and P&PC continue to be the most frequently observed and cited quality subsystems. So companies, take heed, says Gaba.

“That shows exactly where companies should be spending more energy,” he says.

As part of CAPA, device companies are required to perform regular internal quality audits, and the FDA’s 2016 report showed many of them were not doing that, says Gaba. That transgression garnered the highest level of warning letters (79 percent). Companies should take that as a warning that not only will they get a slap on the wrist for not conducting quality audits, but if they’re not looking closely at their quality systems, they’re going to pay a large cost later, says Gaba.

“An investment in quality helps reduce time spent dealing with compliance shortcomings,

so everybody benefits — the public because they now have products of a higher quality, and agency, which doesn’t have to use as many resources to fix problems,” says Gaba. “If you emphasize quality with an eye on the patient as the ultimate customer, and you’re doing your job well, compliance follows.”

Gaba notes the CDRH intends its complaint requirements to be a floor, not a ceiling. The hope is that companies will meet the requirements as a minimum, then go much further with quality.

Overall, the FDA report shows, 483s were down in 2016, and all quality subsystems saw a drop in the number of 483 observations. That’s a very good thing, says Gaba.

“This supports the notion that this push for quality over the last several years is having an impact,” and a big part of the success is the release of these data each year, he says.

Read the CY2016 annual report here: www.fdanews.com/07-13-17-QualitySystemData.pdf.

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CFDA Issues New Guideline For OCT Ophthalmology Devices

Grace Fu Palma, founder and CEO of Boston-based China Med Device, LLC, a firm specializing in commercialization and funding for medtech companies entering China, considers CFDA's new draft guideline for registration of optical coherence tomography devices used in ophthalmology.



The CFDA issued a draft guideline June 9 on the preparation of registration documents for Optical Coherence Tomography (OCT) ophthalmology devices. The draft, which mainly focuses on devices using optical frequency domain reflectometry, can also serve as a reference for registering OCT devices based on other principles.

This is a must-follow guideline if you register OCT ophthalmology devices with CFDA. It details what the CFDA reviewer will be looking for in the review process, including:

- Product name;
- Product structure, such as optical host, power part, non-embedded software, etc. If a computer is used, limit the brand and specs to equipment covered by the CFDA's standard for electromagnetic compatibility (EMC) of medical devices;
- Intended use and contraindications;
- Product summary, including the main functions, the function of each component and the characteristics. The differences from the characteristics of similar products is the key point of technical review.
- Predicate devices and associated information.

Research materials should include:

- Product performance research, such as functional, safety indicators and the basis of other indicators related to quality control.
- Biocompatibility evaluation studies. Materials tested should be finished goods that contact patients. The test report could be a domestic or an overseas inspection report.

- Sterilization / disinfection technology research.
- Product validity period studies.
- Software research. This needs to follow CFDA's Guidelines for the Technical Review of Medical Device Software Registration.
- Light radiation safety research materials. These should follow ISO15004 -2, Ophthalmic Instruments - Basic Requirements and Test Methods - Part 2.
- Environmental testing: Transportation, storage and usage environment will affect the performance of optical products, OCT should provide environmental testing research data.

The risk analysis should consider energy hazards, biological hazards, environmental hazards, hazards associated with operational use, hazards to software, ergonomic hazards, functional failures, hazards associated with maintenance, and aging.

The product's technical information should include the depth of scan, the width of scan, the horizontal resolution and longitudinal resolution of the scan in tissue, and the scan rate.

Whenever CFDA issues a guideline, device-makers seeking CFDA registration of covered products should follow it like a bible to increase the chance of being approved.

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Brazil Adds Ireland As MDSAP Accredited Auditor

Brazil's National Surveillance Agency has added Ireland's standards authority to its list of accredited organizations to perform quality management system audits under the Medical Device Single Audit Program.

The addition means that the National Standards Authority of Ireland may be contracted by devicemakers for compliance with Brazilian good manufacturing practices as well as MDSAP requirements in MDSAP participating countries, which are the U.S., Canada, Australia and Japan.

South Africa's Universal Health Coverage Will Benefit Devicemakers

South Africa's Department of Health released its plan for a national universal healthcare system that will affect how medical devices are reimbursed. Devicemakers also are expected to benefit from the scheme as new regional clinics are built and medical equipment is purchased.

During 2018 to 2019, the department will phase in a revised pricing and remuneration structure for universal health services. A National Health Pricing Advisory Committee will develop a risk-adjusted capitation system and a hospital reimbursement system, according to the newly released plan.

As of June 1, South Africa has its first regulatory system for devices and in vitro diagnostics, which includes a risk-based classification system and a new regulator, the South African Health Products Regulatory Authority (*IDDM*, June 16).

The National Health Insurance (NHI) plan calls for expanded access to laboratory services, which requires setting, monitoring and enforcing quality standards for laboratory services. NHI will cover costs associated with lab services and will contract with certified and accredited private laboratory service providers as needed. The NHI Benefits Advisory Committee will determine the laboratory services to be reimbursed.

Radiology services will also be covered and will be delivered at primary, district, regional and tertiary facilities and will include radiology and imaging sciences, telemedicine, nuclear medicine and radiation oncology.

The medical device industry is concerned that the regulator is trying to fit medical devices into drug regulations without fully considering the implications, according to a task group convened by the South African Medical Device Industry Association (SAMED).

In June, SAMED released a code of ethics to guide ethical conduct for devicemakers in the country, which face an August deadline for marketing licenses. The regulatory authority noted

that device licensing applications are coming in incorrectly bound and without the required fees. It also urged SAMED to instruct applicants to send their ISO documents and international certificates with their license applications.

Read the Department of Health's implementation plan here: www.fdanews.com/07-11-17-SouthAfrica.pdf.

BRIEFS

FDA Exempts 1,003 Class II Devices From 510(k) Regs

The FDA finalized its list of 1,003 class II medical devices low-risk enough to be exempt from 510(k) requirements.

The list is part of the agency's implementation of a 21st Century Cures Act provision that aims to reduce devicemakers' regulatory burden. The device types on the list were deemed a sufficiently low-risk not to require a premarket notification review to determine safety and effectiveness.

The agency noted, however, that the devices on the list are not exempt from other regulations or requirements unless that exemption is specifically established by another law or order. All devices, exempt and otherwise, are subject to current device GMPs, packaging and labeling rules, and regulations on intended use.

FDA Develops Ebola Vaccine Response Assay

Scientists at the FDA announced the development of a new assay to analyze antibody response to Ebola virus vaccinations that does not require the use of the virus.

Rather than the live Ebola virus, the assay relies on a genetically modified, non-disease-causing virus called vesicular stomatitis virus, which shares part of the Ebola genome.

The lack of the actual virus means the process can skip several additional precautions, such as a BSL-4 laboratory, which is normally required for developing vaccinations for pathogens such as the Ebola virus. The new assay can be used in lower-security, more widely available BSL-2 laboratories.

483 Roundup: Three Devicemakers Cited for CAPA, Other Deficiencies

Three device manufacturing facilities landed Form 483s from the FDA after inspections turned up numerous problems with their CAPA, complaint, training and MDR procedures.

Full Range Rehab: The FDA issued a Form 483 to Full Range Rehab, citing problems with its CAPA procedures, acceptance activities, record-keeping and complaint handling.

A March inspection of the company's West Chester, Ohio, facility found the firm had no CAPA procedures. It also lacked procedures for receiving and final acceptance. The director of operations told investigators the firm simply inspected parts upon receipt without standard procedures or records for the process.

Meanwhile, the chief operating officer confirmed the company did not maintain device master records or device history records, and its procedures for handling complaints did not adequately define all customer complaints. The firm also lacked procedures for document control or quality audits.

The firm's complaint handling procedure did not adequately define all customer complaints.

For example, the procedure did not identify notifications of the firm's device not functioning properly as complaints. In addition, repairs of the firm's devices, such as replacing an actuator that was no longer working, were not routinely recorded or documented.

Mb Industria Cirurgica: Cirurgica landed a Form 483 from the FDA for inadequate process validation, CAPA procedures, environmental conditions and training.

The agency issued the form following a March inspection of its facility in Paulista, Brazil. Investigators found numerous manufacturing processes for the firm's Omiderm device had not been verified and also fell short on several procedures to control environmental conditions.

Further investigation found the firm had no procedures to ensure timely and effective assessment

of events that might qualify for medical device reporting requirements. Investigators also hit the company on its CAPA procedures, finding they did not require analysis of quality data to identify existing and potential or recurring issues. It also lacked requirements to ensure all quality problems were communicated to those responsible for quality.

The firm's complaint-handling procedure did not require timely processing all complaints, documentation of oral complaints on receipt, or evaluation of complaints to determine whether they should be reported to the FDA as adverse events.

The company's procedures for nonconforming product did not require determining and documenting the disposition of such products, and the firm failed to implement another of its nonconforming product procedures. Industria Cirurgica had also not implemented its procedures for release of a lot of Omiderm for distribution or its procedure for equipment calibration.

Investigators also found employees responsible for the firm's quality system demonstrated insufficient knowledge of the system, suggesting insufficient training, and the company's training procedure did not require retraining when procedures are updated.

CarboFix Orthopedics: The FDA hit CarboFix Orthopedics on MDR submissions, anti-contamination efforts and quality audits.

The agency issued a Form 483 following a February/March inspection of the devicemaker's Hamerkaz, Israel, facility. Investigators found the company failed to submit an MDR report within 30 days of becoming aware of potential malfunctions in a marketed device. Multiple complaints that could potentially qualify as adverse events were not reported, according to the form.

CarboFix also had no testing procedures for its implanted medical device for Endotoxin, a known contaminate, according to the FDA. Investigators further found that the facility did not perform quality audits at defined intervals.

Read the Form 483s here: www.fdanews.com/07-11-17-Three483s.pdf. — Zack Budryk

APPROVALS

Cardiologs Technologies' ECG Analysis Platform Scores 510(k) Approval

The FDA has awarded 510(k) approval to Cardiologs Technologies' ECG analysis platform.

The platform uses cloud-based cardiac monitoring and analysis web service to analyze long-term ambulatory ECG monitoring recordings. The system has already secured the CE Mark in the European Union.

The technology will allow cardiologists to recover digital ECGs from any compatible monitoring device and, after uploading them to the cloud, use the Cardiolog technology to identify relevant cardiac events.

Cerus Gets CE Mark For Intra-Cranial Aneurysm Device

Cerus Endovascular received the European Union's CE Mark for its Contour Neurovascular System. The device is used to treat intra-cranial aneurysms through an implant.

Cerus is currently conducting a 45-patient single-arm trial to demonstrate the device's safety in treating unruptured aneurysms, with the research taking place at four neurological centers in the United Kingdom and one in Hungary.

The Contour system will receive a limited commercial rollout in the third quarter of this year.

FDA Reduces Clinical Trial Endpoint for Angioplasty Device

Intact Vascular announced the FDA approved its request to alter the primary endpoint in a clinical trial for its new angioplasty device from 12 to six months.

The multi-center, single-arm study aims to investigate the safety and efficacy of Intact's Tack device, an endovascular system designed to repair tears in the artery wall, a frequent balloon angioplasty complication. The company is sponsoring three clinical trials, enrolling the first patient in February.

Pinnacle Spine Group Receives A Fourth Patent for Graft Device

Pinnacle Spine Group received a U.S. patent for its *in situ* graft delivery technology.

The patent applies to the company's system for delivery of graft material to the chamber of a spinal fusion device. The company has previously received three patents covering the same fusion technology and owns several non-U.S. applications, including in Europe, Australia and Canada.

The devices enable targeted *in situ* placement of bone graft material directly into the implanted device for maximum contact with the vertebral endplates.

Z-Medica Gets FDA Clearance For Internal Bleeding Control Device

The FDA awarded *de novo* clearance to Z-Medica's QuickClot Control+ device.

The device is indicated for temporary control of internal organ space bleeding for patients with Class III or IV bleeding, according to the Wallingford, Conn., company. Preclinical trials for the device, they said, showed the device led to significantly less blood loss compared to packing with laparotomy sponges.

The approval comes seven months after the company reached a three-year deal to supply the New York Police Department with its QuikClot belt trauma kits.

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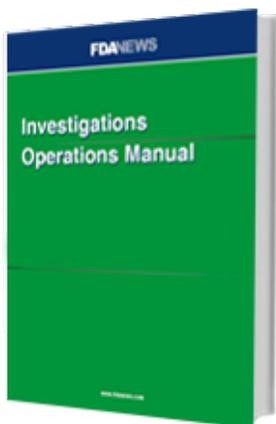
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