INTERNATIONAL DEVICES & DIAGNOSTICS MONITOR

Vol. 3, No. 22
May 29, 2017

IN THIS ISSUE

Device User Fees Would Skyrocket Under Proposed Trump Budget

In a change that would more than triple fees paid by devicemakers, the Trump administration's budget for fiscal 2018 proposes a "recalibration" of how the FDA funds its core mission.

Under the proposal, unveiled May 23, funds collected under MDUFA would increase from the $126 million anticipated for fiscal 2017 to an expected $439 million for fiscal 2018.

The proposal would cut the agency's overall federal funding by $854 million and replace it with $866 million in industry user fees, which would mean an overall increase of 78.6 percent in funding from industry.

"In a constrained budget environment, the budget acknowledges medical product industries have sufficiently matured to assume a greater share of costs associated with FDA's administrative actions," the document says.

(See **Budget**, *Page 2)*

FDA Lifts Hiring Freeze, Gottlieb Discusses Device Safety

FDA Commissioner Scott Gottlieb drew questions from lawmakers on device approvals as he laid out his early priorities in a House appropriations hearing Thursday, and announced that the hiring freeze on the agency had officially been lifted.

Gottlieb told members of the House Appropriations Subcommittee on Agriculture, Rural Development, Food and Drug Administration, and Related Agencies that he had notified the agency's senior staff of the thaw in a memo earlier that morning.

President Trump signed an executive order in January implementing the hiring freeze for all federal agencies. The freeze was lifted by the Office of Management and Budget April 12, but was maintained by HHS, with restrictions based on the administration's planned cuts for the FDA and other agencies. Previously, medical officer positions had been exempted.

(See **Gottlieb**, *Page 2)*

Budget, *from Page 1*

But lawmakers across the board rejected such a proposal earlier this month. In a May 15 letter to members of Congress, HHS Secretary Tom Price asked congressional leaders to support the president's proposed budget by restructuring FDA product reviews to make them 100 percent user-fee supported, with no budget authority to keep them running.

Senate HELP Committee Chairman Sen. Lamar Alexander (R-Tenn.) said Price's plea came "way too late" in the delicately negotiated two-year UFA reauthorization process. "This is an interesting proposal and can be considered the next time the FDA negotiates the user fee agreements with the manufacturers of drugs and devices," Alexander said.

The proposed $10.9 million reduction in budget authority for device programs means the Office of Regulatory Affairs would have to "reprioritize and reevaluate" post-market device surveillance and device adverse event reports, according to the FDA's budget justification documents.

The document states that the additional $171.6 million cut in budget authority for device programs, a "recalibration," would be made up in user fees, though CDRH would be expected to use that projected $231.2 million to reduce average total review times for PMA and 510(k) devices, better standardize the premarket review process and "reaffirm its commitment to its least burdensome requirements by having all employees involved in the premarket review of devices receive training on the least burdensome approach."

The five-year user fee reauthorizations are making their way through the legislative process, awaiting votes on the floor of the Senate and in the House Energy and Commerce Committee. As the reauthorization bills now stand, MDUFA is projected to take in $183 million in fiscal 2018, as opposed to the $439 proposed by the Trump Administration. If the agreements are not reauthorized 60 days ahead of the Sept. 30 deadline, the FDA would be forced to lay off more than 5,000 employees. — Gayle S. Putrich

Gottlieb, *from Page 1*

Members of Congress had repeatedly inquired about the effects of the hiring freeze on the FDA, and whether it would slow the implementation of the 21st Century Cures Act and user fee programs.

Rep. Rosa DeLauro (D-Conn.) and other lawmakers quizzed the commissioner on recent device recalls and his plans for speeding up the device approval process without compromising quality and safety—which she said is already questionable.

On the issue of "speed versus safety," Gottlieb said he has no interest in compromising quality, efficacy or safety in the name of faster approvals.

He said the agency instead needs to focus on efficiencies in the development process — which would ultimately lead to lowering the cost of device development and the finished products — by asking the right questions on the development end, and by providing the right guidance, rules and scientific tools to make sure it's "not only efficient but also learning all we can during that process about safety and efficacy."

The administration's proposed $5.1 billion fiscal 2018 FDA budget would cut the agency's taxpayer-funded budget authority by $854 million and make up for it by dramatically increasing industry-paid user fees—a move FDA and drug industry experts say would harm the agency. — Gayle S. Putrich

FDA Should Require More Labeling Of Emergency Zika Diagnostics: GAO

The FDA should require manufacturers to include more labeling information on unapproved diagnostic devices authorized for use against the Zika virus, according to the Government Accountability Office.

In February 2016, HHS declared that the Zika virus posed a significant potential for a public health emergency and said the situation justified an Emergency Use Authorization (EUA) for Zika virus diagnostic tests.

Since then, the FDA has authorized two different types of diagnostic tests for Zika —molecular tests to detect genetic material in samples of bodily fluids, and serologic tests to detect bloodstream antibodies against the virus.

The FDA has authorized several diagnostic tests under the program, but some performance characteristics were not consistently reported across different tests, making it more challenging to compare them, the GAO found.

The GAO recommended the FDA require manufacturers to list the identity of comparator assays and to consolidate information from individual labels — and make the information available in a form that allows users to better compare information across tests.

The FDA facilitates the development of diagnostic tests by providing manufacturers with EUA review templates that outline the agency's recommendations for analytical and validation studies needed to support an emergency use submission.

The agency also monitors for fraudulent products and false-product claims related to the Zika virus, the GAO noted.

Read the 96-page GAO report here: www.fdanews.com/05-25-17-GAO.pdf. — Zack Budryk

Six of 12 Authorized Zika Molecular Diagnostic Test Labels That Did Not List the Comparator Assay for Clinical Performance

Reference assay and Manufacturer	Comparator assay listed	Comparator assay type	Comparator assay
Zika Virus RNA Qualitative Real-Time RT-PCR: Focus Diagnostics , Inc.	Yes	EUA	Trioplex Real-time RT-PCR Assay: Centers for Disease Control
	Yes	LDT	Lanciotti Test
Aptima® Zika Virus Assay: Hologic, Inc.	Yes	EUA	Trioplex Real-time RT-PCR Assay: Centers for Disease Control
Zika Virus Real-time RT-PCR: Viracor-IBT Laboratories, Inc.	No	EUA	n/a
VERSANT® Zika RNA 1.0 Assay (kPCR) Kit: Siemens Healthcare Diagnostics Inc.	Yes	LDT	Lanciotti Test
xMAP® MultiFlex™ Zika RNA Assay: Luminex Corporation	No	EUA	n/a
Sentosa® SA ZIKV RT-PCR Test (4x24): Vela Operations Singapore Pte Ltd	Yes	EUA	RealStar® Zika Virus RT-PCR Kit U.S.: altona Diagnostics
Zika Virus Detection by RT-PCR: ARUP Laboratories	No	EUA	n/a
Abbott RealTime ZIKA	No	EUA	n/a
Molecular Diagnostics Zika ELITe MGB® Kit U.S.: ELITechGroup Inc.	Yes	EUA	LightMix® Zika rRT-PCR Test: Roche
	No	LDT	n/a
Trioplex Real-time RT-PCR Assay: Centers for Disease Control	No	In-House Assay	n/a
RealStar® Zika Virus RT-PCR Kit U.S.: altona Diagnostics GmbH	Yes	LDT	Lanciotti Test
Gene-RADAR® Zika Virus Test: Nanobiosym Diagnostics, Inc.	No	EUA	n/a

Source: GAO

Devicemakers Seek Changes to FDA's Proposed List of Exempt Devices

Three device manufacturers called for the FDA to modify and clarify its proposed list of class II devices exempt from premarket notifications.

Roche Diagnostics commended the agency for its flexible approach to exempting analyzers and testing systems, but called for clarification on why some analyzers are exempted while others are not.

It is unclear, Roche said, whether the "limitations to exemption" provision applies to diagnostic instruments on the list if the labeling does not include clinical claims. Roche urged the agency to review the exemption and update it to take into account "advances in medical and regulatory understanding."

Becton Dickinson and Company, meanwhile, called on the agency to grant a partial exemption for devices used for myelography procedures due to their similarities to arthography devices.

Aseptic Techniques

Both procedures use aseptic techniques to clean and anesthetize puncture sites and needle insertion into a targeted space, as well as use of imaging equipment. The company also called for a partial exemption for anesthesia kits featuring aspiration needles used for lumbar puncture procedures.

OraSure Technologies requested the removal of 10 enzyme immunoassay devices from the list, arguing that the devices are used for jobsite drug-testing, and providing such an exemption would lead to substandard, potentially inaccurate products.

Read the Roche comments here: www.fdanews.com/05-18-17-RocheDiagnostics.pdf.

Read the BD comments here: www.fdanews.com/05-18-17-BectonDickinsonCo.pdf.

Read the OraSure comments: www.fdanews.com/05-18-17-OraSureTech.pdf. — Zack Budryk

Otsuka and Proteus Resubmit Application for Combination Product

Otsuka and Proteus have resubmitted an application for the drug-device combination product of Abilify (aripiprazole) embedded with a Proteus ingestible sensor in a single tablet.

The ingestible sensor activates when it reaches stomach fluids and communicates with a wearable sensor that records physiological data.

The FDA requested additional information, including further human factors investigations.

The digital medicine would be used in the treatment of adults with schizophrenia, acute treatment of manic and mixed episodes associated with bipolar I disorder and as adjunctive therapy for the treatment of major depressive disorder.

PEOPLE ON THE MOVE

Oligo Medic has named **Jerett Creed** as CEO. Most recently Creed was in charge of launching Oligo Medic's JointRep product throughout Latin America. Prior to that, Creed was founder and CEO of Cardigant Medical.

Creed began his career with Johnson and Johnson, ultimately spending more than a decade with the company finishing his tenure as director of business development.

Martin J. Madden has joined **Novocure**'s board of directors. Madden recently retired after a 30-year career in medical device innovation at Johnson & Johnson.

He most recently served as vice president, research and development DePuy-Synthes and vice president medical device r&d transformation.

LivaNova has hired **Thad Huston** as chief financial officer. Huston joins LivaNova after more than 25 years at Johnson & Johnson, having most recently served as group chief financial officer, medical devices.

483 Roundup: FDA Hits Three Firms For Product Changes, Complaints

The FDA cited three device manufacturers for a range of violations including unreported product changes and failure to properly investigate complaints.

The agency issued a Form 483 to the Oakworks facility in New Freedom, Pennsylvania, following a March 2017 inspection. According to inspectors, the firm made alterations to devices without reporting the changes in writing to the FDA, and took several months to update owner manuals to reflect the changes.

The company also failed to submit timely reports on device malfunctions in at least four cases, and did not conduct quality audits often enough or document the investigations in full, the agency said. Oakworks did not investigate complaints of possible device failures in 10 cases, and lacked full documentation in six other cases.

The company also did not adequately document corrective and preventive actions, which the form noted was a repeat observation. In two other repeat observations, the agency faulted the facility's sampling plans, which were not based on a valid statistical rationale, and said the firm did not have proper procedures for finished device acceptance.

Inspectors also hit the facility for its design verification process, which did not confirm that the design output meets design input requirements, and for lacking adequate controls for products that did not conform to specifications. The investigators also observed the firm's device history records did not demonstrate the devices were manufactured in accordance with the device master records.

Oakworks did not respond to a request for comment.

ConMed: The FDA inspected ConMed's Utica, New York, facility in late January and early February, and issued a Form 483 citing the devicemaker for failure to carry out timely investigations of complaints. In one case, a customer submitted a complaint in December 2015 and the firm voided the customer feedback record without evaluating or investigating it. The complaint record was not closed until September 2015, and the record claimed no device was returned even though the inspection found it was returned on March 18 of that year.

The Form 483 also faulted ConMed for its medical device records, noting that a complaint record opened in August 2015 listed inaccurate information for the device's brand name and catalog number.

ConMed did not respond to a request for comment.

Ultrasonic Services: The agency also issued a Form 483 to Ultrasonic Services after a March inspection of its Houston, Texas, facility. The company implemented a design change for one of its devices without supplying adequate supporting documents, the agency found. The design change allowed Ultrasonic's devices to be manufactured with either dual or single frequencies, while the device was only approved for single frequency.

The firm also lacked an established design history file and documentation to prove its device design was developed according to regulations. On at least two occasions, Ultrasonic redesigned device components without documentation to support the changes.

Ultrasonic declined to comment on the Form 483.

Medical Alignment Systems: The FDA cited Medical Alignment Systems, citing problems with their data reporting, written procedures and handling of complaints.

Following a March inspection of the device maker's Centerville, Utah, facility, the FDA issued a Form 483. According to the FDA, the facility did

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

483s, *from Page 5*

not submit required annual reports for some of its products, with the company submitting no annual reports for its SSL laser devices in the past four years. MAS also failed to develop written procedures for reporting, including for incidents of accidental radiation, according to the form.

The firm also lacked no procedures for handling complaints or corrective and preventive actions.

The agency also faulted the facility for lacking established procedures for handling nonconforming materials. According to inspectors, the firm also did not thoroughly investigate potential suppliers' qualifications or their ability to meet requirements and had no established procedures for purchasing controls. Lastly, officials found the firm did not document its inspections of incoming material or record whether it accepted or rejected incoming products.

Brandt Equipment: The FDA issued a Form 483 to Brandt Equipment of Bronx, New York following a Feb. 6-13 inspection, citing the facility for failing to properly maintain complaint files. Some complaints received by the firm lacked complete information and were not signed by the approving official, the agency found.

The agency also cited Brandt for inadequate procedures for acceptance of incoming product.

Read the Medical Alignment Systems Form 483 here: www.fdanews.com/05-26-17-medicalalignmentsystems483.pdf.

Read the Brandt Form 483 here: www.fdanews.com/05-26-17-brandtequipment483.pdf.

Read the Oakworks 483 here: www.fdanews.com/05-24-17-oakworksinc483.pdf.

Read the ConMed 483 here: www.fdanews.com/05-24-17-conmedcorp483.pdf.

Read the Ultrasonic 483 here: www.fdanews.com/05-24-17-ultrasonicservicesinc483.pdf.
— Zack Budryk

TGA Proposes to Allow Marketing Of Devices Approved Overseas

Australia's Therapeutic Goods Administration is proposing to allow the marketing of devices that have already received marketing approval by certain overseas regulatory authorities.

The TGA is asking devicemakers to comment on which overseas regulators should be considered.

Australia's medical device regulations closely mirror EU regulations, and the country also participates in the Medical Device Single Audit Program. The TGA is also a founding member of the International Medical Device Regulators Forum, and IMDRF signatories are closely aligned when it comes to device classification, conformity assessments and quality standards.

The TGA also has cooperative agreements with Brazil, Canada, France, Germany, Ireland, Japan, Singapore, the UK and the U.S.

Under the new proposal, overseas authorities would need to have similar demographics and health outcomes as Australia and would need to adopt global harmonization guidelines and have a credible track record for evaluating and assessing devices.

The agency proposed the following criteria in allowing approval from foreign regulators:

- Comparability of the regulatory framework of the overseas regulators;
- IMDRF membership;
- Life cycle approach and post market vigilance;
- Communication and cooperation with overseas regulators; and
- Expertise of the overseas regulators.

Even when a medical device has been approved by a comparable overseas regulator, Australian approval would not be automatic, TGA said.

The agency is accepting comments through June 30. Read the TGA proposal here: www.fdanews.com/05-23-17-TGAproposal.pdf.

Australia Maps Out Aggressive Device R&D Plan

The Australian government has unveiled an ambitious plan to boost the country's ability to turn inventions into medical devices.

The government is sinking billions of dollars to build up a stronger R&D infrastructure via a National Research Infrastructure Roadmap, which highlights areas of focus for medical devices, including:

- Digital data and eResearch platforms;
- Characterization for technologies in advanced microscopy and microanalysis;
- Advanced fabrication and manufacturing in areas such as 3-D printing and nanoelectronics; and
- Therapeutic development to develop new innovative medical devices.

As part of the initiative, the National Innovation and Science Agenda will establish a national high performance computing facility to build up modeling and simulation technologies to develop new medical technologies.

The facility will align with the European Open Science Cloud and other global initiatives to support research data management. The effort aims to improve the quality, reliability, durability, and accessibility of data, ensuring the outputs of research are more transparent.

Next generation devices and products will include sensors for medical diagnosis and health monitoring, and implantable structures to address clinical challenges such as tissue regeneration, the roadmap says.

A translational GMP facility will support the development of biomaterials, 3D structures and medical devices and nano technology. The facility will integrate pre-commercial production and testing to take a prototype manufactured under GMP conditions.

Read the roadmap here: www.fdanews.com/05-24-17-nationalRDroadmap.pdf.

APPROVALS

Shockwave Medical Gains CE Mark For Coronary Lithoplasty System

Shockwave Medical has achieved a CE mark for the Coronary Lithoplasty system for the treatment of calcified plaque in conjunction with stenting in patients with coronary artery disease. The device integrates a balloon catheter and sonic pressure waves to break down calcium.

The system is an investigational device in the U.S.

Exactech Wins FDA Clearance for Computer-Assisted Shoulder Arthroplasty

Florida–based Exactech has received clearance from the FDA to market the ExactechGPS shoulder application.

The preoperative planning tool is designed to help surgeons understand their patient's anatomy prior to surgery. ExactechGPS provides visibility into the glenoid vault in real time and allows for accurate placement.

The company plans to launch the device in the U.S. this summer is planned for this quarter.

Oxitone Medical Wins FDA Clearance For Wrist-Sensor Pulse Oximetry Bracelet

Oxitone Medical has received marketing clearance from the FDA for its wrist-sensor pulse oximetry bracelet Oxitone 1000. The device measures vital signs such as SpO2 and pulse rate with the same precision as fingertip pulse oximeters.

The bracelet uses springs and dampers to isolate the unit from wrist movement and topographical variations.

Body Vision Medical Receives FDA Clearance For the LungVision Navigation System

Israel–based Body Vision Medical has received FDA clearance to market LungVision, an imaging system that enables accurate navigation during bronchoscopic procedures.

The device combines fluoroscopy with high resolution imaging and computed tomography.

Ophtec Wins CE Mark For Precizon Presbyopic

Ophtec has received a CE mark for its Precizon Presbyopic intraocular lens.

The lens uses continuous transitional zones to treat presbyopia, a condition associated with aging that reduces the ability to focus clearly on close objects.

EMED Technologies Wins Expanded Indication For Syringe Infusion System

EMED Technologies has been granted expanded indications on its FDA-cleared SCIg60 infusion system. The device administers human plasma-derived immunoglobulin biologics.

The FDA has created a new device code "PKP" to classify and regulate infusion systems for immunoglobulins.

Avacen Medical Wins CE and Health Canada Approval For Pain Treatment Device

Avacen Medical has received a CE mark and Health Canada approval for its Avacen 100.

The device infuses heat into the circulatory system to provide muscular relaxation and increases circulation to provide pain relief.

FDANEWS

Customer Service
(888) 838-5578 • +1 (703) 538-7600
customerservice@fdanews.com

Editorial: Declan Conroy
+1 (703) 538-7644
dconroy@fdanews.com

Ad Sales: Jim Desborough
+1 (703) 538-7647
jdesborough@fdanews.com

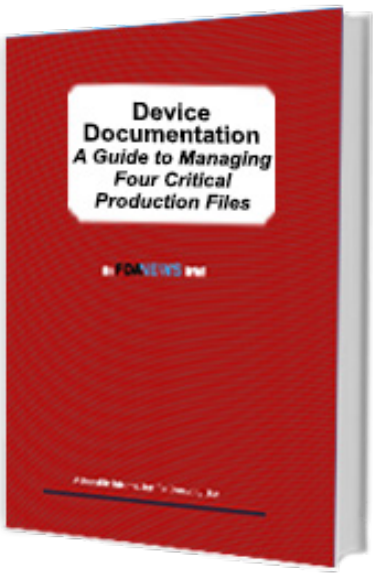
Multi-User Sales: Jeff Grizzel
+1 (703) 538-7669
jgrizzel@fdanews.com

300 N. Washington St., Suite 200 • Falls Church, VA 22046-3431 • Phone: (888) 838-5578 • +1 (703) 538-7600 • www.fdanews.com

Reporters: Cynthia Jessup, Conor Hale, Zack Budryk, Gayle Putrich

President: Cynthia Carter

FDANEWS



Device Documentation: *A Guide to Managing Four Critical Production Files*

Do you understand the four critical production files of device documentation? Device History File (DHF)… Device Master Record (DMR)… Device History Record (DHR)… Quality System Record (QSR)…

How do they differ?

How do they fit together?

These four types of files create an intricate web of documentation critical to producing quality products and complying with FDA and international regulations.

With **Device Documentation: *A Guide to Managing Four Critical Production Files*** you will learn about:

- The required elements in the Device Master Record (DMR)
- The source of the Device Master Record
- The required elements in the Device History Record (DHR)
- The linkage between the DMR and the DHR
- The relationship between the Device History File (DHF), DMR, and DHR
- The role of the Quality System Record (QSR) and ensuring you have one
- The effect of UDI on these required records
- The changes in ISO 13485:2016 related to these records

BONUS: You'll receive a checklist for developing the files to make sure you are fully compliant.

Order **Device Documentation** for a detailed guide that will help you understand each element and their relationships with each other, as well as guidance on how to develop the files.

FOUR EASY WAYS TO ORDER

1. **PHONE:** Toll free (888) 838-5578 or +1 (703) 538-7600
2. **WEB:** www.fdanews.com/53687
3. **FAX:** +1 (703) 538-7676
4. **MAIL:** FDAnews 300 N. Washington St., Suite 200 Falls Church, VA 22046-3431

☑**Yes!** Please send me ____ copy(ies) of **Device Documentation: *A Guide to Managing Four Critical Production Files*** at the price of $177 for each PDF.

Name _____

Title _____

Company _____

Address _____

City_____ State _____ Zip code _____

Country _____

Telephone _____

Fax _____

Email _____

METHOD OF PAYMENT

❑ Check enclosed (payable to FDAnews)

❑ Bill me/my company. Our P.O.# _____

❑ Charge my credit card:
❑ Visa ❑ MasterCard ❑ American Express

Credit card no. _____

Expiration date _____

Signature _____
(Signature required on credit card and bill-me orders)

Virginia customers add 6% sales tax.

17FLYR-N

FDANEWS

Implementing an 11-Step Plan for Device Software Validation and Verification, *2016 Edition*

If device software validation and verification wasn't already hard enough, now you have to comply with ISO 13485:2016.

So how does the newly revised ISO 13485 affect your software validation efforts? Where are the gaps and similarities with the FDA's GMP requirements?

If you don't have these answers — and more — your devices international approval is at risk.

This updated edition of **Implementing an 11-Step Plan for Device Software Validation and Verification** contains a new chapter outlining the software validation requirements in ISO 13485:2016, including:

- Ensuring the approach and activities for software validation or revalidation are proportionate to the risk associated with the software's use; and
- Maintaining records of actions taken as a result of the validation.

The report will help you interpret and apply all the rules and standards you must follow and show you how to set up an 11-step plan for device software validation and verification:

1. Perform risk analysis
2. Determine level of concern
3. Describe the software
4. Formulate requirements specifications
5. Develop design specifications
6. Create an architecture design chart
7. Craft a software development environment summary document
8. Document validation and verification testing
9. Perform a traceability analysis
10. Determine unresolved anomalies
11. Maintain a log of revision and release numbers

You'll also find out what the FDA accepts as an appropriate documentation model … the agency's expectation for your testing software, ERP software and more … and, when and how to use design qualification, installation qualification, operational qualification and performance qualification.

With **Implementing an 11-Step Plan for Device Software Validation and Verification, *2016 Edition***, you'll gain a clear understanding of what the FDA and international bodies are looking for NOW.

FOUR EASY WAYS TO ORDER

1. **PHONE:** Toll free (888) 838-5578 or +1 (703) 538-7600
2. **WEB:** www.fdanews.com/53520
3. **FAX:** +1 (703) 538-7676
4. **MAIL:** FDAnews 300 N. Washington St., Suite 200 Falls Church, VA 22046-3431

☑**Yes!** Please send me ____ copy(ies) of ***Implementing an 11-Step Plan for Device Software Validation and Verification*** at the price of $397 for each PDF.

Name _____

Title _____

Company _____

Address _____

City_____ State _____ Zip code _____

Country _____

Telephone _____

Fax _____

Email _____

METHOD OF PAYMENT

❑ Check enclosed (payable to FDAnews)

❑ Bill me/my company. Our P.O.# _____

❑ Charge my credit card:
❑ Visa ❑ MasterCard ❑ American Express

Credit card no. _____

Expiration date _____

Signature _____
(Signature required on credit card and bill-me orders)

Virginia customers add 6% sales tax.

17FLYR-N