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IN THIS ISSUE

Senate Committee Advances FDA User Fee Reauthorization

The Senate HELP Committee on May 11 advanced to the full Senate a bill that would reauthorize FDA user fees through 2022. The vote was 21-2.

Sens. Bernie Sanders (I-Vt.) and Rand Paul (R-Ky.) voted against the measure, which now heads to the full Senate for debate. The current user fee agreements expire Sept. 30.

The bill primarily would update and reauthorize current user fee agreements, which account for more than one quarter of the FDA's annual budget. Anticipated fees to be collected under the reauthorized MDUFA would increase to $183.3 million in fiscal 2018 from $130.2 million in the current fiscal year — up 40.8 percent. Fees would be expected to total $213.7 million for fiscal 2022.

In addition to extending the agreements through September 2022, the legislation would revamp the review process for so-called de novo medical devices—those determined to be novel and low-risk.

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

Gottlieb Sworn In As FDA Commissioner

Scott Gottlieb was sworn in as FDA commissioner May 11, two days after his appointment was confirmed by the Senate.

Gottlieb, 44, has said he will boost the agency's efforts to keep tabs on medical devices after they are approved.

As the 23rd commissioner, he will be leading an understaffed agency. The FDA currently has approximately 700 to 1,000 vacancies; however, the 21st Century Cures Act grants the agency wider hiring powers and authorizes additional government funding.

Gottlieb previously served as the FDA's deputy commissioner for medical and scientific affairs and before that, as a senior advisor to the FDA commissioner. In 2013, he was appointed by the Senate to

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Gottlieb, *from Page 1*

serve on the Federal Health Information Technology Policy Committee, advising HHS on health care information technology.

Formerly a practicing physician, Gottlieb graduated from the Mount Sinai School of Medicine in New York City, where he also did his residency. He served as a clinical assistant professor at the New York University School of Medicine, where he also practiced medicine as a hospitalist physician.

Throughout the nomination process, some Senate Democrats consistently expressed concern about his ability and willingness to stand up to the Trump Administration on matters of science. His supporters, notably Sen. Lamar Alexander (R-Tenn.), chairman of the HELP Committee, said Gottlieb's industry connections and experience are assets in his new position. — Gayle S. Putrich

User Fee, *from Page 1*

A 20-item package of changes sponsored by committee chairman Sen. Lamar Alexander (R-Tenn.), added by voice vote, adds other provisions, including language that would make hearing aids intended to be used by adults suffering from mild-to-moderate hearing impairment available over the counter, provide support to speed up and improve application procedures for pediatric medical devices, and require the FDA's device center to create a structure to spur pediatric device innovation.

It also would direct the FDA to create a risk-based device inspection framework and make improvements to the process for visiting foreign and domestic device manufacturers, drawing some language from a stand-alone bipartisan bill introduced in February Sens. Johnny Isakson (R-Ga.) and Michael Bennet's (D-Colo.).

The additions also would require the GAO to report back to Congress by September 2018 on the FDA's progress in coordinating with international agencies to better share and use data on clinical trials and research and development for devices.

A draft amendment from Sanders that would establish a medical device innovation fund did not make an appearance at the committee level but could be introduced when the reauthorization package reaches the Senate floor.

The changes must be approved by the relevant House committees and on the floors of both chambers of Congress before being signed into law. If the new agreements are not signed 60 days ahead of the September deadline, the FDA would be forced to lay off more than 5,000 employees, crippling the agency's ability to review device applications. — Gayle S. Putrich

FDA Proposes Plan for Spending $500 Million in Cures Act Funding

The FDA's proposed plan for spending the $500 million allocated by the 21st Century Cures Act through fiscal 2025 prioritizes a breakthrough device pathway, humanitarian device exemptions, and clarifying medical device software.

Over the next nine years, the agency hopes to spend $109 million to implement Cures Act programs in medical devices. Dollar amounts for fiscal 2018 and beyond will need to be appropriated annually by Congress.

In a May 9 meeting, the FDA's science advisory board reviewed and largely supported the agency's proposal. A final version is due to Congress by June 11.

FDA estimates that its breakthrough devices program will grow as high as 20 percent per year over the next decade, however the agency said it needs to acquire the appropriate IT infrastructure.

Standards

The act also directs the FDA to make decisions on recognizing international standards in device reviews within 60 days of requests. The funding will help the agency expand its participation in national and international standard-setting organizations, the work plan said.

In addition, the act eliminates the requirement that device trial sponsors always use a local institutional review board. The FDA plans to issue several guidance documents on using centralized IRBs.

The Cures Act, signed into law in December 2016, instructs the agency to produce draft and final guidances on several topics, including the use of real-world evidence and novel clinical study designs, over the coming year (*IDDM*, Dec. 9).

The full proposed work plan is available here: www.fdanews.com/05-05-17-FDACuresPlan.pdf.
— Conor Hale

FDA Warns Lonza Over Production, Validation, Cleaning Procedures

The FDA warned device manufacturer Lonza over inadequate validation, CAPA procedures, and other violations at its Walkersville, Md., facility.

The agency inspected the facility in late January and early February and issued a Form 483, but found the company's response to be inadequate.

In a warning letter, the FDA noted the facility lacked an established master plan for validation processes involving cleanroom operations, cleaning validations and HEPA filter certifications. It also lacked a cleanroom risk assessment procedure.

Specifically, according to the warning letter, the facility had no requirements in its procedure for qualifying a clean room.

The facility also failed to use established methods for product sterility testing. It used a surrogate sterility test with no representative sample of the batch, which was not sufficiently sensitive.

The warning letter can be found here: www.fdanews.com/05-10-17-LonzaWarning.pdf.
— Zack Budryk

Michigan Court Allows State Fraud Claim Against Medtronic to Continue

A Michigan district court judge ruled last week that product liability claims against an FDA-approved medical device manufacturer were preempted by federal law and dismissed them, but did allow part of the fraud claim against manufacturer Medtronic to proceed at the state level.

In the Canary v. Medtronic, Inc. decision, District Judge Nancy G. Edmunds disagreed with the manufacturer that current GMPs are too broad to serve as a basis for argument that state law product liability claims are preempted by federal law.

The takeaway for device manufacturers? A properly crafted plaintiff claim of federal GMP violations can support product liability claims in a state court.

Devicemakers Should Focus On EU Post-Marketing Requirements

To comply with the EU's new regulations for devices and IVDs, companies should first look at their postmarketing clinical requirements to meet the May 26, 2020 deadline for devices and the May 26, 2022 deadline for IVDs, say Sidley Austin attorneys.

Surveillance systems must include a postmarket follow-up to update clinical evaluations. Makers of Class III devices and implantable devices will need to develop a safety and clinical performance summary to be validated by a notified body that also will be made public.

Companies can expect enhanced scrutiny and surveillance, the law firm warns in a client update, noting that all notified bodies will be redesignated and required to have documented procedures regarding unannounced on-site audits of manufacturers and, when applicable, subcontractors and suppliers.

Previously, clinical data for new devices have been drawn mainly from available literature for equivalent or partially equivalent devices. By contrast, the Medical Device Regulation requires manufacturers to perform their own clinical evaluations for higher-risk Class III and implantable products.

Manufacturers need to communicate early and often with their notified bodies to ensure their clinical data will be accepted. Notified bodies will also notify competent authorities when they grant certificates for high-risk devices, and authorities may request additional information from notified bodies.

Devicemakers should also prepare for new product groups and classification rules as many definitions will change, including the definition of accessories.

The new regulations also include enhanced traceability requirements that include a unique device identification (UDI) that must be affixed to every device to be traced through the supply chain. "Each participant in the supply chain, including distributors and importers will have their own regulatory responsibilities," the law firm said.

Sidley warns that the new regulations also introduce legal liability of the authorized representative for defective devices, "jointly and separately with the manufacturer, despite the fact that authorized representatives are not permitted to control the parameters that could lead to liability."

For companies without an establishment in the EU, contracts will need to be reviewed and updated, and it is likely that the "validity of the liability provisions will be invoked before the national courts," the firm said.

Companies should conduct gap analyses to understand the impact of the regulations on their companies, because the changes will have far-reaching implications across multiple business units, including product development, clinical, regulatory affairs, manufacturing and supply chain operations.

PEOPLE ON THE MOVE

enGene has named **Theresa Podrebarac, MD**, chief medical officer. Dr. Pedrebarac joins enGene from AbbVie where she served as vice president, immunology clinical development. Previously, she was vice president of early clinical development and immunology at Biogen. Prior to Biogen, she served as vice president and head of rheumatology global clinical development at EMD Serono.

Oligo Medic has appointed **Jerett Creed** as CEO. Most recently Mr. Creed was in charge of launching Oligo's JointRep product in Latin America. Prior to that role, he was founder and CEO of Cardigant Medical. He previously served as interim chief financial officer for a publicly traded oil and gas company. He began his career at Johnson and Johnson, initially focused on manufacturing and product development of early angioplasty balloons and bare metal stents.

Medical Device Single Audit Program Gains Momentum

Companies most likely to benefit from the Medical Device Single Audit Program will include those selling products in Canada, along with manufacturers of finished medical devices and high-risk devices, said MDSAP expert Brian Ludovico, in an FDAnews webinar.

Devicemakers selling products in Canada must comply with the single audit requirement by March 2019. Health Canada will expect all device licenses to be supported by MDSAP audits by that time, and if a manufacturer doesn't have a MDSAP certificate, its license will be suspended, said Ludovico, executive director of MDSAP regulatory certification at NSF Health Sciences.

Companies selling their devices in other regions covered by the MDSAP Consortium — which currently includes Australia, Brazil, Canada, Japan and the U.S. — should be aware that information from the Canadian audit will be shared with the regulators in the other regions.

For example, if a company sells devices in Canada, the U.S. and Australia, it will be required by Canada to be certified under MDSAP, and the FDA and the TGA will have access to the audit reports.

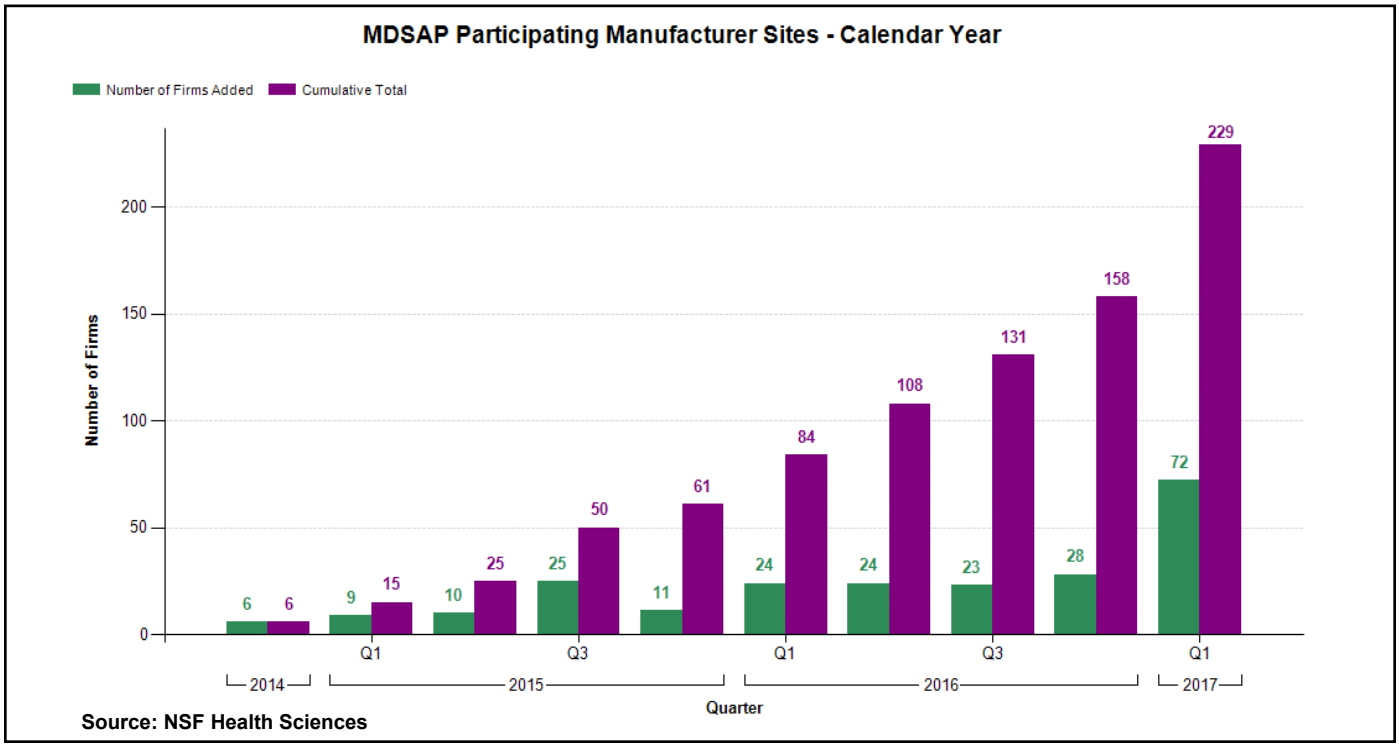
Other jurisdictions are likely to require MDSAP audits as the program gains momentum. The EU has not yet signed on because it has been busy overhauling its device regulations. As part of that process, it has toughened requirements for notified bodies, which will reduce the number from roughly 85 down to about 40.

Ludovico, who worked with a notified body for 21 years, said companies may not be aware of the timing of the Canadian requirements — and that they won't be able to "opt out" of the other regions where they sell their devices.

There are more pros than cons to undergoing a MDSAP single audit certification, Ludovico said. The benefits include speed to market and lower overall costs, because the MDSAP audits cover five jurisdictions**.** In addition, large medical device manufacturers are adopting MDSAP, and they are increasingly likely to require their suppliers to have MDSAP or ISO 13485 certification.

As of the first quarter of 2017, 229 manufacturer sites were participating in the MDSAP program.

Access the webinar, Top 5 Reasons to Use the Medical Device Single Audit Program, here: www.fdanews.com/products/54222.



India Extends Deadline For Device Labeling Rules

Devicemakers importing products into India will have six more months to comply with new device labeling rules.

New labeling rules for imported devices were scheduled to take effect May 25, but devicemakers requested an extension of the requirements, which will now take effect on Jan. 1, 2018.

The Drugs Controller General of India says international labeling rules requiring the expiration date and date of manufacture on the device label conflicted with India's labeling requirements. As a result, importers will be allowed to affix a sticker indicating the manufacturing date and expiration date on device labels.

India recently finalized new regulations that separate out devices for the first time from broader drug regulations, which also go into effect on Jan. 1, 2018. Previously, device manufacturers had to comply with regulations written for pharmaceuticals.

Starting on Jan. 1, 2022, all medical devices sold in India will require a unique device identification, including a device identifier and a production identifier. The production identifier will include a serial number, lot or batch number, software version, manufacturing date and expiration date (*IDDM*, Feb. 17).

Read the DCGI notice here: www.fdanews.com/05-12-17-DCGInotice.pdf.

BRIEF

Australia Pulls Abbott's Absorb Vascular Scaffold From Market

Australia's Therapeutic Goods Administration has removed Abbott's Absorb Bioresorbable Vascular Scaffold System from the Australian Register of Therapeutic Goods.

The decision to recall the device and de-list it in Australia was based on data from studies that showed elevated rates of heart attack and blood clots compared to patients treated with another stent. Abbott Vascular Australia is recalling all unused stock of the device.

483 Roundup: FDA Cites Three Firms For Reporting, Documentation Issues

Repro-Med Systems in Chester, N.Y. failed to submit a report to the FDA on steps taken to reduce a health risk posed from a device, inspectors found during a late 2016 inspection.

In a Form 483, the agency said the facility also lacked adequate quality procedures and documentation.

Defects in a supplier's product led to a 2016 product recall in which customers were notified of the problem. Repro-Med requested the products be returned to the company for disposal, but did not notify the FDA.

The company also failed to follow proper quality procedures after a design change, with no documented validations to confirm that the changes would not negatively impact the product or packaging.

Inspectors also found inadequate CAPA investigations for various sterilization procedures, as well as a lack of procedures for intake and documentation of defective product; no documentation for rework and reevaluation activities in the device history record, specifically for needles; inadequate testing verification for manufacturing equipment; and a lack of quality records for suppliers.

The FDA also faulted the facility over its procedures for receiving, reviewing, and evaluating complaints. Between July 2015 and the inspection, three complaints were not evaluated, and the firm's procedures for complaint investigations did not include collecting all information related to adverse events.

In one case, the facility received a complaint noting that similar malfunctions had occurred previously, but the firm failed to follow up on the reports. A separate complaint about tubing malfunctions listed specific lot numbers that were affected but the firm did not properly investigate the lots in question, the agency said.

The See Clear Company: The FDA found extensive problems with documentation and quality procedures during a fall 2016 inspection of The See Clear Company in Norcross, Ga., resulting in a 12-observation Form 483.

Inspectors found the company did not have procedures for evaluating and investigating complaints, and there was no process or file system for dealing with or documenting complaints. The facility also lacked adequate procedures for: dealing with incoming product, including their acceptance or rejection and personnel training documents; and procedures for control and distribution of finished devices.

None of the quality documents the inspectors found were signed or dated. The documentation also lacked procedures for identifying, segregating and disposing of defective products. The facility provided no quality agreements with contractors outlining their roles and responsibilities. The firm was unable to produce a quality agreement clearly establishing the agreed-upon roles and responsibilities between contractors and the company, and lacked adequately documented monitoring of the company's contract manufacturer.

Risk analysis, specifically for the shelf life of the product, was also found to be inadequate. The company's CAPA procedures did not include a plan for verifying or validating corrective or preventative actions or for recording and implementing changes, the agency said. Moreover, the firm only provided data for one shelf-life, and was unable to justify all components of its risk analysis.

The facility had no documentation of quality audits for 2014, 2015 or 2016, and managers did not assess its quality system for suitability and effectiveness at required intervals.

Eptam Plastics: Contract medical device manufacturer Eptam Plastics in Northfield N.H., was found to have problems with handling complaints and was issued a Form 483 following a February 2017 FDA inspection.

The inspectors found the facility had not been properly maintaining records of evaluations, investigations, and complaint determinations, and had not properly documented the process for dealing with complaints.

Read the Form 483s here: www.fdanews.com/05-12-17-Three483s.pdf. — Gayle S. Putrich

APPROVALS

FDA Gives Nod to Cardiovascular Systems' Replacement Saline Infusion Pump

Cardiovascular Systems received FDA marketing clearance for a redesigned saline pump used as part of the company's Diamondback 360 orbital atherectomy systems. The 70057-03 saline infusion pump will replace the 7-10014 unit, which was recalled on April 17, 2017.

The company anticipates replacing all recalled units by no later than Aug. 31, 2017.

Crospon Receives FDA Clearance For Endoflip with Flip Topography Module

Crospon has received FDA marketing clearance for its Endoflip 2.0 imaging device, which displays esophageal patterns on a 24" touchscreen during endoscopy.

Shipments of Endoflip 2.0 systems will begin in June 2017.

Abbott Gains CE Mark for Confirm Rx Insertable Cardiac Monitor

Abbott has received a CE mark for its Confirm Rx insertable cardiac monitor (ICM), a smartphone compatible device that continuously monitors a patient's heart rhythm and transmits information to physicians via the myMerlin mobile app.

The device is currently under review by the FDA.

FDA Clears MagVenture's Device For the Treatment of Depression

MagVenture has won FDA marketing clearance for its MagVita TMS therapy system, which delivers transcranial magnetic stimulation for patients not responding to medication. The treatment does not require anesthesia. The device delivers magnetic pulses to the part of the brain controlling mood.

Bovie Medical Receives FDA Clearance For J-Plasma Precise Flex Handpiece

Bovie Medical has received FDA marketing clearance for its J-Plasma precise flex handpiece for use in robotic-assisted procedures including those with Intuitive Surgical's *da Vinci* surgical system. The unit is controlled using a robotic grasper. The company will launch the device in the second half of 2017.

Medrobotics Wins FDA Clearance For Flex Robotic System

Massachusetts–based Medrobotics Corp. has received FDA marketing clearance for its Flex robotic system for colorectal procedures.

The minimally invasive Flex robotic system allows surgeons to navigate complex anatomy through a single, small entry point to operate in difficult-to-reach places. Medrobotics received its initial FDA clearance for the Flex robotic system in July 2015 and the CE mark in March 2014.

Abbott Gains CE Mark for Tacticath Contact Force Ablation Catheter

Abbott has received a CE mark for its sensor enabled TactiCath contact force ablation catheter, which is designed to assist in treating atrial fibrillation. The device's magnetic sensor integrates with the Abbott EnSite Precision cardiac mapping system to collect magnetic and impedance data. The device is available in select markets in Europe, with full market release expected in the third quarter. Abbott is pursuing approval in the U.S.

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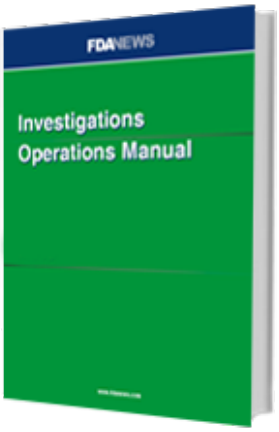

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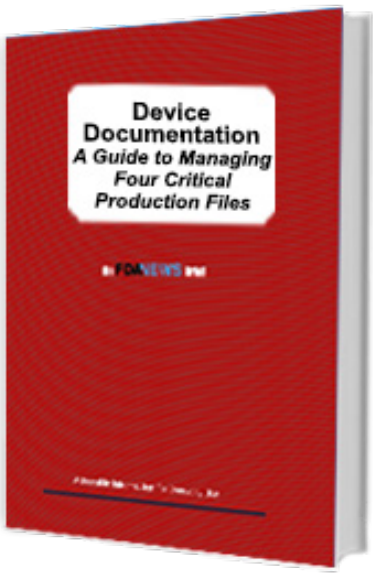

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