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IN THIS ISSUE

U.S. Urges EU to Delay Implementing EU MDR/IVDR by Three Years

With only nine months to go before the EU's Medical Device Regulation hits its May 26 application date, the U.S. is pressing the EU to delay implementation for another three years.

In a July 24 letter to the World Trade Organization Committee on Technical barriers to Trade, the U.S. delegation said it had serious concerns about the implementation of the new regulations. It said that the industry "is worried about their continued access to the EU's $125 billion medical device market, $20 billion of which is supplied by U.S. products."

The letter points to the ongoing lack of notified bodies in the EU to perform certification activities under the MDR/IVDR and the delay in drafting needed implementing acts.

(See **EU MDR**, *Page 2)*

IMDRF Seeks Feedback On Adverse Event Reporting Terms

The International Medical Device Regulators Forum (IMDRF) has issued a new draft document on harmonizing terminology and codes for reporting adverse events for medical devices and in vitro diagnostics.

The forum's Adverse Event Terminology Working Group says a single adverse event terminology and coding system will improve signal detection and enable faster responses by industry and regulators.

Using defined terms and codes would help identify potential risks sooner and allow sophisticated trending analyses among global regulators, the group said.

The draft refers to the 2006 Global Harmonization Task Force (GHTF) document on post market surveillance: Global Guidance for Adverse Event Reporting for Medical Devices. The task force no longer exists and has been replaced by the IMDRF.

(See **IMDRF**, *Page 4)*

EU MDR, *from Page 1*

"MDR/IVDR's implementation is behind schedule. Our industry has two particular concerns about this: One, there is an insufficient number of Notified Bodies (NBs) to perform. And, two, the EU has drafted an insufficient number of the implementing acts needed to provide details about how industry can ensure that their products comply with the new product standards," the statement said.

The delegation asked the EU to provide an update on how many of the 58 NBs accredited to test and certify products under old directives are currently designated as operational under the new MDR and IVDR, and how many the EU expects to be designated as operational by the end of 2019.

The European Commission had suggested that 12 NBs would be operational by the end of 2019, but "12 NBs are not enough to provide sufficient capacity to ensure continued regulatory approvals by May 2020 and May 2022."

Only two of the 18 implementing regulations have been issued, and as a result, EU standardizing bodies cannot begin work on developing the standards industry may use to comply with the MDR/IVDR, the letter stressed.

"Given, this backlog industry maintains that the product standards necessary for compliance with the MDR cannot be completed before the deadline."

It said that the provisions for warehousing and the grace period, "which are intended to provide transitional relief, are insufficient."

"The warehousing provision is insufficient because buyers and producers cannot predict demand, making it difficult to warehouse the right amount of product to meet that demand through the implementation delays. Moreover, warehousing is expensive, degradation is common with medical technology, and the technology itself can quickly become obsolete. The grace periods are insufficient because CE mark product registrations compliant with the old directives may expire before the end of the grace period, in 2024."

The delegation said that if this delay is not possible, it urged the EU to allow for legacy products that are currently deemed safe to be sold on the market until 2024 and to ask notified bodies to provide new products, which require testing for the first time, with priority access to testing and CE marking certification over products being recertified to the new requirements.

Many Class I devices were up-classified to Class IIa or higher under the new regulations, which means they were allowed to self-declare in the past but will not have a valid NB certificate and will not qualify for the grace implementation period that the MDR grants.

So far, only two notified bodies — BSI and TUV SUD — have been designated under the MDR/IVD, and "there is no indication that a significant number of notified bodies will be designated in the next months," according to the European Coordination Committee of the Radiological, Electromedical and Healthcare IT Industry (*IDDM*, July 8).

"By now, 38 notified bodies have applied for MDR," Gert Bos, executive director and partner at QServe, told *FDAnews*.

Bos said most observers expect just 10 NBs to be designated by the end of the year in a best-case scenario, and 20 by the MDR implementation at the end of May 2020.

FDA Hits Houston Devicemaker With Lengthy Warning Letter

Houston-based medical devicemaker Talon received a lengthy FDA warning letter for design process and quality control issues following an inspection of the firm's manufacturing facility.

Investigators found the firm's CAPA procedures to be insufficient, noting that reports "failed to provide documented evidence that corrective actions taken were verified and/or implemented." The letter noted several instances of CAPAs being closed before the underlying issues were resolved.

The letter also hit the firm for failure to establish proper procedures to verify device design changes. Inspectors discovered design changes to the firm's Class II VAC-FIX System — used in radiotherapy treatments — had been approved and implemented without testing or verification.

The FDA further observed the facility did not properly implement procedures to handle nonconforming products. Malfunctioning products were removed from inventory without proper investigation, even when the firm's records showed a corrective action report was required.

In addition, the firm failed to document acceptance or rejection of incoming products. In one example, inspectors found the firm received radio cassette bins and "did not have specifications for the part and no incoming inspection criteria."

Multiple observations noted in the warning were repeats from a 2011 inspection, including a failure of the firm to properly maintain batch records. "There is no documented evidence your firm has controlled the production history of your Class II medical devices," the agency warned. Additionally, the firm was warned again for failure to establish proper device servicing procedures. Investigators found that malfunctioning devices were repaired and returned to customers without completed quality inspection criteria forms.

The warning letter also outlined failures to properly train staff, to routinely perform quality audits, and to keep proper quality control records. The agency highlighted that the firm's response to the Form 483 inspection observations indicated quality audits were being performed, but "with poorly defined requirements."

The firm was also flagged for failing to correctly register its MedKey Lite software — used to keep medications secure and to control user access — with the agency, despite marketing it as "FDA approved."

Read the Talon warning letter here: www.fdanews.com/08-16-19-TALONWL.pdf.

BRIEFS

European Commission Names Third Notified Body for MDR

The European Commission has named DEKRA Certification of Germany as the third notified body for certification under the Medical Device Regulation (MDR).

DEKRA joins BSI Assurance UK and TÜV SÜD of Germany as the only NBs that can certify devicemakers for MDR compliance.

With less than one year before the MDR takes effect, there is a severe shortage of notified bodies needed to certify products in compliance with the new requirements. Some NBs say they will not even apply for the designation (*IDDM*, June 21).

TGA Reviews Comments on Unique Device Identification System

Australia's Therapeutic Goods Administration (TGA) said public comments on its proposal to set up a unique device identification (UDI) system for medical devices show "a strong consensus" in favor of the idea.

The majority of submissions called for linking the UDI database with the agency's Register of Therapeutic Goods. Most comments urged the agency to use the International Medical Device Regulators Forum's UDI guidance as a basis for the system, including its labeling requirements.

Some respondents proposed the exemption of low-risk devices.

IMDRF, *from Page 1*

The new draft provides IMDRF terms, definitions and alpha-numerical codes for adverse event reporting for medical devices and in vitro diagnostics for both pre-market and post-market stages.

The terms are intended to be used by reporters of adverse events and by regulatory authorities that are collecting and processing the information. The terminology includes:

- Observations at the level of the medical device;
- Device components including accessories;
- Observations at the level of patients, users or other persons; and
- Investigations into possible causes of the event as well as causal links independent of whether malfunctioning or not and adverse health effects.

For the time being, the terminology does not include subsets such as actions taken by manufacturers — such as field safety corrective actions and recalls — or regulatory authorities.

The terms and their descriptions are hierarchical, so that as the number of levels increases, the resolution and descriptive power of the system grows.

The advantage of a hierarchically arranged coding structure is that a large variety of terms can be used "without the need to know all terms before using the system," the working group said.

The draft includes four distinct sets of terminologies and the associated alphanumeric codes:

- Medical device problem — terms/codes for describing problems of medical devices that have occurred;
- Cause investigation — types of investigations and their findings and conclusions;
- Health Effects — clinical signs, symptoms and conditions and health impact; and
- Component — terms/codes for describing the parts and components that were involved in or affected by the adverse event incident.

The consultation ends on Sept. 10. Read the IMDRF document here: www.fdanews.com/08-15-19-IMDRF.pdf.

483 Roundup: FDA Hits Four Firms for GMP, Other failures

The FDA cited four devicemakers for problems with their complaint procedures, change controls and quality oversight, among other deficiencies.

PF Consumer Healthcare: Failure to establish procedures for receiving, reviewing and evaluating complaints as well as failure to report complaints and other quality management issues landed Pfizer subsidiary PF Consumer Healthcare a 10-observation, 17-page FDA form 483 following a Feb. 25 to April 4 inspection of its manufacturing plant in Atlanta, Georgia.

FDA inspectors found that complaints involving the possible failure of a device to meet any of its specifications were not reviewed, evaluated or investigated. Between Jan. 1, 2018 and Feb. 28, 2019, there were roughly 4,622 adverse events reported associated with the Thermacare pain product, and 1,199 product complaints and/or adverse events were not investigated. Only 94 of the complaints were filed with the FDA as MDR reports.

Three serious adverse events, one involving an alleged death, and others resulting in second- and third-degree burns were not forwarded to the product quality complaint group, and investigations into the events weren't conducted, the agency said.

According to the firm's business process manual, adverse events sent to the product quality complaint group could be canceled if there is "an allegation of a burn without a quality defect noted," the 483 says. The rationale was that burns without an allegation of a quality defect are considered adverse events only and should follow standard practice, which is to log them as complaints only if the safety division doesn't request a follow-up for an investigation.

At least 11 adverse events involving burns, some of which were third-degree burns, were sent from the safety group to the product quality group and were canceled based on this policy.

During the same period that the FDA investigators were visiting the plant, Pfizer issued an April 26, 2019 press release recalling one lot of its Thermacare back pain heatwraps due to out of specification results for high cell temperatures. Pfizer said units were distributed nationwide and in Puerto Rico from June 2017 through March 2018, and it was removing the product from stores.

The 483 also cites the firm for failing to implement corrective and preventive action SOPs. For example, the firm's procedures for the Thermacare site quality review team require periodic review of quality data sources as well as historical records to identify trends in complaint data. Nearly twice the normal number of complaints were reviewed, but an investigation was not carried out.

The FDA said the firm failed to follow correct test methods and failed to list maximum temperatures measured during testing, and it didn't properly validate the test.

The investigator listed a litany of other quality problems, including failure to establish procedures for quality audits, failure to document in-process inspections or other verification activities, and failure to establish adequate document control procedures.

Bio-Med Diagnostics: Lax change control procedures and document control issues were uncovered during an April 16-19 FDA inspection of Bio-Med Diagnostics' White City, Oregon facility.

Documentation to show that preventive actions were implemented to address gaps in training was lacking for the company's InTray GC, a Class II in vitro diagnostic device for detecting gonorrhea.

Bio-Med implemented a new software system to control all aspects of its product inventory, incoming acceptance activities, nonconforming product and final release. FDA investigators said the firm failed to follow its change control procedures when implementing the new software, and it didn't have a change control report or validation report documenting the change.

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

483s, *from Page 5*

The agency cited the firm for inadequate validation procedures because it failed to validate equipment used to sterilize its products.

Document control procedures were also found lacking in that the clinical microbiology catalog and InTry GC flyer were not reviewed and approved according to the company's SOPs. Obsolete documents were also being used, the agency said.

LPE Holdings: Failure to develop procedures for medical device reporting or for receiving, reviewing and evaluating complaints were among the quality system failures FDA inspectors found during an April 15-17 inspection of LPE Holdings' Woodland, Wash. manufacturing facility.

The firm manufactures patient loading utility systems, Class II devices for loading patients onto airplanes. At least four complaints were still open at the time of the inspection.

The procedure didn't require all service records to be evaluated for potential complaints, and the firm had not conducted the procedure since 2016.

CAPA procedures were also not adequately defined or implemented and they didn't include requirements for documenting that CAPA actions were verified or validated.

Diamond Orthopedic: The FDA hit medical equipment manufacturer Diamond Orthopedic with a Form 483 for multiple violations at its Charlotte facility, including deficient supplier contracts and poor oversight of the quality system.

During a March 25-April 5 inspection, the investigator noted 11 observations. For example, the firm neglected to determine if a complaint about a device failure warranted reporting to the agency as an adverse event — and its complaint record didn't justify the decision not to submit an MDR.

"The medical device investigation report does not record how the patient's care was affected and it does not include comments from the doctor or medical professional that the incident was not a reportable event," the agency said.

The investigator also found that device label review procedures weren't up to par. For example, a work instruction describing packaging and labeling activities did not instruct the quality operator to compare all label information to the device master record for accuracy and completeness.

The investigator found that the firm didn't have quality agreements in place with all its critical suppliers. Two of the firm's seven quality agreements with suppliers, contractors and consultants had deficiencies.

The company's investigations into nonconforming devices were shoddy, the agency said. Ten packages of medical devices returned by a contract manufacturer were not investigated to determine the root causes of nonconformance. Furthermore, no procedures were in place to ensure nonconforming devices were evaluated quickly.

Additionally, the firm didn't properly calibrate a measuring device. Records from the caliper's manufacturer did not include a calibration date, making it impossible for the firm to know when to perform calibration.

Diamond also lacked adequate procedures for identifying quality system deficiencies and executing corrective and prevention actions.

Read the PF Consumer Healthcare Form 483 here: www.fdanews.com/08-15-19-pdconsumerhealthcare1llc483.pdf.

Read the Bio-Med Diagnostics Form 483 here: www.fdanews.com/08-15-19-biomeddiagnosticsinc483.pdf.

Read the LPE Holdings Form 483 here: www.fdanews.com/08-15-19-lpeholdingsllc483.pdf.

Read the Diamond Orthopedic Form 483 here: www.fdanews.com/08-15-19-diamondorthopedic483.pdf.

APPROVALS

FDA Grants Breakthrough Designation for Balloon Catheter

Concept Medical's MagicTouch PTA sirolimus drug-coated balloon catheter (DBC) has received the FDA's breakthrough device designation for use below-the-knee.

The device is designed for treating peripheral artery disease, a common circulatory issue involving reduced blood flow from narrowed arteries, usually in the legs.

In an ongoing clinical study, the device was effective and there were no incidents of device and procedure-related mortality, the devicemaker said.

FDA Clears Binx Health Diagnostic for STDs

The FDA granted Binx Health another 510(k) clearance for its Binx io platform, clearing the fully automated point-of-care test for chlamydia and gonorrhea.

The test uses polymerase chain reaction (PCR) amplification and electrochemical testing to detect the common STDs.

It delivers results in about a half hour, using vaginal swab samples that can be collected by a physician or by the patient.

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

Complaint Investigations

Once a complaint has been deemed potentially reportable to the FDA as an MDR, a designated individual within the complaint handling unit must promptly begin an investigation.

The skill set for an MDR investigation is specialized and different from skills required for other investigations, says *Dan O'Leary, president of Ombu Enterprises*. Therefore, it is important that devicemakers carefully select and train employees to conduct MDR investigations.

The investigation must determine whether the device failed to meet a specification. If so, it also must ferret out the root cause of the inadequacy. It also must examine the relationship of the device to the reported incident or adverse event. The investigation should conclude with a determination of whether or not a CAPA is warranted. The complete results of the investigation must be included in the MDR event file.

The regulations require an individual MDR record for each event, the content of which can be quite extensive, including records from other sources. The information is collected in the MDR event file, which is linked to at least one individual complaint records. If a devicemaker has received multiple complaints about the same issue, the MDR event file for that issue or event could be linked to multiple individual complaint records.

These files need to include all information about the adverse event, such as documentation, deliberations, reportability decision-making, information submitted to the FDA and acknowledgements that the MDR was successfully uploaded to the FDA database. FDA employees must be allowed to access, copy and verify these records.

It is acceptable to for the MDR event file to be part of a complaint file. If a devicemaker does this, however, it must clearly identify the complaint file as having an associated or included MDR event file.

Non-MDR Investigations

Complaints that don't result in an MDR still need to be investigated if they allege:

- Possible failure to meet a device specification;
- Possible failure to meet a labeling specification; or
- Possible failure to meet a packaging specification.

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

Approvals, *from Page 7*

Misonix Earns CE Mark For Ultrasonic Surgical Device

Misonix's Nexus platform has gained the CE Mark, following the FDA's approval of the system in June.

The ultrasonic surgical device combines all of the company's solutions into a single platform, including its BoneScalpel, SonicOne and Sonastar, and it is designed to accommodate future devices.

Nexus features a new digital algorithm that provides more control and efficiency, and increased power to improve tissue resection rates.

Endologix Grabs IDE For Aneurysm Sealing Protocol

The FDA granted Endologix an investigational device exemption approval for its Nellix Chimney EndoVascular Aneurysm Sealing System (ChEVAS) for treating complex abdominal aortic aneurysms.

The system, an endovascular AAA treatment, is designed to join the company's Nellix 3.5 endograft with parallel visceral stents.

Endovascular aneurysm sealing "will offer innovative new technology to a group of patients that are underserved by the current standard of care," the devicemaker says.

Shimadzu's Earns 510(k) Clearance For Radiographic Table

The FDA has granted Shimadzu Medical Systems 510(k) clearance for its Fluorospeed X1 platform, a radiographic/fluoroscopic (RF) system.

The Torrance, California devicemaker's system offers high image quality and multiple features to improve workflow, including image recording and programmable function buttons.

The system supports a wide range of general RF applications, such as chest, abdomen, or extremities along with Upper GI's.

NinePoint's Imaging System Cleared by FDA

NinePoint Medical's NvisionVLE Imaging System has received 510(k) clearance for use in the bile duct and pancreases.

The device's new clearance allows it to be used to generate high-resolution, real-time volumetric images of tissues and subsurfaces in the pancreatic-biliary systems.

The imaging system is designed to be used with the company's Low-Profile Optic Probe, which enables physicians to image small anatomies such as the pancreas and bile duct.

Infant Hemoglobin Monitor Receives CE Mark

Masimo gained the CE Mark for its SpHb hemoglobin monitor for newborns and infant patients that weigh less than 6.6 lbs.

The device is a noninvasive, continuous monitor that measures total hemoglobin, oxygen saturation and methemoglobin. It isn't intended to replace laboratory blood testing, Masimo said.

With its receipt of the CE Mark, the device is now available to patients of all ages in the EU.

MT.DERM's Microneedling Device Receives FDA Clearance

The FDA has granted German devicemaker MT.DERM 510(k) clearance for its microneedling device for treating acne scars and facial wrinkles.

The lightweight handpiece includes adjustable speed modes and it uses a separate power unit to prevent overheating.

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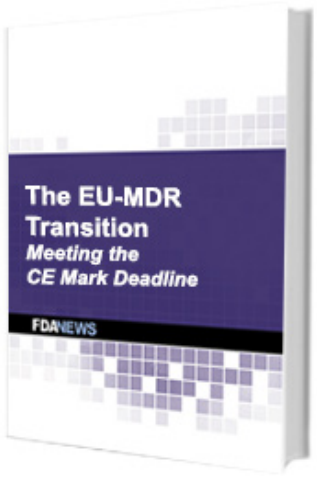

The EU-MDR Transition: *Meeting the CE Mark Deadline*

If you plan to continue putting devices on the European market, you'll need to implement the EU-MDR.

Due to the slow progress in the EU companies are being guided through a soft transition plan.

Dan O'Leary — industry expert with more than 30 years of experience in quality, operations and program management — explains the hybrid system, where you maintain a device certificate under the MDD and a QMS under the MDR.

The EU-MDR Transition: *Meeting the CE Mark Deadline* explains how to take advantage of the soft transition to the new regulation. The soft transition allows companies to retain certain aspects of the current CE Mark applications while following new registration requirements, if their notified bodies approve.

But, what does that really mean?

This report breaks down all the rules and explains all the implications of a soft transition, providing a path to follow to full compliance:

- **Transition Timeline:** All the dates and deadlines on the transition timeline
- **SOPs:** How to develop an SOP for the post market surveillance you will have to conduct under EU-MDR
- **Adverse Events:** How to report adverse events
- **Forms:** What new forms will be required
- **Technical documentation:** How to structure technical documentation for your hybrid system

Start implementing the hybrid MDD/MDR system to keep your products on the European market until the full EU-MDR comes into effect.

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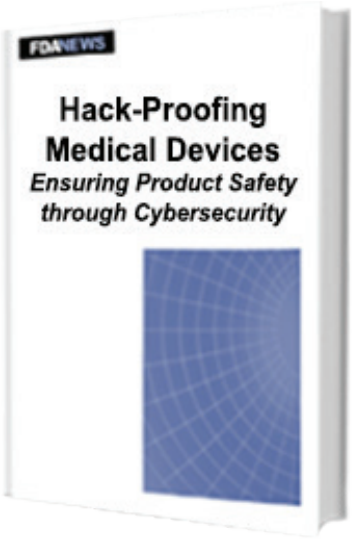

Hack-Proofing Medical Devices: *Ensuring Product Safety through Cybersecurity*

How does the FDA expect you to fight cyber incursions?

With the recent release of the final guidance on postmarket management of cybersecurity, you now have advice from the agency.

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- And much more!

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