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IN THIS ISSUE

Notified Bodies Warn of Future Bottlenecks In Implementing New Device Regs

The European Association for Medical Devices of Notified Bodies (Team-NB) is sounding alarms over the shortage of notified bodies to conduct audits and certify devicemakers in time to comply with the new European medical device regulations.

The association released the results of a survey of its members that gauged readiness to implement the EU's new device and IVD regulations by the deadline of May 2020.

"Many manufacturers, healthcare professional and other stakeholders fear that an insufficient number of notified bodies will be designated on time enabling them to start managing the waves of submissions for initial certification according to the new legislative framework," Team-NB said in a white paper. "There are also doubts about the capacities of already designated notified bodies under the current system."

(See **Regs**, *Page 2)*

Routine Inspections Suspended During Partial FDA Shutdown

Some of the FDA's regulatory and compliance activities — including routine inspections — were placed on hold because of the partial government shutdown that began on Dec. 22 and continued into the new year.

The agency noted that it lacked legal authority to accept user fees assessed for FY 2019 until an FY 2019 appropriation or Continuing Resolution is enacted for the FDA, so it could not accept any regulatory submissions for FY 2019 that require a fee payment and that are submitted during the lapse period.

Almost 60 percent of the FDA's workforce was kept on to handle core agency activities including high-risk medical product recalls, certain criminal and civil investigations, medical product screening and other critical public health activities.

FDA Commissioner Scott Gottlieb took to Twitter to assure the public the FDA's core public-health functions continued during

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Shutdown, *from Page 1*

the shutdown. Gottlieb documented meetings with the agency's data systems management and cybersecurity teams to ensure critical systems remain in operation.

He noted the agency continued its mail facility surveillance operations to examine packages for potential counterfeit products, entry review of all products and examination of products that may pose a high risk to public health.

"All our work is important, but only some of our work is permitted to continue during a lapse in funding," the agency said, noting that operations continued "to the extent permitted by law, such as activities necessary to address imminent threats to the safety of human life and activities funded by carryover user fee funds."

The FDA said reviews of approvals and research requests, as well as the issuing of guidance would continue, and submissions accompanied by user fees received prior to the shutdown would be processed, but said the process was "likely to be slower."

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The paper questions whether it is possible that all manufacturers and all products will be certified according to the new MDR before May 2020. The answer: "Most likely not — because the "new" notified bodies will not be able to assess and take certification decisions for all applications before May 2020!"

The main concerns identified by the notified bodies include:

- The implementation period (May 2017 to May 2020), is too short for all stakeholders, given that many details for both manufacturers and notified bodies are still under discussion;
- The lack of guidance documents to enable clear interpretation of specific requirements;
- Unharmonized interpretations of Joint Assessments of medical devices Notified Bodies by EU Member States and European Commission's experts;
- Capacity shortages for some medical device codes; and
- The workload for two legislative frameworks running in parallel from May 2020 until May 2024.

Team-NB notes some notified bodies "will be designated just a few days before the date of application in May 2020 — or even later."

The associated points out that notified bodies have to implement completely new procedures and need to hire, train and develop new resources to comply with the new regulations. Additional resources are needed because the new regulations put much more burden on notified bodies.

Most devicemakers will need to make use of the extended grace period until May 2024, Team-NB said, adding that other than makers of Class I devices, it is "absolutely necessary to have valid MDD/AIMDD certificates available after May 2020 by applying from now on for renewal of the currently available certificates."

This step will also mean an additional workload for notified bodies, which will push the timeline further back, leading to a bottleneck in the approval process, Team-NB warned.

Read the Team-NB paper here: www.fdanews.com/01-02-19-EUnotifiedbodies.pdf.

CDRH Seeks Stakeholder Input On 2019 Guidance Priorities

FDA's Center for Devices and Radiological Health called for feedback from stakeholders on its priorities for developing guidance for the year ahead.

The center has issued two lists of planned final and draft guidances for 2019 — an A-list of guidances it intends to publish and a B-list of guidance it will publish "as resources permit."

The A-list features improvements to the approvals process, software, cybersecurity and patient engagement.

CDRH noted that resource constraints and new issues may emerge over the course of the year that could prevent the agency from issuing every guidance document on the two lists and may require it issuing guidance documents not on the lists. Even so, the lists provide helpful information about priorities for the fiscal year.

The center also flagged existing guidances that it plans to revisit during the year.

A-list final guidance topics that CDRH plans to issue in fiscal 2019 include:

- Considering uncertainty in making benefit-risk determinations in device premarket approvals, de novo classification and humanitarian device exemptions;
- Unique device identification and compliance dates for Class I and unclassified devices;
- Breakthrough devices program;
- Expanding the abbreviated 510(k) program;
- Concepts and principles for a least burdensome approach;
- Requests for feedback and meetings for device submissions; and
- The special 510(k) program.

Following are the A-list draft guidance topics that CDRH plans to publish:

- Content of premarket submissions for cybersecurity of medical devices;
- Labeling recommendations for surgical staplers and staples;
- Nonbinding feedback after FDA inspections;
- Recommendations for CLIA waiver applications for IVDs;
- Recommendations for dual 510(k) and CLIA waivers;
- Computer software assurance for manufacturing, operations and quality system software;
- Patient engagement in clinical trials;
- Content of premarket submissions for software contained in medical devices;
- Lifecycle regulatory requirements for medical device servicing; and
- Accreditation schemes for device conformity assessments.

Topics for the B-list include: PMA submissions for continuous ventilators; testing considerations for implanted brain-computer interface devices for patients with paralysis or amputations; animal studies to evaluate organ preservation devices; UDI for convenience kits; and medical x-ray imaging devices conformance with IEC standards.

For the retrospective review list, the agency is seeking suggestions regarding which final guidances should be revised or withdrawn. There are roughly 20 final guidances under review.

CDRH plans to update all three lists every year as required under the Medical Device User Fee Amendments of 2017.

Read more details of the proposed guidance here: www.fdanews.com/01-02-19-FDAguidance.pdf.

Health Canada Maps Out Action Plan To Improve Device Safety, Quality

Health Canada released a three-part action plan aimed at improving how devices get on the market, strengthening monitoring and providing more information to consumers about the devices they use.

One of the first priorities is improving how devices get on the market. Proposed changes would allow healthcare professionals and researchers to file applications for authorization to conduct

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investigational tests for devices. Currently, only manufacturers are able to apply for investigational testing.

Beginning in January, Health Canada will begin moves to review evidence requirements and expand scientific expertise. In the device arena, the agency has a scientific advisory committee on digital health and on cardiovascular devices and pacemakers, and it plans to form a new advisory committee on women's health issues.

The agency expects to release draft guidance on evidence requirements for higher-risk devices in November 2019.

Beefing Up Monitoring

Beginning in February, the agency plans to implement mandatory reporting of serious medical device incidents by hospitals and to expand the Canadian Medical Devices Sentinel Network (CMDSNet).

Currently, the network covers 17 healthcare organizations, representing more than 260 hospitals and facilities across the country. The network will be further expanded to include facilities outside the hospital setting such as long-term care facilities and private clinics.

Canada's action plan comes on the heels of "The Implant Files," published by the International Consortium of Investigative Journalists, which pointed to wide disparities in the way different regions handle recalls and field safety notices. For example, pelvic mesh devices for organ prolapse repair and incontinence were halted by regulators in the U.K. and New Zealand, but continued to be sold in Canada, South Africa and other regions (*IDDM*, Dec. 10, 2018).

In June, Health Canada will publish revised regulations on reporting medical device incidents in the Canada Gazette, and it will expand its CMDSNet in June. The agency also plans to launch additional education programs in September.

The agency is exploring expanded use of real-world evidence to monitor safety and effectiveness of products used in real-world post-market settings and it expects to release draft guidance in June.

In March, the agency is adding eight inspectors and two investigational analysts to its inspectorate program and it plans to increase the number of foreign inspections from 80 to 95 by April.

It also plans on strengthening and expanding its outreach and information activities with Canada's provinces and territories.

MEDEC, Canada's national medical device association, welcomed the agency's "patient-centered approach" and the commitment to engage with all stakeholders.

The association said it supports continual improvement to processes and regulatory requirements that "will enhance patient safety and patient confidence in medical devices in Canada." MEDEC noted that Canada has "some of the most stringent medical device regulations in the world and the medical technology industry has an extremely strong track record of safety."

Read the Health Canada action plan here: www.fdanews.com/01-02-19-Canada.pdf.

Zevex Cited for Inadequate CAPA, Nonconforming Product Rework

Inadequate corrective and preventive action procedures and improper procedures for rework of nonconforming product landed devicemaker Zevex in hot water with the FDA following a Sept. 4 to Sept. 17 inspection of its Salt Lake City, Utah plant.

The firm designs and manufactures components for enteral nutrition delivery as well as surgical equipment.

FDA inspectors noted that several nonconforming products originally passed final acceptance when values did not agree with specifications, but adjustments were made nearly two weeks after the production run. "No one at your firm could provide an explanation for why this adjustment of acceptance records was performed," the 483 notes. The inspectors also found other discrepancies in acceptance procedures.

Read the Zevex Form 483 here: www.fdanews.com/12-06-18-zevexinc483.pdf.

Wound Dressing Manufacturer Falls Short on Quality Requirements

Devicemaker Winfield Laboratories was unable to produce quality control documentation for its N-Terface dressing, a Sept. 24 to Sept. 25 FDA inspection of the Richardson, Texas, facility revealed.

The material is a high-density polyethylene sheeting used as a primary dressing on newly applied skin grafts, laser skin resurfacing, partial-thickness burns, skin ulcers, chemical peels, dermabrasions and hair transplants. The company also manufactures sterile syringe seals and container seals.

Winfield Labs lacked design control procedures and design history files to demonstrate that its N-Terface material was developed according to design control requirements, the six-item Form 483 said.

The FDA inspector said the devicemaker had not established a procedure to control all documents as required by quality system requirements. Numerous quality procedures had not been reviewed and approved by management, including quality auditing procedures, medical device reporting policies and procedures, corrective and preventive actions and complaint handling procedures, purchasing controls and supplier selection procedures.

Winfield Labs had not conducted any quality audits. When the FDA inspector requested records to indicate that management had reviewed quality system documents, the president indicated that "informal meetings were held, and the meeting agenda and schedules were not documented," the 483 said. The company also failed to conduct on-site audits of its suppliers.

Read the Winfield Laboratories Form 483 here: www.fdanews.com/01-03-19-winfieldlabsinc483.pdf.

Hemodialysis Solution Maker Dinged for Recurring Quality Issues

A 12-item 483 documents a litany of quality system failures the FDA found at Diasol East of Watertown, Tenn., during an Aug. 7 to Aug. 22 inspection.

The quality failures included inadequate process control procedures to ensure conformance to specifications, inadequate testing and validation procedures, inadequate finished device acceptance activities, and failure to document rework and reevaluation activities.

Nonconforming batches with out-of-specification electrolyte concentration were stored without a valid justification. The 483 documents repeat observations for acceptance procedures and testing procedures for the firm's Diasol liquid acid concentrate.

For example, the inspector found at least five examples of failure to document the final disposition of nonconforming product. The firm had received a July 12, 2017, warning letter from the agency for missing product nonconformity reports and failure to investigate nonconforming products.

Many of the findings were repeat observations, flagging document control procedures, labeling activities, and measuring and test equipment not suitable for the intended purpose.

Read the Diasol East Form 483 here: www.fdanews.com/01-02-19-diasolinc483.pdf.

FDA Scolds New Jersey Devicemaker For CAPA Handling

The FDA hit Monmouth Junction, New Jersey device manufacturer Replication Medical with a Form 483 following an inspection that revealed issues with the firm's documentation of corrective and preventive action activities and device history records.

The investigator, who inspected the facility between July 10 and August 22, 2018, found that the firm didn't adequately document its CAPA activities and results. For example, the firm didn't properly follow a complaint handling procedure and failed to routinely assess complaint trends, the agency found.

Additionally, a CAPA initiated in 2016 over an improperly installed water filter — which led to a broken water hose that flooded the facility — did not include a water sample test for total organic content despite the firm's action plan requiring one.

Another CAPA was closed in February 2018 before a final quality control check could be conducted prior to packaging the firm's one-piece posterior spinal implant product, GelFix, in foil. The CAPA was initiated in April 2017 when the firm discovered that three of its size 10 units had suture loops that were too small.

Some device history records showed that the firm exceeded drying times for GelFix implants by leaving them in the drying oven too long. Additionally, device history records for three lots of GelFix did not include documentation of labeling that the products were "For Export Only."

The firm also changed the instructions for one of its devices but did not receive approval before establishing it. Instructions referred to as "NeuFx Lumbar Surgical Procedure" were updated to note that "only one or two turns is necessary to secure the holder." However, the firm didn't send the change through its document change request process as required.

Read the Replication Medical 483 here: www.fdanews.com/01-03-19-replicationmedicalinc483.pdf. — James Miessler

Classifying Complaints

Establishing a classification system for complaints helps organize your analysis. Quality expert Dan O'Leary of Ombu Enterprises recommends classifying complaints by type of failure. The real issue, he says, is that "a complaint alleges a deficiency." The customer is complaining the device is deficient in meeting one or more essential design output areas, such as: identity; quality; durability; reliability; safety; effectiveness; and performance.

If you are going to use this classification method, O'Leary says, make sure your complaint SOPs clearly define each type and staff are trained to make decisions based on those definitions.

Devicemakers also could classify complaints according to source — written, electronic or oral message — O'Leary says, "but today this is not going to give you a lot of valuable information, because almost everything's going to come in electronically." This kind of classification can help manufacturers gain a better understanding of customer communication, however.

Ultimately, the devicemaker must make a key decision about each complaint. Does the complaint allege a serious incident — one that might have led or might lead to a death, a serious deterioration of someone's state of health or a threat to public health?

If the answer is yes, the complaint must be reported to the FDA or other regulator based on their regulations.

If the complaint is determined to be "nonserious," it does not need to be reported but it must be recorded, investigated and classified for analysis purposes.

It's the way you use the results of this analysis that regulators emphasize. They want to know that you are tracking and identifying any significant increase in frequency or severity or other outlier uncovered in complaints and that you are using that information to make continual improvements.

Excerpted from the FDAnews management report: *Complaint Management for Devicemakers — From Receiving and Investigating to Analyzing Trends*.

FDA Lowers Risk Classification Of Electroconvulsive Therapy Devices

The FDA has reclassified electroconvulsive therapy (ECT) devices that treat catatonia or severe major depressive episodes or bipolar disorder as moderate risk devices with special controls.

The agency moved the devices from Class III (high risk) to Class II (moderate risk) with special controls, noting that "sufficient information exists to establish special controls that mitigate known risks and provide a reasonable assurance of safety and effectiveness for these two uses of ECT devices."

ECT manufacturers must file a premarket approval application for all uses that haven't been reclassified to Class II, such as bipolar manic states and schizoaffective disorder.

The FDA previously published a proposed order to reclassify the devices in December 2015 and received over 3,400 comments from industry, professional organizations, trade groups and individual consumers, many of which generally supported the reclassification.

Other comments said the proposed reclassification didn't go far enough and called for an expansion to include other indications, such as autism, Parkinson's disease, schizophrenia, mania and delirium, among others.

The FDA said it "concluded that there was insufficient scientific evidence to support reclassification" for the other indications discussed in public comments.

APPROVALS

Cepheid's Hepatitis B Viral Load Test Gains CE Mark

Cepheid received the CE Mark for a rapid molecular assay, the Xpert HBV Viral Load Test, which measures viral loads of Hepatitis B in patients.

Using Cepheid's GeneXpert system, the test measures a patient's HBV DNA levels via plasma or serum samples and produces quantitative results in less than an hour.

The test can be used for predicting the likely development of a disease and to measure a patient's response to antiviral treatment.

FDA Clears Becton Dickinson's Enteric Viral Panel

The FDA granted Becton Dickinson 510(k) clearance for its molecular diagnostic test, the BD MAX enteric viral panel.

The test detects enteric viral pathogens that cause viral gastroenteritis and can distinguish between them.

The BD MAX can perform targeted detection for norovirus, rotavirus, adenovirus, human astrovirus and sapovirus.

The enteric panels run on the BD MAX molecular system and can provide results in less than 3.5 hours.

CathWorks' Fractional Flow Reserve System Cleared

The FDA cleared CathWorks' non-invasive FFRangio fractional flow reserve system for measuring blood pressure and flow through the coronary artery.

Fractional flow reserve is used during coronary catheterization to determine the likelihood that an abnormal narrowing of a blood vessel will hinder oxygen delivery to the patient's heart.

The device is used during coronary angiography procedures to help physicians make clinical decisions without the need for another intervention.

Quidel Gains CE Mark for Vitamin D Assay

Quidel has earned the CE Mark for its point-of-care Sofia Quantitative Vitamin D Assay for use with its Sofia fluorescent immunoassay analyzer.

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Approvals, *from Page 7*

The assay analyzes serum samples to determine the total amount of vitamin D in the patient's body.

Vitamin D deficiency has been linked to various health issues including cancer, cardiovascular diseases, bone disease and hypertension.

European Commission Approves AstraZeneca's COPD Treatment

The European Commission has approved AstraZeneca's Bevespi Aerosphere, a long-term chronic obstructive pulmonary disease (COPD) treatment that is administered via a pressurized metered-dose inhaler.

The twice daily, fixed-dose device combines glycopyrronium and formoterol fumarate.

The treatment is not indicated for the relief of acute bronchospasm or for treating asthma.

Hycor Biomed Cleared in U.S. For Allergy Testing System

The FDA granted clearance for Hycor Biomedical's Noveos allergy testing system for use in allergy testing labs.

The device can handle up to 700 tests in one run. The system allows a significant reduction in sample sizes, blood-based interferences and allergen lot variabilities.

FDA Grants PMA for Cardiva's Vascular Closure Device

Cardiva Medical has received FDA premarket approval for its Vascade MVP venous vascular closure device, for stopping patient bleeding following electrophysiology procedures.

The device is made up of a bioabsorbable collagen patch and a collapsible mesh disc. The disc is used to temporarily stop bleeding from a vessel, after which the patch is inserted and serves as a seal.

FDA Clears Hemodynamic Monitoring Device

The FDA granted 510(k) clearance to Retia Medical's Argos hemodynamic monitor that measures an adult patient's cardiac output in the operating room and ICUs.

The device uses signal processing and algorithms to create a model of the patient's circulation, giving physicians information that helps them track oxygen delivery and fluid status in high-risk surgeries.

Human Milk Analyzer Cleared for Marketing

The FDA cleared the Miris Human Milk Analyzer, a diagnostic test that measures the amount of nutrients in breast milk, for marketing.

The device determines the concentration of carbohydrates, fat, protein, total solids and energy.

The analyzer is intended to help parents and healthcare providers meet the nutritional needs of infants, especially those who require additional nutrients because of health conditions or preterm birth.

Japan Approves Coronary Orbital Atherectomy Device

Japan's Ministry of Health, Labor and Welfare approved Cardiovascular Systems' Diamondback 360, a coronary orbital system for removing sclerosis from blood vessels. The device facilitates stent delivery in coronary artery disease patients who are eligible to receive stenting or coronary angioplasties.

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FDANEWS

Complaint Management for Devicemakers: *From Receiving and Investigating to Analyzing Trends*

Complaint management is essential to a functioning quality management system.

Understanding the FDA's Quality System Regulation isn't enough — you must also master ISO 13485:2016 and the new EU MDR. They all require devicemakers to conduct trending in some form or another. But none of them tell you HOW.

This new edition of the best-selling **Medical Device Complaint Management** fills in that gap for you.

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- Receiving, documenting and investigating complaints
- Determining when complaints are reportable
- Using complaints to update risk management data …

… the new report teaches you how to analyze trends in your complaint files to spot opportunities for product and program improvement.

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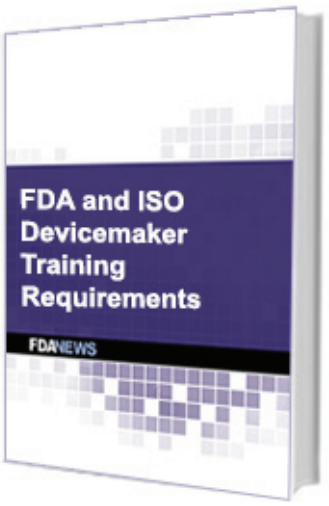

FDA and ISO Devicemaker Training Requirements

Device manufacture is a complicated business, but few areas are more rulebound than QMS. Many a devicemaker has come up short trying to stay abreast of the FDA's QSR, ISO 13485:2016, and other ISOs while trying to comply with competence, training and awareness rules.

It takes more than teaching simple skills to achieve the state of job readiness and performance required of devicemakers' workforces. Regulators agree that a comprehensive training program should consider employee education, experience, background and skills. What they don't agree on is what those concepts mean and how to incorporate them into training.

FDA and ISO Devicemaker Training Requirements breaks down training requirements in both the FDA's QSR and international standards ISO 13485, 9001 and 10018 — among others — shows where they overlap and where they differ and provides a plan for developing a training program that fills in all the gaps. You will learn:

- The four elements of competency
- Definitions of key terms and requirements
- The concept of a "designated individual" and the qualifications for the role
- The importance of a well-written job description
- The difference between a "job" and a "role"
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