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IN THIS ISSUE

FDA Moves to Improve Device Safety Through Competition Around Safer Design

FDA Commissioner Scott Gottlieb offered more perspective on new initiatives the agency is undertaking to improve medical device safety in remarks at the FDLI annual conference in Washington, D.C.

The agency intends to focus more of its policies on supporting developers that pursue safer devices, he said.

As part of its new Medical Device Safety Action Plan the agency raised the possibility of providing an approval path for safer devices that don't meet its Breakthrough Program criteria but are intended to be safer than current technologies on the market.

Under the new program, "we'd provide greater interactions with developers and grant expedited review to their products where the key advantage is their enhanced safety over existing devices," he said.

"We also want to make it easier for medical device manufacturers to make comparative safety claims about their products."

(See **Safety**, *Page 2)*

TGA Overhauls Advisory Committee Confidentiality, Conflicts of Interest Guidance

Australia's Therapeutic Goods Administration revised its guidelines for confidentiality obligations and conflicts of interest for members of advisory committees — including the Advisory Committee for Medical Devices — overhauling the guidance with major content and structural changes.

Committee members must first sign a "deed of undertaking" that declares they have no possible conflicts or interests that may give rise to one, other than those declared in a member's annual declaration of interests form. The deed also declares that the member must not use or share confidential information with anyone outside the committee without prior approval.

(See **TGA**, *Page 2)*

Hemospray Wins De Novo Marketing Clearance

The FDA granted Wilson-Cook Medical marketing clearance for its Hemospray device used to control bleeding in the gastrointestinal tract.

The agency reviewed the device through the De Novo premarket review pathway for low to moderate risk devices.

The device is an aerosolized spray that delivers a mineral blend to the bleeding site. It is used during an endoscopic procedure and can cover large areas such as large ulcers or tumors.

The FDA reviewed data from clinical studies consisting of 228 patients with upper and lower GI bleeding, supplemented with real world evidence from medical literature. The device stopped GI bleeding in 95 percent of patients within five minutes.

Safety, *from Page 1*

The new program would aim to encourage competition around designing devices that offer improved safety measures along with the same benefits as currently marketed products.

The agency is also looking at regulatory options that will require companies to implement appropriate post-market mitigation steps more efficiently, such as through updated labeling or required user training.

Gottlieb said the agency is also applying a total product life cycle approach to medical device regulation that will attempt to more closely integrate pre- and post-market review functions and more closely align the cross-disciplinary expertise of its review staff into "more integrated, cohesive and collaborative review teams."

Read the full Medical Device Safety Action Plan here: www.fdanews.com/04-19-18-MDSafetyActionPlan.pdf. — James Miessler

TGA, *from Page 1*

Committee members should declare both financial and non-financial interests, the TGA advises. Direct financial interests include, but are not limited to, shares, consultancies, contracts, sponsorships, grants, board memberships, partnerships, trusts and patent ownership.

Indirect financial interests include paid conference expenses, research or educational benefit grants, holding a paid retainer for professional advice, hospitality from a company in the therapeutic goods industry, participation as a researcher or unpaid expert advisor and clinical trial participation, among others.

Non-financial interests include strong personal, philosophical or religious beliefs, a close friend in a pharmaceutical medicine industry or membership in a sporting club or society.

In deciding whether to disclose an interest, the TGA recommends that the member take into account its subject matter, nature, currency and extent, the nature of the issues that the committee comments on and whether the member will be commenting specifically on the matter.

Committee members should also declare immediate interests of their family — typically their spouse or partner and dependent children. A spouse who is an employee of a pharmaceutical company can be regarded as an indirect financial interest, for example, and an interest that can be perceived by a "reasonable observer" as impacting a member's ability to be objective and impartial requires disclosure.

The guidance also instructs members not to communicate with the public and media regarding committee business unless authorized to do so. Members may speak on behalf of their organizations or in a professional capacity as long as it does not seem to be on behalf of the TGA, Department of Health or committee.

Read the revised guidance here: www.fdanews.com/05-09-18-TGA.pdf. — James Miessler

Canada Makes Additional Adjustments to MDSAP Program

Health Canada is making further reductions in audit times for its Medical Device Single Audit Program for smaller companies with lower-risk products.

The regulator said that shorter audits could be undertaken for devicemakers that:

- Have 100 or fewer employees;
- Make only lower-risk products (typically Class II medical devices);
- Use simple design and manufacturing processes using commonly available materials and established technologies; and
- Have a good history of conformity to ISO 13485 and regulatory requirements.

For example, a manufacturer with 15 employees could see a 35 percent reduction in audit times, and one with 45 employees could see an 18 percent reduction. The additional reductions become effective June 11.

Health Canada said it remains committed to a smooth transition from the Canadian Medical Devices Conformity Assessment System (CMDCAS) to MDSAP and that auditing organizations have been informed of the adjustments.

In April, the agency said it was sticking to its compliance deadline of Jan. 1, 2019, for devicemakers selling products in Canada to transition to MDSAP but was making adjustments to help manufacturers comply (*IDDM*, April 23).

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 in response to industry comments about difficulty in 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.

Read the May 4 notice here: www.fdanews.com/05-08-18-CanadaMDSAP.pdf.

FDA's Spring Regulatory Agenda Flags Rulemaking for Devices

HHS unveiled its spring unified agenda for upcoming proposed and final rulemakings, including the following planned FDA actions for medical devices:

Final Rule: Medical Device Classification Procedures

This final rule, expected in November 2018, implements Section 608 of Food and Drug Administration Safety and Innovation Act (FDASIA) requiring FDA to use administrative orders to announce or change the classification of devices instead of taking action by issuing regulation.

Proposed Rule: Harmonizing and Modernizing Regulation of Medical Device Quality Systems

The agency anticipates issuing this proposed rule in July 2018 to harmonize and modernize quality system regulations for medical devices. The revisions will replace existing requirements with specifications for an international consensus standard for medical device manufacture, ISO 13485:2016.

The revisions are meant to reduce compliance and recordkeeping burdens on device manufacturers by harmonizing domestic and international requirements, and will modernize the regulation.

Proposed Rule: Medical Device De Novo Classification Process

Anticipated in July, this proposed rule will establish procedures and criteria for the de novo process while making it more transparent and predictable for manufacturers.

De novo classification reduces regulatory burdens on manufacturers by giving them a less burdensome application pathway for marketing devices.

India Releases Final Guidance on Safety and Performance Principles

Following consultation with stakeholders, India's Drugs Controller General adopted essential principles for safety and performance of medical devices marketed in India.

The final guidance sits alongside India's new Medical Device Rules, which went into effect on Jan. 1.

The final guidance closely mirrors a draft issued in July 2017 but it provides more detail and breaks down categories of devices and in vitro diagnostics more specifically.

In one change from the draft document, the final guidance omits a portion of the preface that said it "does not dictate how a manufacturer should prove that their medical devices have met the essential principles."

The final guidance differentiates between three different types of standards: basic or horizontal standards; group or semi-horizontal standards; and product or vertical standards.

Basic standards indicate fundamental concepts, principles and general safety requirements that apply to a wide range of products and processes. This includes risk management, clinical trials and the quality management system.

IVD Reagents

Group standards are those that apply to families of similar products such as standards for sterile devices or those for in vitro diagnostic reagents. Product standards are the necessary safety and performance standards for specific types of devices such as infusion pumps or blood glucose monitors.

Clinical evaluation should include clinical investigation reports, literature reviews or clinical experience to establish a favorable benefit-risk ratio — and clinical studies must be carried out according to the new Medical Device Rules.

For diagnostic devices with a measuring function, the emphasis is placed on precision and stability based on appropriate scientific design to address sensitivity, specificity, and reproducibility. The guidance stresses traceability and quality control measures.

The guidance covers risks associated with medical devices incorporating biologic materials, including tissues and derivatives of microbial recombinant origin. It also covers infection and microbial contamination, manufacturing and environment properties, combination devices and devices that incorporate software.

The guidance lays out the following essential principles for all categories of medical devices:

- Devices are to be designed and manufactured so that they perform as intended and don't compromise the clinical condition or safety of patients;
- Solutions adopted by the devicemaker should conform to safety principles and take into account the state of the art. To minimize risk, the manufacturer should first identify foreseeable hazards and estimate the associated risks. Then it should eliminate as much risk as possible, reduce remaining risk, and inform users of any residual risk;
- Devices should achieve their intended performance and be designed, manufactured and packaged so that under normal conditions they are suitable for their intended purpose;
- The characteristics and performance of the device should not adversely affect the health or safety of the patient or user under normal conditions of use according to the manufacturer's instructions;
- Devices should be designed, manufactured and packaged so that their characteristics and performance are not adversely affected by transport and storage conditions;
- All known and foreseeable risks "and any undesirable effects" should be minimized and be acceptable when weighed against the benefits of the device under normal conditions; and
- Every device requires clinical evidence appropriate for its intended use.

Read the final guidance here: www.fdanews.com/05-10-18-Indiaprinciples.pdf.

NeuroField Failed to Report Device Failures, Control Product

A February inspection of Bishop, Calif.-based NeuroField found the firm failed to report device failures for its neurofeedback devices, and it didn't properly control products according to specifications, the FDA said.

The agency inspector identified 23 instances where customers reported functional or structural failures, but the events were processed as routine service repairs and not evaluated for MDR reportability.

The inspector also observed four instances where incoming in-process materials failed to meet specifications, but they were not documented, evaluated or segregated as noconforming materials.

"Some of these failed materials/components, as documented in your device history record were repaired and used in building finished devices," the Form 483 said.

In addition, the firm had no established quality policy and it could not provide inspection and testing records for the NeuroField X3000 Plus, and the software for the device was not validated.

Read the NeuroField Form 483 here: www.fdanews.com/05-08-18-neurofieldinc483.pdf.

Process Validation Tips

The fifth most cited problem that FDA encounters during inspections is process validation. Process validation is conducted on production equipment and is intended to confirm what you already know about how that equipment works. Validation is specific to the equipment, process, and production and should identify and control critical raw material and process parameters. The firm must complete this before the final design transfer and it should be a part of the design history file or DHF.

So where does this go wrong?

Often, firms will not have a validation master plan. This plan is essential to good project management. It ensures validation of processes. It sets priorities, establishes roles and responsibilities, and creates oversight, as well as schedules, timelines and budgets. The validation master plan also identifies qualified resources and methods for handling deviations; describes procedures, methods, forms, and implementation strategies and documentation. The master plan should also contain continuous improvement components—monitoring, tracking, trending, and revalidation.

The process validation master plan should include: product design/development; process development; facility qualification; utility qualification; test methods validation; cleaning validation; procedures, methods, and forms; qualified personnel and training; roles and responsibilities; and budgets, timelines and schedules.

FDA also frequently sees misconceptions between verification and validation. The following logic tree can help clear up mistakes:

Is the process output fully verifiable? If yes, ask "is the verification sufficient and cost effective?" If yes, verify and control the process.

If the process output is not fully verifiable, you should validate it, and, if necessary, redesign the product and/or process and go back to the beginning of the verification process.

If the process output is fully verifiable but the verification is not sufficient or cost effective, again, you should validate, and if necessary, redesign the process and/or product.

Yet another pitfall is not identifying the worst case conditions in the operational qualification stage. The process parameters should be challenged to assure that they will result in a product that meets all defined requirements under the anticipated conditions of manufacturing.

Look at worst case testing. The operational qualifications will define the process limits or inputs to ensure that the output of the process meets pre-defined requirements, even at worst case conditions.

Excerpted from the *FDAnews* management report: *Troubleshooting Your Quality System: A Guide to Five Devicemaker Quality Compliance Traps*.

Southwest Technologies Cited For Adverse Event Reporting

An FDA inspection of Southwest Technologies' Kansas City, Missouri-based facility in February and March logged 13 observations, most relating to quality system failures and failure to track nonconforming products and submit Medical Device Reports.

The manufacturer of sterile wound dressings received two reports of frostbite in association with its hypothermia caps, mittens and slippers, but the events were not documented and MDR reports were not submitted even though one patient reportedly lost three fingers, the Form 483 said.

The firm's sterilization validation for stimulen collagen wound dressings did not meet acceptance criteria, and the verification study method did not include provisions for retesting of samples, the FDA said.

The FDA discovered that the firm had not established design control procedures, and a device master record was not maintained. Procedures and specifications for manufacturing were not established for any of the firm's medical devices.

The facility also failed to document corrective and preventive actions activities. For example, CAPAs were not opened during 2015 and 2016, even though the firm withdrew products from the market and instituted a full quality management system reboot in 2015.

Procedures to control nonconforming products were not established, the investigator said, and management reviews were not performed from July 15 to December 2017. The company had not appointed a management representative to oversee quality system activities, and it failed to document training activities.

The manufacturer also fell short in controlling environmental conditions.

Read the Southwest Technologies Form 483 here: www.fdanews.com/05-08-18-southwesttechinc483.pdf.

Medical Acoustics Flagged For Inadequate CAPAs

During an inspection of the Medical Acoustics facility in Clarence, NY facility in December 2017, FDA investigators found that the firm failed to properly implement CAPA procedures.

Moreover, of 11 CAPAs the agency reviewed, at least five were not completed in a timely manner.

For example, an investigation opened Nov. 18, 2013 regarding the need to update several procedures was still open as of the inspection, and the changes had not been implemented. Another was signed to indicate that corrective actions and effectiveness verification were completed in November 2014, but the CAPA was not approved and closed until March 2017.

Read the Medical Acoustics Form 483 here: www.fdanews.com/05-11-18-medicalacuisticsllc483.pdf. — Zack Budryk

FDA Reclassifies Sharps Needle Destruction Device

Makers of needle destruction devices will no longer have to file a premarket approval application thanks to a new final order issued by the FDA.

The order renames needle destruction devices as "sharps needle destruction devices," and reclassifies them as Class II devices with special controls, down from Class III postamendment devices.

The move was made to reduce the regulatory burden. Instead of a premarket approval application devicemakers can now submit a less burdensome 510(k) premarket notification.

The agency clarified that devices that were not in commercial distribution before May 28, 1976 — generally classified as postamendment devices — were automatically classified into Class III.

The FDA had issued a proposed order and received two comments, both supporting the decision to reclassify the devices.

Read the final order here: www.fdanews.com/05-08-18-FDAsharps.pdf.

APPROVALS

FDA Clears EKF's Hemoglobin Analyzer

The FDA granted 510(k) clearance to EKF Diagnostics' Diaspect Tm POC hand-held, reagent-free hemoglobin analyzer.

The device requires minimal training and it is always on, with no maintenance or calibration required.

The device gives users accurate hemoglobin measurements within two seconds of insertion for analysis. It can be used in a variety of settings as well as by a wide range of health care personnel.

Edwards Gains CE Mark For Transcatheter Tricuspid Therapy

Edwards received a CE Mark for its Cardioband tricuspid valve reconstruction system, a transcatheter therapy used to treat tricuspid heart valve disease.

The therapy uses the same implant technique and design as the company's Cardioband mitral system and is not yet approved for sale in the U.S.

The device can be positioned precisely to a patient's anatomy and allows real-time adjustment with simultaneous result confirmation.

Cepheid Receives FDA Clearance for Strep A Test

Cepheid, a molecular diagnostics company, received FDA 510(k) clearance for its Xpert Xpress Strep A test to provide molecular detection of Streptococcus pyogenes (Group A Strep).

The test uses an automated real-time polymerase chain reaction to detect Strep A DNA. It can be performed by untrained users to gather results in around 18 minutes.

The low-risk CLIA-waived test does not require culture confirmation for negative results unless symptoms persist or there is an outbreak of acute rheumatic fever.

Novasight Hybrid Imaging System Wins Marketing Clearance

Conavi Medical's coronary artery imaging system received 510(k) clearance from the FDA for use in imaging coronary anatomy during angioplasty and stenting procedures.

The device enables simultaneous imaging of coronary arteries using both intravascular ultrasound (IVUS) and optical coherence tomography (OCT).

It can acquire both IVUS and OCT images using a single catheter, combining the resolution and contrast of OCT with IVUS' larger field of view.

FDA Clears Reza Band for Reflux

The FDA granted 510(k) clearance to Somna Therapeutics' Reza Band, an externally-worn

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

Approvals, *from Page 7*

device designed to reduce symptoms of laryngopharyngeal reflux.

The device applies slight pressure to the cricoid cartilage area located below the Adam's apple which increases internal pressure of the upper esophageal sphincter. It reduces symptoms like chronic throat irritations and cough, hoarse voice, postnasal drip and difficulty swallowing.

The device, which is worn around the neck, reduces LPR symptoms by stopping regurgitation of stomach contents.

Beckman Coulter Achieves CE Mark for Early Sepsis Indicator

Beckman Coulter's early sepsis indicator device, a hematology-based test, received CE Mark certification.

The new test will be made commercially available on the company's recently launched DxH 900 hematology analyzer. The indicator uses the analyzer's technology to characterize cells in their near-native states.

The hematology-based test is meant to alert emergency department clinicians about the possibility or risk of developing sepsis as part of a routine complete blood count.

FusionVu Application Cleared By FDA for Prostate Biopsies

Exact Imaging, an ultrasound system developer, received 510(k) clearance for adding its Fusion Vu application to the ExactVu micro-ultrasound platform.

The application allows urologists to perform cognitive MRI transrectal ultrasound or micro-ultrasound/MR fusion on the ExactVu high resolution platform.

The new application provides 70-micron real-time resolution of the micro-ultrasound system for targeted prostate biopsies.

Abbott's Xience Sierra Coronary Stent Approved in Japan

Abbott's Xience Sierra everolimus-eluting coronary stent was granted national reimbursement by the Japanese Ministry of Health Labor and Welfare to treat coronary artery disease.

The new stent features an enhanced design, a new delivery system and unique sizes for use in challenging cases.

Xience Sierra was developed to help doctors more easily treat individuals with difficult blockages that involve multiple or completely blocked arteries or complications like diabetes.

Abbott Gains FDA Clearance For Sensor Enabled Catheter

The FDA cleared Abbott's Advisor HD grid mapping sensor enabled catheter for creating detailed maps of the heart.

The device is intended to improve cardiac ablation procedures by providing an inside view of the heart, allowing a more accurate identification of its anatomy.

The sensor captures information such as the direction and speed of cardiac signals, allowing for the creation of high-density cardiac tissue maps for better treatment regimens.

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Supplier Quality Metrics for Devicemakers: *Predicting and Selecting the Best*

Regulators are watching your supplier management practices closely. The FDA's Quality System Regulation (QSR), ISO 13485 and the international Medical Device Single Audit Program (MDSAP) all have specific requirements for purchasing controls and acceptance activities. They expect your suppliers to function as an extension of your quality system. So how do you choose the ones most likely to meet your standards?

An effective supplier evaluation system includes determining your expectations, converting them into measurable characteristics/metrics, defining the measurement method and setting the target you expect suppliers to hit.

In the **Supplier Quality Metrics for Devicemakers** management report you'll learn how to use predictive analysis of such metrics as delivery time, management efficiency and lot acceptance rate to identify suppliers you can count on and spot potential problems in the future. You'll learn:

- Requirements for receiving acceptance
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