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IN THIS ISSUE

FDA to Allow Combo Products to Submit Malfunction Summary Reports

The FDA is allowing manufacturers of combination products to submit certain device malfunction medical device reports (MDRs) on a quarterly basis.

The agency had earlier streamlined reporting requirements for Class I devices and Class II devices that are not permanently implanted or life supporting or sustaining. The summary reports do not apply to Class III and implantable or life-sustaining Class II devices.

There are still reportable malfunctions for which devicemakers will need to submit individual malfunction reports more often than quarterly to protect public health, the agency said. It stressed that malfunctions related to certain recalls should still be reported as individual MDRs.

Under the new requirements, manufacturers will not be allowed to bundle reportable malfunction events by product code or product family. Rather, each unique combination of device brand name, device model, and device problem code can be summarized together.

(See **Combo***, Page 2)*

UK Unveils 'No Deal' Brexit Contingency Plan

The UK's Department of Health and Social Care (DHSC) released a contingency plan in anticipation of a possible "no deal" Brexit situation that could potentially disrupt the supply of medical devices that are imported into the UK from EU countries.

The UK plans to leave the EU on March 29, 2019, but a "no deal" Brexit could disrupt supplies of devices and clinical products. In preparation, the department analyzed supply chains for medical devices and clinical consumables to identify the proportion of products that are routinely imported.

DHSC is taking steps to ensure that medical devices and clinical consumables supplied from EU countries continue to move smoothly to National Health Service organizations. Stocks of devices and

(See **Brexit***, Page 2)*

Health Canada Updates Requirements For Class II/III Infusion Pumps

Citing post-market safety concerns about the delivery accuracy of infusion pumps, Health Canada is updating the evidence requirements to demonstrate the accuracy of these devices through performance testing for new and amended license applications.

Effective immediately, new Class II and Class III license applications will require performance testing for:

- The pumping mechanism;
- Any software component that could affect fluid delivery accuracy; and
- A tubing set when the change impacts the delivery accuracy range stated in the pump labeling.

Devicemakers will need to include in their license applications performance testing data that "clearly demonstrates that the infusion pump can reliably deliver therapeutic agent within the accuracy ranges specified in product labeling," the agency said.

Performance testing should be done with the complete infusion pump system and required accessories. Tests should include a statistically justified sample size to demonstrate accuracy performance.

Health Canada stressed that a comparison to existing licensed devices alone would not be sufficient to support a new infusion pump's performance testing data; device-specific testing will be required.

The agency acknowledged that the performance testing "may go beyond the scope of testing required by the international standards for infusion pumps." It also said that the requirements will be imposed on all pump types, and manufacturers of more specialized pumps, such as insulin pumps, should provide a rationale for a more limited battery of testing.

Failure to provide evidence of adequate testing will result in a refusal to issue a license, the agency said.

Read the Health Canada guidance here: www.fdanews.com/08-21-18-HealthCanada.pdf.

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The agency explained that bundling malfunction reports by product codes or device families would make summarizing and interpreting the information in a summary report difficult for manufacturers, the FDA and the public.

The FDA also pointed out that the International Medical Device Regulators Forum is working on harmonizing all device coding, including problem codes, which will provide more granularity.

The program is voluntary and is aimed at streamlining malfunction reporting; it is only applicable to reportable malfunction events that manufacturers become aware of on or after Aug. 17.

Read the agency's notice here: www.fdanews.com/08-21-18-Comboreports.pdf.

Brexit, *from Page 1*

consumables will be increased nationwide as a part of the contingency measures.

"The government's contingency plans have been developed so that the infrastructure and logistics capability of the NHS supply chain will be able to accommodate and manage these increased volumes," DHSC said in an Aug. 23 letter to stakeholders.

Suppliers will be contacted in September about their contingency plans and the need to ramp up production and supply of products when necessary. The department urged companies that have already made contingency plans to send in details. — James Miessler

Industry Offers Mixed Response To FDA's Safety Action Plan

Industry stakeholders lauded the FDA's efforts to make greater use of real-world data and to take a total product lifecycle approach to regulation as outlined in its proposed Medical Device Safety Action Plan.

However, AdvaMed and Johnson & Johnson took issue with the agency's plan to identify areas where it might seek additional authority.

The FDA said it would consider regulatory options to streamline and modernize "timely implementation of postmarket mitigations," exploring whether it has the authority to issue "umbrella regulations" to identify devices that may require additional training or user education beyond the physician labeling currently required.

AdvaMed said in its comments that it had concerns with the FDA proposal to impose special controls through an umbrella regulation. It questioned the merit of such a move and said that currently the FDA lacks the authority to do this. If the agency were to move toward this, it would need to seek further input from stakeholders; as such a move would have "far-reaching and unexpected effects."

The FDA's safety action plan would also "consider invoking restricted device authority" on a case-by-case basis to increase patient protection for the highest risk devices. The association suggested that the FDA should instead look at its internal processes to identify "whatever internal obstacles prevent efficient practice."

Total Product Life Cycle

AdvaMed praised the FDA's plan for CDRH to shift to a total product life cycle organizational structure. 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 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.

Reorganization of CDRH's premarket and postmarket offices into a total product life cycle 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 said.

AdvaMed also supported the agency's use of real-world evidence to better understand how products are used and experienced in the real world. "AdvaMed continues to support FDA's efforts to use RWE in its regulatory decision making" and its collaboration with the National Evaluation System for Health Technology Coordinating Center (NESTcc), the association said.

Innovation

Another prong of the safety action plan would spur innovation towards safer medical devices by providing regulatory incentives and scientific expertise that help drive competition (*IDDM*, April 23).

AdvaMed disagreed with language in the action plan that suggested that a voluntary 510(k) pathway for certain moderate-risk devices would send a signal that the pathway would be safer compared to demonstrated substantial equivalence to a predicate device.

Johnson & Johnson said it supports a more modern 510(k) pathway, but it took issue with a statement in the action plan that said the marketplace "does not provide strong incentives to make an established device safer in the absence

(See **Safety***, Page 4)*

FDA Releases New Guidance On Arthritis Treatments

The FDA asked stakeholders to suggest structural endpoints for use in clinical trials of medical products, including medical devices, aimed at treating the root cause of osteoarthritis.

Regulators have already approved drug products for treating the pain of osteoarthritis, but no treatments have yet been approved to prevent the underlying structural damage it causes, the agency says in new draft guidance.

The draft guidelines mark the first time the FDA has wrestled with structural endpoints for osteoarthritis in nearly two decades. But it offers few concrete suggestions, instead punting to stakeholders for comment.

"This draft guidance is intended to serve as a focus for continued discussions among the FDA, sponsors of medical products, the academic community, and the public regarding the assessment of structural endpoints," the FDA says.

The Centers for Disease Control and Prevention estimates that some 30 million Americans suffer from osteoarthritis. It's the most common joint disorder in the U.S. and the cases of knees affected have more than doubled since the mid-20th Century, leading to millions in taxpayer dollars being spent on joint replacement surgeries and rehab.

Yet the pathology of the disease is still largely opaque and the amount of structural damage oftendoesn't correlate with patients' self-reported pain and/or mobility problems.

"The ultimate goal of treatments," the FDA says, "is to avoid or significantly delay the complications of joint failure and the need for joint replacement, and, also, to reduce the deterioration of function and worsening of pain."

Given the nature of the disease, it's "unclear what magnitude of change in structural endpoints would translate to a clinically meaningful benefit to patient," the FDA says.

Read the draft guidance here: www.fdanews.com/08-22-18-OsteoarthritisDraft.pdf. — Bill Myers

Safety, *from Page 3*

of a new or greater-than-previously-understood safety concern."

The devicemaker stressed that its chief medical officers are involved in all aspects of device development, and its first-in-human development committees review all accumulated safety data before allowing teams to introduce certain new devices.

J&J said its teams incorporate real-world evidence into proactive safety monitoring and noted that J&J was the first company to share clinical trial data from across its portfolio of products with researchers around the world.

PEOPLE ON THE MOVE

WuXi AppTec appointed **Edward Hu** as co-CEO of the pharmaceutical and medical device technology company where he will share business management responsibilities with the company's founder and CEO Ge Li. Since joining the company in 2007, Hu has served as its chief operating officer, chief financial officer and chief investment officer. Before joining WuXi, he served as senior vice president and chief operating officer at Tanox. Wuxi's laboratory testing division is currently constructing a state-of-the-art test facility in the industrial hub of Suzhou, China.

Connecticut-based **Lumendi** named **Michael R. Thomas** as its new vice president of sales. Thomas has more than 30 years of experience in medical and surgical sales. He will be responsible for sales of the company's DiLumen EIP and DiLumen C2 platforms that enable minimally invasive endolumenal therapies. He previously served as vice president of global sales and business development at bariatric surgical platform developer USGI Medical. Prior to that role, he served as bariatric practice advisor at Allergan, field marketing manager at Ethicon Endo-Surgery, senior professional representative at Fujisawa Pharmaceutical and regional trainer and recruiter at SmithKlineBeecham Pharma.

Design Controls, Device Master Record Missing at Mibo Medical

Failure to establish design controls, acceptance procedures or a quality policy for its MiBo Thermoflo Class II device landed specification developer and manufacturer Mibo Medical Group a Form 483 following a May inspection of its Dallas, Texas facility.

Marketed since 2014, the device hydrates eyes via an electric heating element that delivers continuous heat to the eyepad, which breaks down hardened lipids.

The firm had not defined, documented or implemented design control procedures that addressed design input, outputs, review, verification, validation or design changes, according to the nine-item 483.

Mibo had not established procedures for corrective and preventive actions and also failed to establish and maintain procedures for handling complaints, the agency said.

The facility did not maintain a device master record including device specifications, production process specifications, quality assurance procedures, packaging and labeling specifications and maintenance and servicing procedures and methods.

"As a specification developer/manufacturer, your firm did not establish and maintain procedures to ensure that all purchased products and services conform to specified requirements in the manufacture of the MiBo Thermoflo," the agency said.

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

Executing an Audit

Planning and developing an internal audit program and training all involved personnel are tasks that take a lot of time and effort, but they are merely the foundation. Execution of the audit program comes with its own set of challenges, and is a more extensive activity than just checking items off a "to do" list in the audit procedures document.

Part of the established procedures should include steps taken to develop an audit plan for each individual audit. A one-size-fits-all plan will not work, as certain audits will, of necessity, have different goals and different purposes.

The beginning of any plan, according to *Susan Reilly, owner of the consultancy Reilly & Associates*, should be to ensure that all auditees necessary are available and aware that an internal audit is being scheduled. Someone on the audit team needs to be responsible for making sure that everyone who needs to be notified about an audit being scheduled is contacted. This includes anyone outside the company or business unit who may have responsibilities pertinent to the area being audited.

"I have been called in to do, say internal audits of a complaint process where I find out the corporate body has some responsibility for complaint-handling, yet no one there was notified that there was going to be an audit that day," she said. "So, make sure all auditees are aware and the audit plan can help do that."

In addition to ensuring that all auditees are available, audit team members need to be available, as well. Auditors should be identified, with responsibility for contacting them and clarifying the schedule clearly defined.

The audit plan should spell out the specific purpose or objectives of the audit being planned, as well as the scope or boundaries of what the audit will cover. It should specify what criteria — standards, regulations and internal procedures — will be applied during the audit. Other critical pieces of audit planning include:

- Anticipated start and stop dates;
- A general meeting schedule, including opening, daily and closing meetings among
- auditors and key auditees; and
- Audit interfaces.

Once the schedule has been set and confirmed, but well before the audit begins, the audit team should review past audit reports. This is especially important if part of the purpose of the current audit is to assess the effectiveness of previous corrections.

Excerpted from the FDAnews management report: *Effective Internal Audits and Quality Control Units for Devicemakers*.

Lab Cited for Not Maintaining Complaints, Supplier Requirements

Failure to maintain complaints from 2014 to 2017 landed Phoenix, Arizona-based Gergens Orthodontics Lab a Form 483 following a May FDA inspection.

Of the roughly 30 complaints the lab received from 2017 and onward, all were found deficient in recording required information such as the device name, the phone number and address of the complainant, result of the investigation and replies.

The firm also lacked documented evidence that management reviews had been performed, the agency said.

In addition, the orthodontic devicemaker did not document procedures for ensuring that suppliers complied with specified requirements.

Read the Gergens Orthodontics Form 483 here: www.fdanews.com/08-23-18-gergensorthodonticlab483.pdf.

Ultrasound Medical Devices Falls Short on Managing Complaints

An FDA inspection in May found that Ann Arbor, Mich.-based Ultrasound Medical Devices had not established procedures for receiving, reviewing and evaluating complaints.

"Your firm had not evaluated any customer service communications you have received since May 1, 2016," the agency said, noting that during the inspection, the firm's management investigated several service tickets, 11 of which were customer complaints tagged as "routine support/maintenance."

None of the reports were forwarded to the quality manager or dealt with in a timely manner, the FDA said. The 483 report noted that some complaints were logged up to four months after they were received.

The ultrasound manufacturer's corrective and preventive actions were also found to be lacking. The most recent quality data analysis documented was dated Aug. 11, 2016, and the company's quality assurance and regulatory affairs manager told the FDA investigator that no quality data analysis had been conducted since that date.

The facility was also cited for not establishing procedures for training and identifying training needs for its employees. The firm's interim quality assurance and regulatory affairs manager, who had been in place since December 2017, did not have documented training in the employees file, the 483 said.

Read the Ultrasound Medical Devices Form 483 here: www.fdanews.com/08-23-18-ultrasoundmedicaldevicesinc483.pdf.

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The company was also cited for not establishing procedures for finished device acceptance to ensure the products meet acceptance criteria.

The firm also lacked procedures for quality audits and had not conducted any audits.

Read the Mibo Medical Form 483 here: www.fdanews.com/08-23-18-mibomedicalgroup483.pdf.

Health Canada Shifts to ToC Format For Class III and IV Applications

Health Canada will adopt the Table of Contents format for Class III and IV premarket medical device applications from April 1, 2019.

The change follows the International Medical Device Regulators Forum recommendation for harmonized formatting for medical device market authorization requests. In October 2015, the IMDRF launched a pilot program for submission of regulatory dossiers under the ToC format, which drew positive feedback from industry stakeholders.

Manufacturers will be expected to submit premarket applications for such devices in either the ToC or Health Canada format, according to the agency. Health Canada will discontinue use of the Summary Technical Documentation (STED) format on the same date and will no longer accept applications in that format.

The ToC format will improve the filing process for applications for multiple jurisdictions and better support the transition to the Health Level-7 messaging standard that supports submission of information for regulated products, the agency said. — Zack Budryk

Philippines FDA: J&J First Aid Kits Include Counterfeit Devices

The Philippines Food and Drug Administration issued a warning that the Johnson & Johnson First Aid To Go Kit includes devices that have not gone through the registration process and are considered counterfeit and unapproved devices.

The agency said it confirmed with J&J that the devices are counterfeit and should not be used.

Johnson & Johnson said its operating companies take "a variety of approaches" to identify counterfeit products, including product and packaging security steps that help distinguish authentic and counterfeit products.

APPROVALS

MolecuLight Gains FDA's De Novo Clearance for Fluorescent Imaging Device

Toronto, Ontario-based devicemaker MolecuLight received the FDA's De Novo clearance for its handheld fluorescence imaging device, the MolecuLight i:X.

The portable device captures fluorescence information from wounds and surrounding tissue using still images and videos in real-time.

The device, which previously received the CE Mark and Health Canada Medical Device License, allows clinicians working on skin wounds to digitally record images of the wound and images of fluorescence emitted from the wound when exposed to an excitation light.

FDA Approves Ivantis' Hydrus Microstent

The FDA gave its approval for California devicemaker Ivantis' Hydrus microstent, used for treating patients with mild to moderate primary open-angle glaucoma (POAG).

The microstent is roughly the size of an eyelash and is made from a super-elastic, biocompatible alloy that is used in many implants.

It is designed to relieve high intraocular pressure frequently seen in patients with POAG by allowing blocked eye fluid channels to flow freely.

Implantica Receives CE Mark for RefluxStop

Medical technology company Implantica earned a CE Mark for its RefluxStop device, used for treating patients that suffer from acid reflux.

Implantica received the CE Mark based on results from a multi-center investigation that demonstrated its safety and effectiveness, and it may now market the device in the European Economic Area and Switzerland.

The device avoids potential complications that arise from compressing the food passageway — such as difficulty swallowing and inability to

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

Approvals, *from Page 7*

burp or vomit — treating gastroesophageal reflux disease without squeezing the passageway.

CoreLink's 3D Anterior Lumbar Approved by FDA

CoreLink received FDA approval for its 3D anterior lumbar interbody device, a spinal implant that mimics the characteristics of natural bone.

The device has a load-sharing support structure and an interconnected lattice to provide strength, stability and stiffness.

The structure of the implant also allows for better imaging by minimizing material density.

FDA Allows Marketing of Brainsway's TMS for OCD Treatment

The FDA has permitted marketing of Brainsway's deep transcranial magnetic stimulation (TMS) device for treating obsessive compulsive disorder.

"Transcranial magnetic stimulation has shown its potential to help patients suffering from depression and headaches," said Carlos Peña, director of CDER's Division of Neurological and Physical Medicine Devices. "With today's marketing authorization, patients with OCD who have not responded to traditional treatments now have another option."

The agency said the device should not be used by patients with metallic objects or implants that are in or near the head, such as cochlear implants, aneurysm clips or coils or deep brain stimulators.

TPlus Receives CE Mark For Medical Image Archiver

Korean device manufacturer TPlus received European certification for its View Vine picture archiver and communication system.

The picture archiving and communication system sends, stores and receives medical images and supports real-time image recognition.

The device has been stripped of less frequently used functions and now generates only integral images used to show the average intensity of pixels, to assist in diagnosis.

Kleresca Approved in EU For Dermatological Platform

Dermatological device developer Kleresca gained a CE Mark for its biophotonic dermatological system.

The device uses a non-invasive fluorescent light treatment to encourage the skin's biological processes, repair skin in patients and treat rosacea. It can also be used as an add-on treatment for other dermatological procedures, such as laser treatments.

The device cannot cause a photosensitive reaction because the treatment gel is not absorbed by the skin, and the treatment does not damage the skin's natural barriers.

FDA Clears SPR's Nerve Stimulator for Pain Relief

SPR Therapeutics' received FDA clearance for its single and dual lead peripheral nerve stimulator.

The devices are minimally invasive alternatives to opioids that are implanted for up to 60 days to relieve acute and chronic pain, including post-traumatic and post-operative pain. The components are removed after treatment.

The nerve stimulator comes with a wearable electronic pulse generator that has rechargeable batteries and a Bluetooth compatible remote.

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

Complaint management is essential to a functioning quality management system.

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Top Trends in Drug and Device Advertising and Promotion: *Enforcement Priorities for the FDA and FTC*

As drug and device companies develop new and innovative ways of promoting their products — such as targeting new markets, influencer marketing and using social media and reality television — it's important to understand the regulatory priorities of the FDA and the FTC to avoid running afoul of those agencies.

Top Trends in Drug and Device Advertising and Promotion takes a deep dive into six areas regulators give the most attention:

1. **Consistent Communication:** Three factors that ensure communications are consistent with a product's approved labeling
2. **Direct-to-Consumer Advertising:** Use of distracting visuals, competing superimposed images and lively music that can minimize the required presentation of risk information
3. **Risk Disclosure:** How much information needs to be presented and how
4. **Payer Communications:** Disseminating healthcare economic information, or HCEI, to payers postapproval
5. **Preapproval Promotion:** A new safe harbor for communicating information about investigational products to payers
6. **Transparency:** Making it clear that a communication is sponsored advertising

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