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IN THIS ISSUE

FDA May Seek New Authority Under Device Safety Action Plan

The FDA released a new action plan aimed at assuring the safety and effectiveness of medical devices while addressing unmet patient needs.

FDA Commissioner Scott Gottlieb said the Medical Device Safety Action Plan will use existing tools in new ways and also identify areas where the agency may need to seek additional authority.

Last year the FDA approved a record number of devices, leading to both greater benefits and greater risks to patients, Gottlieb said.

One proposed element in the five-prong plan would integrate CDRH's premarket and postmarket offices to use a total product life cycle (TPLC) approach.

The center has historically been organized according to the stages of a product's life cycle, allowing staff to become specialized by function, but not always promoting the communication

(See **Plan**, *Page 2)*

FDA Releases Guidance On Quality Considerations for Inhalers

The FDA published draft guidance on metered dose and dry powder inhalers highlighting considerations for critical quality attributes.

Sponsors should create a desired quality target product profile (QTPP) before development begins, the agency said, including elements such as strength, purity and stability, aerodynamic performance and the proposed dosage form and the delivery system.

Early in the development process, applicants also should develop a list of potential critical quality attributes (CQAs) within appropriate limits, with each CQA relating to one or more elements of the QTPP. The list can be changed as the development progresses.

(See **Guidance**, *Page 4)*

Plan, *from Page 1*

and collaboration that is necessary for continuously evolving innovation of medical devices, the agency said.

CDRH is evaluating a potential restructuring of one large office into seven smaller device-specific offices that would each be responsible for premarket review, postmarket surveillance, manufacturing and device quality, and enforcement. The new structure would include a separate office dedicated to clinical evidence and analysis.

Gottlieb said that the reorganization of CDRH's premarket and postmarket offices into a TPLC structure would allow experts to share both pre- and postmarket information,, improving decision making and allowing timely implementation of corrections discovered as postmarket data from real world clinical settings is collected and analyzed.

The agency also plans to establish a "robust medical device patient safety net" using the National Evaluation System for health Technology (NEST) to link data from different electronic health information sources, including device registries, electronic health records, medical billing claims and patient-generated data.

The plan also establishes the Women's Health Technologies Strategically Coordinated Registry Network (CRN) to address data gaps in the field of women's health, improving the quality and efficiency of real world evidence collection in clinical areas that are unique to women.

In another plan element, the agency will consider regulatory options to streamline and modernize "timely implementation of postmarket mitigations," exploring whether the agency has the authority to issue "umbrella regulations" to identify devices that may require additional training or user education beyond the physician labeling that is currently required.

In his statement about the plan, Gottlieb said the FDA may also "consider invoking restricted device authority" on a case-by-case basis to increase patient protection for the highest risk devices. This would allow the agency to impose requirements on specific high-risk devices while still allowing access to the devices to those patients who could benefit from such access.

Another prong of the plan would spur innovation towards safer medical devices by providing regulatory incentives and scientific expertise that help drive greater competition. The agency is considering developing a program similar to the Breakthrough Device Program, which gives patients who need it access to innovative new devices. The new program would support the development of safer devices that do not meet Breakthrough Program criteria but are intended to be safer than current technologies on the market.

"Safety and innovation should go hand in hand," said Gottlieb, noting that the plan will encourage manufacturers to make even modest changes to their devices when such adaptions lead to a reduction in risk for patients.

A separate plan element would improve device cybersecurity by seeking additional authority to require firms to build the capability to update and patch device security into a product's initial design. The FDA also intends to develop a CyberMed Safety (Expert) Analysis Board as a public-private partnership to complement existing cyber coordination and response mechanisms.

Read the full action plan here: www.fdanews.com/04-19-18-MDSafetyActionPlan.pdf.
— Donna Scaramastra Gorman

Health Canada Eases MDSAP Deadline, Beefs Up Post-Market Surveillance

Health Canada is sticking to its compliance deadline of Jan. 1, 2019, for devicemakers selling products in Canada to transition to the Medical Device Single Audit Program, but it is making adjustments to help manufacturers comply.

The regulator said it would not take enforcement action if manufacturers have undergone a MDSAP audit by Dec. 31, 2018. The modifications to the transition process were made due to industry comments around scheduling MDSAP audits and the requirement to have a MDSAP certificate by the Dec. 31 deadline.

The agency said it recognizes that some manufacturers are facing challenges in scheduling MDSAP audits in 2018, and may not be issued their MDSAP certificate by Dec. 31, 2018 as there is often a delay between the timing of the audit and the issuance of the certificate.

Device manufacturers that underwent an initial recertification audit to ISO 13485 under CMDCAS will be allowed to transition into the MDSAP during the surveillance audit process, which will allow manufacturers to maintain their existing certification cycles.

Although manufacturers that transition to MDSAP during a surveillance audit won't receive a MDSAP certificate in 2018, they will be able to continue selling their devices until they receive the certificates.

The regulator clarified that devicemakers transitioning to MDSAP during a surveillance audit will need to show:

- That they have undergone an initial or recertification audit to ISO 13485 under CMDCAS on or after Jan. 1, 2016;
- They hold a valid ISO 13485 certificate issued under CMDCAS that has a validity period to at least Dec. 31, 2018;
- As of Jan. 1, 2019 they continue to hold a valid ISO 13485 certificate issued by a MDSAP Auditing Organization; and
- They have undergone a MDSAP audit or have made arrangements to undergo a MDSAP audit.

Health Canada is working with auditing organizations and is monitoring the transition to mitigate the impact of potential auditor resource shortages. It said most AOs are not seeing difficulty in meeting the MDSAP transition deadline. The biggest challenge is getting manufacturers to agree to schedule their MDSAP audits soon enough to complete the process before the transition deadline (*IDDM*, Feb. 23).

Increased Post-Market Surveillance

Health Canada is planning on ramping up its post-market surveillance program by providing the Minister of Health with additional authority to request analytical reports from manufacturers when there is "suspicion of a safety concern with a medical device and set out conditions under which the authority would be used."

The authority would enable the health minister to request the information that was used to create the analytical issue report and "any other information in the manufacturer's possession deemed necessary to assess the safety of a medical device," Health Canada said.

Other proposed regulations would provide the authority to compel manufacturers to conduct reassessments and to require tests and studies.

More information will be forthcoming, and guidance will be made available for industry to comment on the proposal.

In addition, Health Canada is establishing a new division within the Medical Devices Bureau to allow for more targeted reviews of digital health technologies to better adapt to rapidly changing technologies and respond to these faster innovation cycles.

The new Digital Health Review Division will focus on wireless medical devices, mobile medical apps, telemedicine, software as a medical device, artificial intelligence, cybersecurity, and medical device interoperability.

FDA Guidance Accepts IEC Standards For Ultrasonic Diathermy Devices

The FDA released final guidance that provides policy clarification for ultrasonic diathermy devices as well as information devicemakers should submit in their premarket notification submissions.

Ultrasonic therapy devices are considered both medical devices and electronic products and need to comply with radiation safety performance standards in 21 CFR 1010 and 1050.10 as well as certain International Eletrotechnical Commission (IEC) standards.

The devices produce high-frequency sound waves — transmitted through a wand applied to the skin — that travel deep into tissue to create therapeutic heat to treat pain, muscle spasms and joint contractures.

The FDA said that complying with both FDA and IEC standards can cause manufacturers to duplicate their efforts, and it said that conformance with the IEC standards would provide the same level of protection as the FDA's performance standards.

Although conformance with IEC standards would satisfy FDA performance standards, manufacturers must still comply with other FDA requirements including submitting 510(k) applications using IEC data. The guidance applies only to ultrasonic diathermy products regulated under 21 CFR 890.5300(a), product codes IMU and PFW, which are Class II devices.

Manufacturers must provide IEC certifications for their products in their 510(k) submissions. They must furnish certifications to dealers or distributors that the product conforms to applicable standards, and the certification must also be provided on a label or tag permanently affixed to the product.

The FDA said the tag should read: "Complies with 21 CFR Subchapter J, except for conformance with IEC 60601-2-5 and IEC 61689 instead of the performance standards in 21 CFR 1050.10. See for more information FDA's guidance 'Policy Clarification and Premarket Notification [510(k)] Submissions for Ultrasonic Diathermy Devices,' dated April 16, 2018."

The guidance provides further information to be included in a 510(k) submission, including device descriptions, predicate device comparison information, software performance test data, biocompatibility information for patient-contacting materials, electrical safety and electromagnetic compatibility, wireless technology standards, labeling, and cleaning and reprocessing.

The agency said it received no comments on the draft guidance, which was released on Aug. 31, 2017.

Read the final guidance here: www.fdanews.com/04-18-18-Diathermyguidance.pdf.

Guidance, *from Page 1*

Container closure systems, including device constituent parts, should also be considered for CQAs for the combination products. For example, an MDI's secondary packaging — such as a foil pouch — can provide additional protection from humidity when needed, and its material properties should be considered when secondary packaging is used.

For dry powder inhalers, potential product CQAs normally include assay, impurities and degradants, the delivered dose, APSD, volatile/semi-volatile leachables content, foreign particulate matter, moisture content, microbial load and device part characteristics such as specific resistance to air flow.

Read the draft guidance here: www.fdanews.com/04-18-18-MDIDPI.pdf. — James Miessler

PEOPLE ON THE MOVE

Centogene named **Dirk Ehlers** as chief operating officer and president of its diagnostics division. Ehlers has nearly three decades of management experience and most recently served as senior vice president and president of the surgical solutions division at Hill-Rom Holdings. Prior to that role, he served as CEO of Eppendorf and in management positions at Roche, Fresenius Kabi, Olympus Optical, and Evotec.

IMDRF Roundup: Regulatory Updates From Russia, Brazil and Asia

The International Medical Device Regulators Forum released updates on regulatory works in progress in member countries following its March 20-22 IMDRF meeting in Shanghai.

Russia reported that it established a new medical device quality management system that was developed for the Eurasian Economic Union, which includes Armenia, Belarus, Kazakhstan, Kyrgyzstan and Russia. The main provisions require QMS clearance before pre-market approval for sterile and higher-risk devices — and manufacturers will be inspected every three years.

Brazil granted Anvisa new authority to conduct GMP inspections of device manufacturing facilities outside the country. The risk-based inspections will depend on the complexity of the manufacturing process, the potential health risk and the compliance history of the manufacturer.

Audit reports issued within the framework of the Medical Device Single Audit Program (MDSAP) will be used to assess GMP compliance and to grant GMP certificates.

Anvisa has recognized 13 auditing organizations and Brazil has granted 63 GMP certificates using MDSAP audit reports to date.

Brazil also introduced a public consultation on a proposal for unique device identification codes to be included on patient implant cards for cardiovascular stents, and hip and knee implants.

Japan Targets Real-World Data

Japan's Pharmaceuticals and Medical Devices Agency is establishing a Regulatory Science Center to collect real-world data to better inform the quality of device reviews and post-market safety measures.

Japan reported that the first medical device was approved using its new Sakigake priority review pathway in December 2017. The approved device was a titanium bridge for adduction-type spasmodic dysphonia. The device was approved in six months.

Korea's Ministry of Food and Drug Safety is implementing a Special Act for Innovative Devices that will include 3D-printed devices, medical devices that use artificial intelligence and big data, genetic testing devices, and intelligent robots, among other innovative products.

The act's main features include an expedited review process, a customized safety management system, technical support for clinical trials and capacity building.

Korea has also introduced an IVD Act to address the unique characteristics of IVDs. For example, it provides for a simultaneous review system for companion diagnostics and drugs. It establishes a clinical laboratory accreditation program and approval system for IVDs that allows for advanced genetic testing following accreditation. The approval system is simplified for IVDs by combining IVD reagents, equipment and software as one system for approval.

In December, Korea also introduced new guidelines on 3D printed medical devices.

Australia Reforms

Australia also updated the IMDRF management committee on its regulatory reforms. The country recently introduced an expedited review process for novel devices, and it is developing guidance for using data from comparable overseas regulators for approval of medical devices in Australia.

As part of that process, Australia will designate conformity assessment bodies in Australia. Previously, the country relied on EU notified bodies.

Singapore is implementing a system similar to Australia's whereby marketing authorization from certain reference regulatory agencies will suffice for marketing authorization in Singapore. The reference regulators are Australia's TGA, the EMA, Health Canada, Japan's PMDA and the U.S. FDA.

The city-state is implementing legislation covering telehealth products and regulatory requirements for stand-alone software and mobile applications. It expects to release guidance in 2018 covering essential principles for safety and performance of medical devices,

(See **IMDRF***, Page 6)*

SynCardia Systems Nailed For MDR Deficiencies

The FDA issued a warning letter to SynCardia Systems over issues regarding medical device reporting at its Tucson, Arizona facility.

The inspection, which was conducted in August, found that the firm failed to report information suggesting a medical device it produced, the Temporary Total Artificial Heart system, possibly contributed to the death of a patient.

The agency noted a post-approval study of the device conducted by the firm, which described a male patient who died a month after being implanted with the device and whose cause of death was listed as "device malfunction."

The firm did not submit an MDR regarding the death, claiming it relies on its customers to provide patient death reports associated with its devices, which the agency found to be unacceptable.

In addition, the agency could find no evidence that the firm's MDR procedures were implemented. The facility's Electronic Medical Device Reporting Procedure had no effective or release date, and did not identify or evaluate adverse events occurring without customer complaints.

Read the SynCardia Systems warning letter here: www.fdanews.com/04-17-18-SynCardia.pdf.
— James Miessler

IMDRF, *from Page 5*

labeling for devices, device registration and change notification.

China reported that it is improving the coding requirements of medical devices, and the CFDA released a consultation on rules for unique device identifiers for public comment.

CFDA released guidances that cover system software and network guidelines for medical devices. It is currently developing guidance on security technology reviews for medical devices, technology reviews of mobile medical devices and technology reviews of medical device software.

Bio-Thesiometer USA Flagged for Complaint Handling, MDR Procedures

A Cleveland, Ohio medical device manufacturer drew a Form 483 after the FDA's January inspection found the firm's procedures were inadequate.

The investigator observed that the firm's procedures for receiving, reviewing and evaluating complaints were not fully developed.

The firm's complaint forms did not document an assessment of the MDR, the contact information of the complainant, the firm's reply to the complainant, the corrective action taken or whether an investigation is needed.

In addition, the firm lacked written procedures for evaluating and submitting MDRs.

Read the Bio-Thesiometer USA Form 483 here: www.fdanews.com/04-19-18-biothesiometerusa483.pdf.

Senators Seek Lower Prices For Combination Naloxone Products

Sixteen Democratic and independent senators wrote to HHS Secretary Alex Azar urging him to negotiate lower prices for the opioid overdose reversal drug naloxone — including for combination drug-device products.

The price of the drug has increased significantly over the course of the epidemic despite being approved by the FDA nearly 50 years ago, the senators said.

The cost of the hand-held auto-injector form of the drug, Evzio, has increased from $690 for a two-pack in 2014 to $4,000 for a two-pack, according to Michigan senators Debbie Stabenow and Gary Peters. The increases are at odds with recommendations by the United States Surgeon General that more Americans keep naloxone delivery devices on hand, the letter states.

"We urge HHS to immediately negotiate a lower price for easy to administer naloxone combination products," the letter said. "In addition, we ask you to ensure affordable coverage for individuals with health insurance, including Medicare, Medicaid, and individual and employer sponsored plans."

The Commission on Combating Drug Addiction and the Opioid Crisis "recommended empowering the HHS Secretary to negotiate reduced pricing, and in October 2017 19 Senators wrote in support of this policy. To date, no such action has been taken by HHS," the letter states. — Zack Budryk

Abbott Issues Firmware Update For Implantable Cardiac Devices

Abbott released a firmware update for certain high-voltage implantable cardiac devices that strengthens their security and adds a vibrating battery performance monitor.

The update for implantable cardioverter defibrillators and cardiac resynchronization therapy defibrillators includes cybersecurity enhancements to help protect against unauthorized device access.

The upgrade also introduces a device-based battery performance feature to monitor the battery for abnormal behavior and vibrate to alert the patient if any issues are detected.

The company is working with regulatory authorities worldwide to implement the new upgrade, which will be available in the next several weeks.

APPROVALS

RevMedx Receives CE Mark For Injectable Hemostatic Device

RevMedx gained CE Mark certification for its XStat, an injectable device that can achieve hemostasis in seconds.

The device is used to stop bleeding in patients, stabilizing injuries and giving them time to reach an emergency facility.

The XStat uses a syringe-like applicator to inject a group of small, expanding sponges into a wound that swell and exert hemostatic pressure to stop bleeding.

Fischer Medical's Cardiac Simulator Gains Clearance

Fischer Medical's Bloom2 cardiac electrophysiology stimulator received 510(k) clearance from the FDA.

The device is modeled after the company's original Bloom device but features an new user interface that does not use dropdown menus.

The Bloom2 is used in electrophysiology procedures to treat and diagnose cardiac rhythm disorders. It is designed to have the feel of the original Bloom stimulator introduced in the 1970s.

Tactile Systems Launches Flexitouch Plus

Tactile Systems Technology's Flexitouch plus, used for treating lymphedema, is now commercially available in the United States after receiving 510(k) approval from the FDA.

The device features the ability to create and save preset therapy programs and it can treat both legs at once for faster bilateral therapy.

(See **Approvals***, Page 8)*

Approvals, *from Page 7*

Medtronic's Laser Ablation System Gains CE Mark

Medtronic launched its Visualase laser ablation system for use in neurosurgery procedures in the European market after earning a CE Mark.

The device, guided by MRI images, delivers laser energy to a small targeted area using an applicator to destroy unwanted soft tissue as light is sent through the applicator.

The system earned FDA clearance in 2007 for necrotizing and coagulating small areas of soft tissue.

Innovus' Glucose Monitoring Kit Gets FDA Clearance

Innovus Pharmaceuticals received 510(k) clearance from the FDA for its GlucoGorx glucose monitoring kit for use in managing diabetes.

The kit can provide glucose level test results within four seconds, according to the company.

The test kit includes a glucose meter, lancet device and test strips and is eligible to enter reimbursement and government supply programs.

Innovus plans to launch the test kit later this year.

Bacteria-Resistant Urinary Catheter Approved for Use in Europe

A urinary catheter coated with bacteria-resistant material received a CE mark for use in European hospitals and will be trialed in six hospitals in the U.K.

The trial will help determine whether the material can significantly reduce infection rates and lower costs for patients requiring a catheter.

The team that discovered the materials said they are getting significant interest from companies who manufacture other medical devices.

Olerup QTYPE Receives CE Mark

Brisbane, California-based molecular diagnostics company CareDx received a CE mark for its Olerup QTYPE Human Leukocyte Antigen (HLA) typing diagnostic.

The test is used by transplant laboratories for real time HLA typing of donors and recipients of organ transplants.

Cancer Genetics Gets 510(k) Clearance for Tissue of Origin Test

Cancer Genetics received FDA clearance for its tissue of origin test after making modifications to the test reagents and software.

The microarray-based gene expression test evaluates the genomic information of tumors to identify their origin.

The test covers 15 of the most common types of tumors, including thyroid, breast, non-small cell lung, pancreas, kidney, bladder and liver cancer.

FDA Clears Roche's Chlamydia And Gonorrhea Detection Tests

The FDA granted Roche 510(k) clearance for its cobas CT/NG assay for Chlamydia trachomatis and Neisseria gonorrhea for its 6800/8800 systems.

The tests identify the DNA of the sexually transmitted pathogens, so patients can be either symptomatic or asymptomatic.

The assays can be used on urinary samples, vaginal swabs, or endocervical and cervical swab specimens.

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FDANEWS

CDRH Reorganized: *New Strategies for Devicemakers*

Device regulation is about to change in ways large and small, as the CDRH moves toward a total reorganization.

CDRH's reorganization plan — to be carried out over the next two years — aims to replace current siloes of responsibility with a team approach that follows a device from development to application to premarket planning and ultimately to postmarket surveillance, with the same people working together at each stage.

CDRH Reorganized lays out all of the moving pieces and lets you know what to expect, how to take advantage of new opportunities and how to influence the direction of the new system. And you'll hear it from one of the people most qualified to interpret the changes, former CDRH Associate Director of Policy Paul Gadiock.

Gadiock recommends devicemakers get in on the ground floor of this reorganization. "Disruption can be unsettling," he says, "but if you're attentive, it also presents opportunity for new ideas because there's less inertia standing in your way."

You will learn:

- The planned structure of CDRH's regulatory and clinical evidence offices
- The most effective strategies for communicating with the FDA post-reorganization
- How the center's new focus on total product life cycle will drive premarket and postmarket data collection
- How the new CDRH Digital Health unit will help streamline the review process for digital health devices
- And More…

Order your copy of **CDRH Reorganized: *New Strategies for Devicemakers*** and learn how to deal with the new CDRH structure at each stage of your device's life cycle.

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Regenerative Medicine: *Steps to Accelerate Development*

With the 21st Century Cures Act, attention is being focused on the use of human cells and tissue to treat serious and underserved conditions.

The FDA created a new regulatory paradigm in November 2017 when it issued four guidances — 2 final and 2 draft — aimed at explaining, streamlining and accelerating development of regenerative therapies.

Key among these developments is the creation of a new Regenerative Medicine Advanced Therapy (RMAT) designation that offers applicants an abbreviated pathway to approval, working closely with the FDA throughout the process.

Regenerative Medicine outlines the RMAT pathway and breaks down requirements regenerative medicine developers must meet to qualify. The FDA granted RMAT designation to 12 organizations in 2017 — the first year of the program. Now is the time to get in the mix, work with the FDA to develop the program and improve your chance of being one of the next RMAT designees.

You will learn:

- Key definitions the FDA uses in evaluating regenerative medicine applications
- Requirements to be eligible for RMAT designation
- How to apply for RMAT designation
- How the final versions of the Same Surgical Procedure and Minimal Manipulation guidances differ from their drafts

Order your copy of **Regenerative Medicine: *Steps to Accelerate Development*** and learn what it takes to get in on the ground floor of the new approval pathway and use it to accelerate your road to market.

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