# International Devices & Diagnostics Monitor

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## IN THIS ISSUE



## Senate Sends FDA User Fee Bill to the President

As one of its final items before leaving for the summer, the Senate overwhelmingly voted to reauthorize the FDA's user fee agreements through fiscal 2022, completing over two years of work.

The program is expected to bring in $1.42 billion in fees, about a quarter of the agency's budget, over the next fiscal year — supporting the individual programs that cover reviews of medical devices, drugs, generics, biologics and biosimilars, as well as approximately 5,000 employees — and includes provisions for hiring 230 additional staff over the next five years.

The Senate approved the measure that passed the House with a voice vote in July, H.R. 2430, as a way to expedite the process instead of considering a separate version (*IDDM*, July 17).

Following the 94-to-1 vote Thursday, the bill now goes to the president's desk for approval, far ahead of the current MDUFA expiration

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

## EMA Seeks Stakeholder Comments On Companion Diagnostics

The EMA released a concept paper that will form the basis of a new guideline on companion diagnostics.

The agency recently released its first guidance on IVD medical device regulation, but said more direction was needed on to the "interface" between drugs and predictive biomarker assays, including companion diagnostics.

One of the problems for the agency is that EU legislation covering marketing of drugs and IVDs is not linked. The new IVD regulation notes cooperation between notified bodies and drug regulators in evaluating a new companion diagnostic, but this does not lead to approval of a specific companion diagnostic.

The EMA defines a companion diagnostic as a device that is essential for the safe and effective use of a corresponding drug to:

*(See* **EMA**, *Page 2)*

**User Fee**, *from Page 1*

date of Sept. 30. Sen. Bernie Sanders (I-Vt.) was the sole lawmaker to vote against the bill.

Anticipated medical device fees would increase from $130.2 million to $183.3 million in fiscal 2018, and up to $213.7 million for fiscal 2022, including new fees for de novo reviews. The new fee levels would apply to all applications received after Oct. 1.

The bill passed by the Senate also includes language from several bills introduced over the past year, including one making hearing aids available over the counter. The provision would do away with the need for an examination or signed waiver for a patient to receive the device, and would place them in a new category under Class I devices.

It would also require the FDA to issue regulations for safety and labeling requirements, and to update its draft guidance on personal sound amplification products — consumer electronics that may use similar technology, but are intended for use by individuals with normal hearing (*IDDM*, May 1).

Lawmakers ignored President Trump's calls to have industry fund 100 percent of user fee-related activities. The White House issued an official statement of policy following the House's passage in mid-July, but Senate leaders said requests to renegotiate the terms of the agreements had come "too late." — Conor Hale

**EMA**, *from Page 1*

- Identify, before and/or during treatment, patients who are most likely to benefit from the treatment; or
- Identify patients likely to be at increased risk for serious adverse reactions as a result of the treatment.

If a drug's label recommends it for use with a predictive biomarker, any commercial assay used for this purpose will be considered a companion diagnostic and will require a CE mark.

"Development of medicinal products and IVDs are often independent, coming together only superficially towards the end," the paper says. It points to gaps in evidence and validation as a particular concern, and says co-development programs should link the two to generate evidence to support validation of the diagnostic.

For example, a CE-marked IVD may not be available to measure potentially predictive biomarkers during development, and the assay used in development may itself be co-developed as an eventual companion diagnostic.

The technical performance requirements of assays used to measure predictive biomarkers will vary depending on the stage of development and whether the biomarker affects subject eligibility or treatment allocation.

In addition, an assay used during a pivotal trial in support of drug approval could be considered a reference test for the development and validation of subsequent companion diagnostic.

Read the EMA paper here: www.fdanews.com/08-01-17-EMAcompanionDx.pdf.

## Most Users Accept Sharing Data From Networked Medical Devices

More than three out of four consumers approve the immediate transmission to their doctors via the Internet of significant changes in medical conditions recorded by networked pacemakers, blood-sugar sensors or other devices, according to a 2017 survey by Unisys.

But more than half of the respondents said they were extremely or very concerned about hackers gaining unauthorized access to a device such as a defibrillator, insulin pump or pacemaker. Another one-quarter said they were somewhat concerned about such breaches.

The survey results reflect distinctions consumers make among who gets information and how it is used.

Only about one in three approve of allowing insurance companies to tap the flow of information to determine what to charge for coverage.

Unisys has conducted the security survey since 2007. The 2017 survey was conducted online April 6-18 in 13 countries and included more than 1,000 respondents in the United States.

There is great potential for the healthcare industry to benefit from data sharing from medical devices, but consumers "have reason to remain wary," according to Unisys vice president Jeff Livingstone.

For example, there is a perceived difference in the risk between a health insurance company collecting information about member behavior and a doctor monitoring a patient's critical medical data. This is true despite any direct or indirect advantage to the member or patient.

As the number of smart medical devices grows — including those that are worn or even embedded in patients' bodies — healthcare providers will be challenged with efficiently tracking and managing devices away from their medical facilities and ensuring the devices are secure, he said.

## Senate Bill Aims to Block Hacks of Medical Devices

Medical devices would have to be better protected against hackers under a cybersecurity bill introduced Aug. 1 by U.S. Sen. Richard Blumenthal (D-Conn.).

The Medical Device Cybersecurity Act would require devices to come with a "cyber report card" and better protections against remote access.

In addition, the bill would require that cybersecurity updates remain free and not require FDA recertification.

Other provisions in the bill call for guidance and recommendations for end-of-life devices, including secure disposal and recycling instructions, and would expand the responsibilities of the DHS Computer Emergency Readiness Team to include cybersecurity of medical devices.

"The security of medical devices is in critical condition," Blumenthal said.

"Without this legislation, insecure and easily-exploitable medical devices will continue to put Americans' health and confidential personal information at risk."

## Boston Scientific Issues Alert Over Fatal Pacemaker Incident

Boston Scientific sent out an alert when one of its pacemakers, the S-ICD device, "delivered an atypical amount of energy" after environmental radiation corrupted its memory, preventing S-ICD arrhythmia detection/treatment and ultimately causing the patient's death.

Following the incident, the company conducted a three-week internal investigation and concluded the incident was a "single event upset" with a 1 in 300,000 probability of reoccurring. Despite this finding, Boston Scientific is preparing a software update to safeguard against memory corruption.

## Devicemakers Call Nation-States Top Cybersecurity Threat

Devicemakers view government-sponsored hackers as the top cybersecurity threat, according to a new survey from KPMG.

The audit, tax and advisory firm surveyed 100 executives responsible for information technology and security at drug and device manufacturers. They found that 53 percent named nation-states as the top threat to cyber-security. Sixty-three percent said bad actors sought patent and clinical research data. The threat is largely from nations that seek to obtain intellectual property without the associated research and development costs, according to KPMG partner David Remick.

Respondents were also asked about priorities for improving their organizations' cybersecurity protocols. The top priority among devicemakers was better technology, at 36 percent, followed by concrete, overarching strategies for data collection and protection at 28 percent. Only 9 percent of respondents, devicemakers and drugmakers alike, viewed increased staffing as a priority. This reflects a tendency among organizations to emphasize tech solutions at the expense of improved processes and training, according to Remick, who called this a "grave mistake."

Companies increasingly engage patients through applications and web portals, which improves patient engagement but brings a slew of new risks, said KPMG partner Michael Ebert. Forty percent of those surveyed said their overseas security protocols were weaker than local ones.

The survey follows another published in June – conducted by the IT research organization Ponemon Institute for the security company Synopsys – that found two-thirds of devicemakers anticipate a cyberattack on a device built or used by their organizations in the next year, but only 17 percent have taken significant steps to avert such an attack.

Focused on North America, that study included responses from about 550 individuals whose roles centered on the security of medical devices.

Only one third of those surveyed understood the potential for adverse effects to patients from insecure medical devices, the survey found. — Zack Budryk

## 483 Roundup: FDA Hits Three Firms Over MDRs, Complaints, and Records

The FDA cited three devicemakers for a range of deficiencies including inadequate procedures for device failures, MDRs, complaints, and recordkeeping.

**GFS Chemicals:** An Ohio contract manufacturer of medical devices failed to maintain adequate records for its manufacturing processes, failed to set requirements for suppliers and lacked procedures for conducting quality audits or handling complaints, the FDA said.

The company, GFS Chemicals, of Columbus, sells laboratory equipment and chemicals to a variety of customers, including pharmaceutical firms.

The FDA reviewed the facility's production processes and protocols going back 10 years in an inspection conducted in March, and found the company's device history records were incomplete and showed that the facility failed to follow its manufacturing procedures.

The agency also found the facility lacked validations for some manufacturing processes and failed to spell out procedures and documentation for changes in methods, such as a 2009 switch from an operation that previously was conducted manually.

In addition, the agency found the company's CAPA documentation was inadequate.

**Columbia Scientific Development:** Columbia Scientific Development did not properly investigate potential device failures or develop written MDR procedures, according to the FDA.

The agency issued a Form 483 following a May/June inspection of the medical device specifications developer's Portland, Ore., facility. Investigators found Columbia's complaint handling procedure did not require investigating complaints involving possible failures of devices, their labeling or their packaging. Two of four complaints documented since May 2016 related to potential problems with the company's electrode devices, but the company documented that both were closed without an investigation.

The FDA faulted the company's MDR procedures, noting that it did not have an internal system for identifying and submitting supplemental or follow-up reports or submitting MDR events to the agency.

The company's complaint-handling procedures required all oral or written complaints to go on the firm's official complaint document, but the firm only documented two out of four complaints about its electrodes.

The company's design history files did not demonstrate that the design complied with requirements and the company did not document validation of the device design, the agency said. In addition, the firm's procedures required reviews for management and subcontractor performance but there was no documentation of the reviews taking place.

The Form 483 further noted that the company's design control procedures did not require that design reviews be documented in meeting minutes, and its device master record for the Columbia 600B electrodes do not include all required information. Device history record procedures were also incomplete, with seven failing to include or reference the location of UDI coding on the label.

Lastly, the firm's document control procedures require authorized approval signatures, but at least three procedures were implemented without one, and documents stamped "HISTORY" were mixed in with current documents, contrary to company procedures.

**Tate Technology:** Tate Technology failed to properly evaluate complaints or keep records of nonconformances, according to the FDA.

The FDA issued a Form 483 to the devicemaker following a June inspection of its Spokane, Wash., facility. Investigators found the firm's procedures for handling complaints did not include a requirement that all medical device complaints be evaluated for medical device reporting, and it did not document an MDR evaluation for any of 12 complaints received since last January.

*(See* **483s***, Page 6)*

## TGA Proposes to Reclassify Synthetic Meshes as 'High Risk'

Transvaginal mesh devices and mesh used for hernia repair may soon be classed as "high risk" by the Australian government.

The Therapeutic Goods Administration is proposing that all synthetic meshes be bumped from Class IIb (medium to high risk) up to Class III (high risk), requiring manufacturers to seek additional regulatory approval.

Surgical mesh is used to provide temporary or permanent support for weakened structures and/or muscles in surgery. Other common uses include repair of hernias, pelvic organ prolapse, and stress urinary incontinence.

The move by the TGA comes on the heels of controversy regarding the mesh devices. A class action suit involving 700 women against Johnson and Johnson alleges the company didn't perform proper clinical trials to determine the product's safety.

Implants for pelvic organ prolapse have been linked with chronic pain, nerve damage, bleeding and infection, with mesh erosion cutting through the vaginal wall.

Currently, synthetic surgical meshes are classified as Class IIb. While some surgical meshes such as those including medicines or materials of animal, microbial or recombinant origin, are already classified as Class III.

As it seeks this regulatory change, the TGA is hoping to introduce formal requirements for medical device makers to provide patient implant cards and product information for all active and implantable medical devices.

The moves are part of TGA's effort to align itself with the European Commission as that organization updates regulatory processes. The proposed changes follow a decision by the European Commission to implement a number of medical device reforms, including to up-classify all surgical mesh medical devices to Class III and to provide patient implant cards and consumer product information for all implantable medical devices.

Said TGA, implementation of the changes is in response to the government's decision in September 2016 to accept Recommendation Twenty of the Expert Panel Review of Medicines and Medical Devices Regulation (MMDR). Because the European regulations were not finalized until May 2017, TGA wasn't able to consult on this aspect of alignment with the European Regulations until now.

The TGA is looking for views from industry, healthcare professionals, and current and future recipients of medical devices on how it proposes to implement the changes. The agency hopes the comments will flag any unintended consequences of the proposed changes. The comment deadline is August 25, 2017.

Meantime, look for more such changes from Australia. TGA said there are a number of other changes to be considered. The two measures are being advanced first, given their ability to positively impact on patient safety around mesh devices. — Suz Redfearn

**483s**, *from Page 5*

Moreover, according to the agency, the company did not keep records of "Red-Tag" nonconformances for medical devices. The facility's quality manager told investigators that the tags were disposed of as soon as the nonconformance was handled.

In addition, Tate's procedures for supplier selection and evaluation did not feature requirements for suppliers, contractors and consultants regarding medical devices, and the company failed to document its evaluation of potential suppliers.

The firm's procedures further allowed for the use of unapproved suppliers, and had no agreements in place with contractors or suppliers to alert Tate of changes to their products or services.

Read the three Form 483s here: www.fdanews.com/08-02-17-ThreeForm483s.pdf.
— Zack Budryk and Gregory Roberts

## MHRA Pelvic Mesh Group Finds Risk Information is Key Issue

The UK's Medicines and Healthcare products Regulatory Agency released final recommendations from the Mesh Oversight Group, which concluded hospitals need to improve their processes for tracking data and patients need to be better informed about potential risks of pelvic mesh devices.

The Mesh Oversight Group released an interim report in December 2015 that addressed concerns over the use of mesh devices implanted in the pelvic region to treat stress urinary incontinence and pelvic organ prolapse. The interim report suggested action was needed to better inform women about potential risks following surgery.

Following the publication of that report, the Mesh Oversight Group was formed to advance recommendations and make sure responsible bodies were held accountable. The group worked with MHRA, NICE, the British Society of Urogynecology, the Royal College of Obstetricians and Gynecologists and the British Association of Urological Surgeons to finalize its recommendations.

The report highlights some positive changes. Hospitals have changed the way they record data, which has allowed them to collect more data on the complications women experienced. Some of the improvements in information flow resulted in an increase in the number of women reporting complications. The report concluded that this was due to the increased awareness rather than an increasing number of complications.

A registries subgroup continues to work to develop better ways of tracking implanted mesh devices to capture more accurate data. The subgroup will report its findings and make recommendations by November 2017.

NICE anticipates it will also publish a new guideline in 2019 for clinicians, clinical directors, hospital trusts and commissioners.

Read the final report here: www.fdanews.com/08-01-17-MHRAmesh.pdf. — Tamra Sami

## Patient Engagement Advisory Committee to Hold First Meeting

The FDA's Patient Engagement Advisory Committee (PEAC) will hold its inaugural meeting in Gaithersburg, Maryland, October 11-12 to discuss how patients, devicemakers, and the FDA can share information.

The nine-member committee will meet "once or twice a year," the agency says, and the meetings will be open to the public.

Patients can have "unexpected experiences" with a device or clinical trial, and the PEAC will allow patients to share what happened with the device manufacturer and the FDA, said Jeffrey Shuren, CDRH director, and Kathryn O'Callaghan, CDRH assistant director for strategic programs, in a July 25 blog post.

The committee will consider how patients can provide input across the medical device lifecycle, and how to get patient input related to medical device performance once products are on the market.

The PEAC is a response to 2012 federal legislation that instructed the FDA to "solicit the views of patients during the medical product development process and consider the perspectives of patients during regulatory discussion."

The legislation led directly to the formation of the PEAC, though it is not the only forum involving patients that has been created because of the legislation. Last year alone, CDRH "held 21 patient interaction opportunities, involving 34 patient organizations with 68 percent of CDRH staff interacting with patients," and agency spokesperson said.

The agency is also working to ensure that patient perspective is considered in the evaluation of medical devices beyond the confines of PEAC. The number of approved investigational device exemptions, for example, has included patient reported outcomes 65 percent of the time. — Donna Scaramastra Gorman

# APPROVALS

## FDA Grants Pre-Market Approval To Spectranetics' Drug-Coated Balloon

Spectranetics secured FDA pre-market approval for its Stellarex drug-coated balloon.

The device, aimed at returning blood flow to the femoral and popliteal arteries, went through five randomized trials. The device proved safe and effective and demonstrated low rates of legion revascularization, the Spectranetics said.

The clinical trial data showed the device's efficacy in addressing femoropopliteal disease in diverse populations.

## Agfa Wins 510(k) Clearance For XERO Viewer Expansion

The FDA awarded 510(k) clearance for advanced clinical applications on Agfa HealthCare's XERO Viewer.

The viewer is a component of the company's Enterprise Imaging Platform, which organizes imaging data from various sources in one place. The clearance expands the device's capabilities to include 3D visualization tools and applications for orthopedics and mammography.

The XERO viewer allows users to view patient images from any web-enabled device using popular browsers.

## Quantel Medical's Photocoagulator Wins FDA Nod

The FDA has approved Quantel Medical's photocoagulator for treatment of macular edema and peripheral retinal pathologies.

The Easyret device incorporates Quantel's proprietary ELBA fiber laser technology for 577nm wavelength yellow lasers that the company introduced last year in Europe.

The device is also indicated for pathologies such as diabetic retinopathy and central serous chorioretinopathy.

## Immunalysis Fentanyl Urine Test Scores 510(k) Approval

Alere division Immunalysis announced the FDA has granted 510(k) clearance to its Sefria fentanyl enzyme immunoassay.

Fentanyl immunosay tests have previously only been available for forensic testing. The Sefria test will make fentanyl screening available for hospitals, doctors' offices and other healthcare settings.

Fentanyl abuse is a major driver of the opioid addiction epidemic, with death rates from synthetic opioids increasing nearly 75 percent between 2014 and 2015.

## Bruker Receives FDA Clearance For Expanded MALDI Biotyper Claim

The FDA has cleared Bruker for a further expanded claim for the company's microbial identification system.

The expansion covers 144 new species of microbe, bringing the Biotyper's library to 424 microbial species cleared for the microbiology market. It also includes a series of new disposable biotargets derived from the company's Anchor-Chip technology.

The expanded claim covers expanded workflow tools, including an optically-guided target preparation assistance tool.

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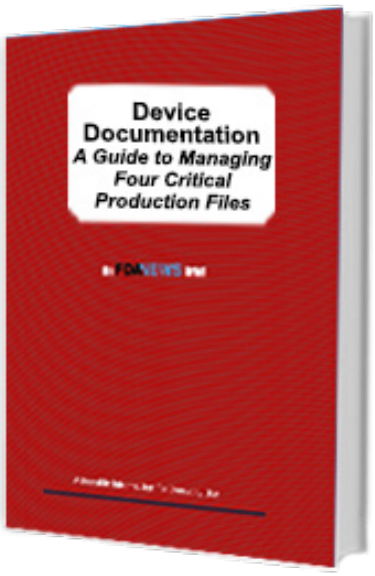


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