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IN THIS ISSUE

House Bill Increases Medical Device User Fees, CDRH Appropriations

Medical device user fees would rise to $134.5 million, representing a modest increase over the $128.4 million requested by President Barack Obama in his fiscal year 2016 proposed budget, as part of recommendations being considered by the House Appropriations Committee.

In a yet-unnumbered bill, the committee has proposed $424.1 million in appropriations for the U.S. FDA's Center for Devices and Radiological Health and the related field activities of its Office of Regulatory Affairs. That was more than the $327.8 million the president had been seeking.

Overall, the bill would give the FDA almost $2.6 billion in discretionary funding, representing an increase of $30 million over the FY 2015.

The bill was released two weeks ago and sent to the subcommittee that oversees the FDA, which approved it in a June 18 voice vote. Last Tuesday, the committee released a report detailing how

(See **Appropriations**, *Page 2)*

Medical Devices Bill $298 Million In 21st Century Cures Act: CBO

The Congressional Budget Office is estimating that medical device provisions in the proposed 21st Century Cures Act, if implemented by the U.S. FDA, would cost at least $298 million from 2016 to 2020, according to a report issued last week.

The House Energy & Commerce Committee unanimously approved the bill, H.R. 6, in May.

It has not gone to the House floor and no similar legislation exists in the Senate.

The legislation would ease U.S. device clinical trials by allowing a single central review board to monitor multiple trial sites.

Currently, device trials must be cleared by a local IRB at each research site.

(See **21st Century**, *Page 6)*

Australian Panel Urges New Pathways To Approve Medical Devices

A panel of experts is calling on the Australian government to establish three new approval pathways for medium- and high-risk medical devices and align with the EU regulatory framework to expedite listing on the Australian Register of Therapeutic Goods.

The recommendations, announced last week, are tied to the government's plan to fast-track approvals of promising new medical technologies and conduct joint reviews with trusted foreign regulators — part of a broad effort to streamline the country's device approval process.

The Department of Health and Ageing launched an independent review of the current framework last October (*IDDM*, Nov. 3, 2014).

The first pathway calls for a conformity assessment by the Therapeutic Goods Administration or an organization designated by the TGA. Specific criteria would be established for conformity assessment bodies, including the capacity to set requirements for medical device classes.

The second pathway focuses on devices from overseas markets and would allow for approval by another national regulatory authority or an organization designated by that NRA.

The panel recommends that the government develop criteria for identifying comparable overseas designating authorities and NRAs to evaluate devices in consultation with consumers, health professionals, devicemakers and the TGA.

Under this pathway, the TGA would still have to determine a medical device has been correctly classified, its marketing approval documentation is in order and it meets Australian requirements to be included on the ARTG.

The third pathway would allow for expedited approval. In these cases, the TGA would be able to place conditions on the device's inclusion in the ARTG.

Additionally, the report recommends that Class 1 nonsterile and nonmeasuring devices continue to be included on the ARTG based on a self-assessment by the manufacturer.

The TGA should make clear to consumers and healthcare providers that while those devices are registered, they haven't been subject to independent assessment, the panel says.

Read the panel's report, *Review of Medicines and Medical Devices Regulation*, here: www.fdanews.com/06-25-15-australiareport.pdf. — John Bechtel

Appropriations, *from Page 1*

fees should be applied. A subsequent markup session of the bill was postponed.

Unfinished Business

The House committee tasks the FDA with wrapping up a couple of long-term projects. For example, in 2011, the agency's National Mammography Quality Assurance Advisory Committee approved a change to the mammogram patient and physician reports to include information on individuals' breast density. The FDA has yet to complete this process, and the committee is pushing the agency to implement it in an "expedited manner" and report on progress made no more than 60 days after the act goes into effect, according to the report. The committee made the same request in last year's funding proposal.

The committee also chides the agency for not taking action on guidance issued in December 2011 on responding to unsolicited requests for off-label information on devices. The guidance's comment period closed March 27, 2012, and the agency subsequently responded to two citizens petitions asking for clarification of the regulations.

The committee instructs the agency to address this issue comprehensively and provide strategies for how the medical device industry can communicate this information to interested parties. Again, the committee gives the agency 60 days to complete the guidelines.

The bill is available at www.fdanews.com/06-24-15-appropriations-bill.pdf. The report explaining the bill may be accessed at www.fdanews.com/06-24-15-budget.pdf. — Elizabeth Hollis

FDA Looks to Ease Confusion Over UDI Direct Marking Requirements

The FDA is clarifying language related to the direct marking of medical devices for unique device identification purposes, including the definition of reprocessing.

In draft guidance released June 26, the agency explains what form a direct marking should take. Under the UDI final rule released in September 2013, a UDI must be permanently affixed to reusable medical devices that require reprocessing between patients. The requirement applies to all device classes, except low-risk Class I devices that bear a universal product code on their labels and packages.

The direct marking requirement came about because medical devices can be used for months or years and may become separated from their original labels and packages that also bear a UDI. Questions arose about what requirements the direct marking must meet.

To that end, the draft guidance "helps people understand that direct marking can be fulfilled a number different ways, such as a permanent label or tag," Jay Crowley, vice president and UDI practice lead at USDM Life Sciences and architect of the final rule, tells *IDDM*.

The FDA decided not to specify any particular approach to direct marking because of the wide variety of existing devices, use conditions, and reprocessing methods for these devices," the guidance says.

Indeed, labelers may use methods such as etching, attaching a permanent plaque to durable equipment or placing a radiofrequency identification or similar tag on the device.

Reprocessing

Another facet of direct marking the document addresses relates to the definition of reprocessing.

"There was ambiguity and confusion for the purposes of UDI," says Crowley, who praised the FDA for adding clarifying language in the definition.

"For purposes of UDI direct marking requirements, we consider a device that is intended to be cleaned and either sterilized or disinfected before each use to be intended to be reprocessed," the guidance states.

(See **UDI**, *Page 6)*

Malaysian Authorities Aim to Shed Light on Conformity Requirements

Devicemakers seeking to market their products in Malaysia must submit a declaration of conformity with the countries medical device requirements, including certification of their quality management system and a list of applicable standards, according to draft guidance that was issued last week.

The DoC attests that the device in question fully conforms with six essential principles of safety and performance and 11 related to design and manufacturing, which may or may not pertain to a certain device.

The declaration also must provide the manufacturer's name and address, particulars of the medical device, an attestation of responsibility and give the name, position and signature of a responsible person.

This may be the chief executive officer or general manager of the company.

Release of the draft guidance comes roughly a year after the Medical Device Authority issued a series of five policy notices to help industry comply with the 2012 Medical Device Act, which went into effect in 2013 (*IDDM*, July 22, 2014).

Several device manufacturers, including Boston Scientific, St. Jude Medical and Medtronic, have a Malaysian presence.

Read the draft guidance at www.fdanews.com/06-29-15-Malaysia.pdf. — Elizabeth Hollis

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FDA Will Allow 'Latitude' In IDE Application Approvals

The U.S. FDA has outlined a risk-benefit framework aimed at reducing the chances of an IDE application being rejected.

In draft guidance issued June 18, the agency says it hopes to clarify some factors it takes into account when assessing the benefits and risks of starting clinical trials of investigational medical devices. For example, the stage of development of the device, the maturity of the proposed technology and the availability of nonclinical testing to supplement or replace the need for human testing are all considered by staff.

Given the anticipated and unanticipated risks associated with these devices, the FDA says it will allow "appropriate latitude" for the conduct of studies supporting IDE applications.

The guidance provides a framework sponsors can adopt for an IDE risk-benefit assessment, which should include the following elements:

- A summary of the disease or condition to be treated and a description of the device in the context of currently available treatments;
- An assessment of risks of the proposed investigation;
- A summary of key benefits of the proposed investigation;
- A summary of any available patient preference information;
- An assessment of uncertainty and why that uncertainty is acceptable; and
- A summation of how the elements justify the decision to proceed with the trial.

The FDA puts a strong emphasis on patient preference, which has been the focus of an ongoing initiative. The FDA has issued draft guidance highlighting the main factors to consider when collecting patient preference information to back PMAs, HDE applications and *de novo* requests (*IDDM*, May 15).

Read the draft guidance at www.fdanews.com/06-29-15-ide.pdf. — Elizabeth Hollis

FDA to Scrutinize Essure Implant's Safety Record

Following more than 5,000 complaints, including reports of patient injuries and four deaths, the U.S. FDA is taking a second look at the safety and effectiveness of Bayer's Essure birth control implant.

The agency's Obstetrics and Gynecology Devices Panel will hold a public meeting Sept. 24 to gather feedback about the device before determining what action to take. Bayer acquired Essure when it bought Conceptus in 2013.

The Essure procedure involves permanently placing a flexible insert into each fallopian tube. Tissue forms over these inserts, creating a barrier that prevents sperm from reaching the eggs. The company claims the product is 99 percent effective in preventing pregnancy permanently, based on five-year clinical study data.

However, women using the device have reported experiencing pain and other health problems. According to the FDA, some symptoms — such as extreme fatigue, depression and weight gain — are not in the labeling and were not observed in postapproval studies or described in clinical literature.

The FDA identified 5,093 medical device reports related to Essure from the time of its 2002 approval through May 31 of this year. Commonly seen complaints include patient-device incompatibility (e.g., nickel allergy), migration of the device or one of its components, the device operating differently than expected, breakage and malposition of the device.

Of the death reports, one was related to a post-procedure infection, another to uterine perforation, a third to an air embolism during device removal surgery and the fourth due to suicide.

Bayer says it has communicated regularly with the FDA about the risk-benefit profile of Essure and welcomes the upcoming panel discussion. — Elizabeth Hollis

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Devices that are only meant to be cleaned between uses by different patients would not fit the reprocessing definition for the purposes of UDI direct marking.

In addition to these clarifications, the draft guidance confirms the compliance dates for each device class.

It also explains that a labeler may file for an exemption if the direct marking would affect a device's safety and effectiveness. If safety and effectiveness would be affected, but the manufacturer chooses to apply the marking, the FDA would generally require a new 510 (k) submission.

In the end, Crowley says the document should prove useful. "It's a good document, and it should help people confused by some aspects of the UDI rule," he says.

Industry trade group AdvaMed also expressed appreciation for the FDA issuing the guidance, adding that it is reviewing the document for specific comments.

The draft guidance is available at www.fdanews.com/06-29-15-UDI.pdf. — Elizabeth Hollis

21st Century, *from Page 1*

Additionally, the FDA reform package simplifies informed consent rules around device trials posing "no more than minimal risk to the human subject," as long as they include appropriate safeguards.

The CBO breakdown on medical devices includes:

- $158 million to establish a program to provide expedited review of devices that represent breakthrough technologies where no approved alternatives exist and the technology offers significant advantages over existing alternatives;
- $68 million to establish an accreditation program for third parties to expedite the approval process for certain devices, review and recognize national and international standards, and develop and update guidances and regulations;
- $68 million to implement a new framework for the regulation of medical software; and
- $4 million for the FDA's Center for Devices and Radiological Health to issue final guidance on the review of combination products. The guidance is due within 18 months of H.R. 6's adoption and would be updated regularly.

The bill also includes a provision to establish a Cures Innovation Fund, which would encourage public-private partnerships and award grants to foster the collection, analysis and availability of data on the natural history of disease and support initiatives of the Council for 21st Century Cures. The CBO estimates that spending from the fund would total $327 million over the 2016-2020 period

The CBO report can be read here: www.fdanews.com/06-24-15-cboreport.pdf. — John Bechtel

Experts: Incorporate Cybersecurity Into Design, Development Process

With a number of attempted and successful cyberattacks on hospital networks making headlines, what steps can medical devicemakers take to ensure the security of their products?

That question was the focus of an FDAnews webinar titled *Medical Device Cybersecurity Quality Assurance: Requirements, Best Practices & Innovative Approaches* featuring Melissa Masters, director of Battelle DeviceSecure Services, and her colleague Stephanie Preston, a senior medical device security engineer.

By identifying stakeholder needs, defining a security risk process and recognizing and implementing appropriate security requirements, devicemakers can set themselves up for success, the two said. Using cybersecurity expertise during the design phase, verifying security requirements through penetration and fuzz testing, creating a responsible disclosure policy, and updating and maintaining devices in the postmarket setting are additional steps to take.

All of these steps are essential to incorporating security in the device design and development process, a move encouraged by the U.S. Food and Drug Administration in its October 2014 cybersecurity guidance (*IDDM*, Oct. 6, 2014).

Full Disclosure

Masters stressed that manufacturers should adhere to this philosophy throughout the product lifecycle. "Just like safety, a security process is ongoing and living until that product is retired," she explained. That said, "safety should always trump security."

Devicemakers also need a responsible disclosure policy for instances when a cyber vulnerability is identified by an outside party, Preston said. "Hackers and security researchers are going to be looking at your device."

At least one device company, Philips, is taking it a step further, following the lead of tech leaders such as Google and offering "bug bounties," or cash awards, to those who find and report security issues.

So, what's the worst thing a devicemaker can do when someone reports a security vulnerability? According to Preston, it's not responding at all. "Reporters are generally just trying to do the right thing," she said. Ignoring the reporter means he or she could make the disclosure public, leading to greater embarrassment to the company.

To avoid such chagrin, companies should do the following:

- Establish a reliable way for a reporter to contact you;
- Respond to reports acknowledging receipt of their submission;
- Validate reporter's finding, reaching out to him or her for additional information, if necessary;
- Consider asking the reporter for aid in validating any patches; and
- Work with the reporter to establish a public partial disclosure date.

Two industries that are leading the way in cybersecurity are the financial and airline industries. Preston told *IDDM* that methods used by the airline industry, in particular, correlate to medical devices.

As with a medical device, the development of an aircraft can take years. Both can last for years, too, Preston said, adding that devicemakers need to be mindful of the fact that cyber challenges can evolve over time.

There are a number of resources to help devicemakers as they work to incorporate security into the design and development process, Masters and Preston said. The Association for the Advancement of Medical Instrumentation is working on Technical Information Report 57, *Principles for medical device information security risk management*, which is expected soon, according to Masters. In addition, international standard ISO 14971: 2012 – *Application of risk management to medical devices*, provides an overview of the risk-management process through the medical device's lifecycle. — Elizabeth Hollis

BRIEFS

SynCardia Warns About Heart Driver System

SynCardia Systems alerted surgeons to possible safety risks involving its Total Artificial Heart Companion 2 driver system after receiving reports of more frequent deaths among a patient subgroup using the device. The Tucson, Ariz., devicemaker said among 38 patients with preimplant circulatory rescue interventions who used the C2 driver system the mortality rate was 60 percent, compared with 17 percent of those who used an earlier model. The FDA has conducted its own analysis of data from patients implanted on or after July 9, 2012, and found a similar link between the C2 driver system and higher mortality in this subgroup. The TAH-t won FDA approval in 2004. The smaller, more mobile C2 driver system was approved in 2012.

XIO Group to Acquire Lumenis

Hong Kong investment firm XIO Group has agreed to buy Israeli devicemaker Lumenis for an estimated $510 million. Lumenis CEO Tzipi Ozer-Armon says the acquisition represents a vote of confidence in the company's achievements, which include the launch of new products and tripling of pretax earnings over the past three years. The XIO group, which led Lumenis through a strategic reformation, specializes in global transactions. The devicemaker develops minimally invasive products for surgery, ophthalmology and aesthetics. The deal is expected to close in September.

Medtronic Acquires Two Companies

Medtronic is purchasing CardioInsight Technologies and Aptus Endosystems for a combined $203 million. Cleveland Ohio-based CardioInsight will become part of Medtronic's atrial fibrillation business and will give Medtronic access to the CardioInsight ECVUE system, which noninvasively maps electrical heart disorders. ECVUE is available in the U.S. and Europe. Aptus Endosystems, which is based in Sunnyvale, Calif., develops endovascular aneurysm and thoracic endovascular aneurysm repair treatment technologies.

Zimmer Recalls Hip Prosthesis

Zimmer is recalling its M/L Taper hip prosthesis with Kinectiv technology femoral stems and necks due to a process monitoring failure that left higher than expected amounts of manufacturing residue on the products. The affected units were manufactured between March 31 and April 20, 2015, the Warsaw, Ind., devicemaker says in a recall notice. The company alerted customers of potential issues with the devices in a letter issued May 18. Zimmer urges customers to return all affected products to the company. The devicemaker has just completed its acquisition of Biomet in a deal valued at $14 billion. The combined company is now Zimmer Biomet.

Siemens' HIV Assay Wins FDA Nod

The U.S. FDA has granted Siemens' ADVIA Centaur HIV Ag/Ab combo assay 510(k) clearance, the German devicemaker says. The assay works by detecting an HIV viral protein and antibodies generated in response to the infection. This ability to detect both antigen and antibody can enable earlier detection of infection and lead to reduced transmission. The diagnostic test has been available in European markets since 2010.

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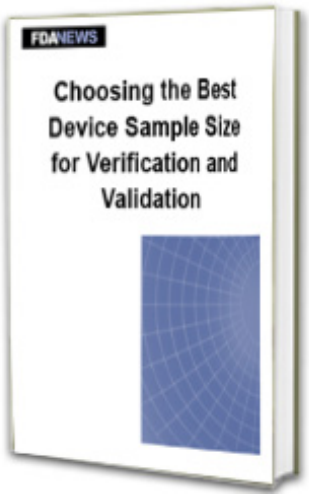

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