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IN THIS ISSUE

Editor's Note: Due to the holidays, *International Devices & Diagnostics Monitor* will not be published Dec. 23. The next issue will be published Jan. 6, 2020.

EMA Group Flags Concerns Over Notified Bodies Assessing Companion Diagnostics

A European Medicines Agency expert group has raised concerns about notified bodies assessing companion diagnostics.

Experts from Belgium, Germany and the Netherlands said that the EMA should consider whether the current system for assessing companion diagnostics tests is still fit for purpose, according to a report released by the EMA's Genomics, Genetics, Transcriptomics and Epigenetics subgroup.

Currently, the EMA doesn't assess companion diagnostics and genetic testing platforms, because this is the purview of notified bodies. The report notes that in the U.S., the FDA assesses and grants approval for companion diagnostic and genetic testing platforms.

The authors suggest that a system that has a more central assessment companion diagnostics could be more beneficial and consistent.

(See **EMA**, *Page 2)*

Low-Risk Devices May Gain More Time to Comply With EU MDR

The EU proposes to allow low-risk Class I devices four more years to comply with the EU Medical Device Regulation.

The Council of the European Union's latest set of corrections for the EU MDR would extending the compliance date for low-risk Class I devices to May 26, 2024.

The proposed revision would clarify that Class I devices that need a conformity assessment for CE marking and had a conformity assessment conducted before May 26, 2020 could be placed in the market until May 26, 2024.

The proposed change applies to devices that may have been upclassified as a result of the MDR.

The addition to the regulation states that: "By way of derogation from Article 5 of this Regulation, a device which is a class I device

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pursuant to Directive 93/42/EEC, for which the declaration of conformity was drawn up prior to 26 May 2020 and for which the conformity assessment procedure pursuant to this Regulation requires the involvement of a notified body, or which has a certificate that was issued in accordance with Directive 90/385/EEC or Directive 93/42/EEC and that is valid by virtue of paragraph 2 of this Article, may be placed on the market or put into service until 26 May 2024, provided that from 26 May 2020 it continues…"

The European Commission released a previous MDR update in March, providing guidance on the Eudamed inspection database and the device nomenclature system that will be used for the EU MDR and EU IVDR. The new regulations go into effect on May 26, 2020 for devices and on May 26, 2022 for IVDs (*IDDM*, March 29).

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The group noted that under the new EU IVDR that becomes effective in 2022, notified bodies will have to interact more with regulators, and notified bodies can request that the EMA and national agencies provide input on a medical device in a consultation procedure.

Such a system could lead to "variability in the assessment of diagnostic tests and hence variability in performance characteristics that may ultimately affect the benefit/risk balance of medicinal products that are used specifically based on the results of a diagnostic test," the report said.

In the EU, when a medicinal product is administered based on a genomic diagnostic test, the requirement for industry at the time of marketing authorization is that a CE marked diagnostic test, as certified by a notified body, is available on the market, the group said.

"With the increasing complexity of genomics tests and the increasing importance of these tests in the adequate use of medicinal products (in particular in oncology, as reflected by a sharp increase in the number of oncology medicinal products, which are used specifically in patients with certain genomic characteristics), it needs to be considered whether the current system for assessment of in vitro (companion) diagnostic tests is still fit for purpose," the report said.

For example, a guideline being drafted includes recommendations on developing predictive biomarker-based assays including companion diagnostics.

Read the report here: www.fdanews.com/12-06-19-EMA.pdf.

FDA Warns Device Manufacturer, Sterilizer in Texas

The FDA sent a warning letter to American Contract Systems for process validation violations at its Houston, Texas medical device manufacturing and sterilizing facility.

An agency inspection revealed that the sterilization operations were not adequately validated to demonstrate that all component materials, sizes, solutions and types could undergo and withstand the sterilization process.

For example, the process challenge packs it used for sterilization did not represent the facility's routinely sterilized components in each product family and there was no data to support its selection of worst-case components used in the packs.

The agency also warned the firm for not having procedures to monitor and control process parameters to ensure that the specified requirements continue to be met.

A review of the facility's device master records showed that critical component specifications for sterilization processing were not identified for its top five selling sterilized surgical trays, an issue the agency also flagged during a previous inspection. The agency found that the five trays were sterilized using processes that had not been validated.

Read the American Contract Systems warning letter here: www.fdanews.com/12-06-19-AmericanContractSystemsWL.pdf.

Think Tank Rips Medical Device Tax

The Tax Foundation, a Washington, D.C.-based think tank, called for the repeal of the 2.3 percent medical device tax introduced under the Affordable Care Act, finding that it would heavily impact the medical device industry.

Congress passed a moratorium in 2016 to suspend the tax, which was extended last year to expire on Dec. 31, 2019. The tax is scheduled to take effect on Jan. 1, 2020 if the moratorium is not extended.

The policy group said the tax is not sound policy "due to its complexity and adverse economic effects." It claims that the tax would result in a decline of about 21,000 full-time jobs and a $1.7 billion reduction in gross domestic product.

It also argued that the tax narrowly targets profit margins of the medical device industry, which would ultimately stifle innovation.

The Tax Foundation also flagged that the tax lacks transparency and neutrality, noting that smaller device companies, particularly startups, would face a greater burden than larger companies.

The foundation also argued that the tax would result in higher costs to consumers, and limit access to the newest medical technology because of the increased costs on both patients and the industry.

BRIEFS

Brazil Reports Half of GMP Certificates Now Issued Under MDSAP

Brazil's ANVISA has reported that almost half of the GMP certificates it issued in 2019 were under the Medical Device Single Audit Program.

In 2019, the MDSAP program met its milestone of 5,000 participating companies, and 48.7 percent of the total international health product certificates issued by ANVISA were made using the MDSAP program.

In 2019 ANVISA issued 321 GMP certificates under MDSAP compared to 107 certificates in 2018 and just 38 in 2017. It conducted 84 international health product inspections in 2019 compared to 110 in 2018 and 238 in 2017.

With the increase in companies participating in the program, ANVISA can "conduct fewer inspections and focus resources on the most risky situations, ensuring efficient use of public money," the agency said.

In addition to resource savings, MDSAP represents an increase in health safety since auditors

(See **Briefs**, *Page 4)*

FDA Explains New 510(k) Pathway For Magnetic Resonance Coils

The FDA released draft guidance outlining the performance criteria sponsors of certain magnetic resonance coils should use to support substantial equivalence instead of a direct comparison. The guidance applies to sponsors who wish to submit a 510(k) application using the agency's Safety and Performance Based Pathway.

The guidance covers Class II MR coils that are intended for hydrogen/proton imaging for general diagnostic use. The devices are not meant to make contact with patients, and if they do, it should be limited contact with intact skin, the agency said. Coils intended for specific clinical indications or specifically intended for use with imaging agents are not included in the guidance.

Devices that qualify for the pathway do not need to provide direct comparison testing against a marketed predicate device to show they have "substantially equivalent performance characteristics," the agency said.

Instead, the agency recommends providing a results summary for all tests evaluated along with other submission information identified for eight specific tests the agency describes in the guidance. The test information, including a results summary, test protocols, or complete test reports, should be submitted as part of the 510(k) application.

Read the draft guidance here: www.fdanews.com/12-06-19-MR-Coil-Safety-Guidance.pdf.
— Jordan Williams

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inspect companies more frequently, reporting to the agency annually as well as to other agencies participating in the program.

ANVISA is a founding member of MDSAP, having developed the program along with the FDA, Japan's Pharmaceuticals and Medical Devices Agency, Australia's Therapeutic Goods Administration and Health Canada.

UK Issues Class II Recall for Pre-Filled Emerade Adrenaline Pens

The UK's Medicines and Healthcare products Regulatory Agency issued an alert that Emerade adrenaline autoinjectors have failed to operate, and PharmaSwiss (a Bausch & Lomb affiliate) is recalling all unexpired batches.

Bausch & Lomb has determined that one component of the autoinjector has failed to activate, particularly when pens are exposed to high temperatures.

The MHRA advised healthcare professionals to stop supplying the products and to quarantine all remaining stock and return it to the supplier. The agency noted that in the UK there is an insufficient supply of alternative brand adrenaline pens to replace all the Emerade pens held by patients.

The agency said that EpiPen and Jext strengths of 300 mcg could be used instead of 500 mcg Emerade pens. The MHRA advised that patients traveling to hot climates should carry an alternative brand pen.

Malaysia Opens Consultation On Orphaned Devices

Malaysia's Medical Device Authority is asking for industry input on a proposal to allow the continued use of orphaned devices that can't be registered because the manufacturer or authorized representative in Malaysia is no longer available.

There are numerous such devices that were in use in hospitals before Malaysia enacted a new medical device law in 2018. The act made it illegal to sell devices without a license, which means that many devices would need to be withdrawn from the supply chain.

The agency is proposing that the devices continue to be used, and that healthcare facilities with orphaned devices identify and provide notification.

The healthcare facilities will be responsible for the device rather than the manufacturer or authorized representative. The notifier can be a local government, private healthcare facility or a related facility.

Read the guidance here: www.fdanews.com/12-06-19-MDGuidance.pdf.

Respire Nets Eleven-Item 483 Over MDR Submissions

Failure to investigate complaints about devices that did not meet specifications and other serious quality system deviations landed Respire Medical Holdings an 11-item 483 following an FDA inspection of its Brooklyn, New York facility.

The company, which manufactures sleep apnea and dental devices, failed to evaluate complaints to determine if a medical device report should be submitted to the FDA, the agency said.

It received at least 19 complaints about its dental devices, ranging from the fixing element breaking off to patients waking up with screws under their lips. Some developed allergic reactions while others experienced burning of the mouth, and one patient possibly ingested part of the acrylic device.

The facility's design validation didn't ensure that devices conformed to defined user needs and intended uses. For example, the firm conducted a design change for its Respire Blue sleep apnea device, but the design plans didn't describe or reference design and development activities or assign responsibility for implementing changes.

In addition, a technician was observed conducting a final release of one of the Respire Blue devices, documenting the measurements as "bite is good" and "fit is good." The agency investigators noted that the technician didn't measure the device using calipers or any other testing equipment.

Read the 483 here: www.fdanews.com/12-06-19-respiremedicalholdingsllc483.pdf.

Identifying Fraudulent Complaints

Trend data are only as good as the individual complaints providing the information. Not all complaints are equally valid. Some are, in fact, fraudulent. No company wants its customer service reps or other officials spending time on fraudulent complaints.

However, these may not always be easy to distinguish, especially at first; indicators of fraud can be subtle, warned Carol Kozlowski, manager of crisis management for insurance services at RQA. However, a carefully crafted complaint-handling system should include procedures to help identify any red flags for fraudulent complaints. Any red flags noted should be documented immediately.

Nonetheless, she recommended, companies should start from the assumption that a complaint is real. Each complaint should be handled the same, with escalation and investigation as warranted per the company's complaint-handling SOPs. However, employees should always be on the alert for red flags, such as a complainant that:

- Provides inaccurate/incorrect personal data information, such as telephone number, address, employer, Social Security number or driver's license number;
- Provides an address that is a post office box, relative's address or friend's address;
- Demands a quick settlement;
- Forgets pertinent details or gives different versions or a rehearsed version of the incident;
- Provides vague or inconsistent loss details;
- Has extensive knowledge of insurance terms and policy information;
- Is unwilling to respond to questions concerning the loss or injury, or to provide documentation;
- Refuses to provide the sample for testing, or says the product is not available/has been thrown out;
- Has an extensive claims history;
- Obtains immediate attorney representation;
- Reports incident details that do not correlate with the documents provided or test results;
- Does not provide witnesses;
- Threatens adverse publicity if the claim is not settled quickly or not as demanded;
- Is or was having financial difficulties; or
- Inquires about a settlement early in the claim process.

Excerpted from the FDAnews management report: *6 Steps to Managing Drug and Device Customer Complaints*.

Centurion Medical Hit For Clean Room Violations

Sterile devices were handled in a cleanroom with inadequately defined environmental controls, FDA inspectors found in an inspection of a Centurion Medical Products facility in Howell, Michigan.

The manufacturer of catheters and other surgical equipment also lacked a validation process for sealing a sterilized product. The company said that a validation was previously completed for a similar product, but the agency investigators noted it did not use the same packaging material.

The FDA officials also noted that airborne particulate monitoring results exceeded the action limit on two occasions, but the investigation was not fully documented.

In addition, the firm did not perform testing using worst-case conditions and its CAPA procedures were inadequate, the agency said.

Read the Centurion Medical Products Form 483 here: www.fdanews.com/12-06-19-centurionmedicalproductscorp483.pdf.

FDA Finds Integra's CAPA, Design Transfer Procedures Inadequate

Corrective actions by Integra Neurosciences may have affected the integrity of its external drainage systems and led to a cerebrospinal fluid leak, FDA inspectors found during an inspection of the firm's Anasco, Puerto Rico plant.

The agency said the neurosurgical devicemaker needed to establish and validate specifications to prevent breakage of the stopcock component during use.

Design transfer procedures weren't implemented to ensure that device design specifications were correctly translated to production specifications through product testing, the agency said.

In addition, the firm's acceptance activities did not include quantifiable critical device specifications, and purchasing control procedures were inadequate to ensure that all products the firm received conformed to specifications.

Read the Integra Neurosciences Form 483 here: www.fdanews.com/12-06-19-integracincdbaintegranurosciencesprinc483.pdf.

Lawmakers Say Insurance Claims Should Include High-Risk Device Identifiers

Sens. Chuck Grassley (R-Iowa), Elizabeth Warren (D-Okla.) and three representatives urged the Centers for Medicare & Medicaid Service to begin including information from unique device identifiers (UDIs) for high-risk implants on electronic insurance claims.

Last month, X12, the American National Standards Institute committee in charge of insurance claim transactions, issued draft recommendations for incorporating UDI device identifiers in claims forms. The lawmakers are asking CMS to adopt this guidance, which would allow device identifiers of high-risk implants to be included in claims transactions.

Listing the device identifier – required on UDIs to identify the labeler and the device's version or model – would improve the quality of healthcare by enhancing tracking information on implants like cardiac stents and artificial joints, the legislators claim.

"This overdue change will help to reduce health risks and costs to the Medicare system," they said. "Including this information in claims transactions will enhance post-market surveillance of potential faulty devices and streamline the process of identifying affected patients when problems arise."

Read the lawmakers' letter here: www.fdanews.com/12-06-19-LetterUDIs.pdf.
— James Miessler

APPROVALS

FDA Clears Sealing Instrument For Intuitive's Surgical Systems

The FDA granted Intuitive clearance for its SynchroSeal vessel sealing instrument and accompanying E-100 generator for its da Vinci surgical systems.

The new devices help surgeons seal and transect tissues and vessels more quickly, improving procedures performed by the company's da Vinci X and Xi robotically-assisted surgical systems that require sealing.

The SynchroSeal instrument uses advanced bipolar energy to transect tissue and cool down quickly in a one-step process performed with a single pedal press.

EOS Imaging Gets 510(k) Clearance for X-ray System

EOS Imaging received 510(k) clearance from the FDA for its EOSedge X-ray system, a device used for high-quality musculoskeletal imaging exams.

The system is the first of its kind to use a high-resolution photon counting detector to provide high image quality. It features an open cabin with an enlarged patient platform for comfortable access and larger fields of examination.

The device uses FlexDose technology, which controls the radiation dose delivered to the patient.

NeuroOne's Cortical Electrode Cleared by FDA

The FDA issued 510(k) clearance for NeuroOne's Evo thin film cortical electrode, a device used to temporarily stimulate, monitor and record brain activity.

This thin film technology "offers the potential for improved resolution during recording brain activity, future placement through a less invasive procedure, and reduced inflammation of brain tissue," the company said.

NeuroOne plans to apply its cortical electrode technology to other devices for use with therapeutic applications for Parkinson's disease, epilepsy and for spinal cord stimulation.

CryoLife Nabs CE Mark for Minimally Invasive Thoracic Stent Graft

CryoLife earned the CE Mark for its E-nya thoracic stent graft system for minimally invasive repairs of descending thoracic aorta lesions, including thoracic aortic aneurysms and dissections.

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Approvals, *from Page 7*

The device features different configurations, including bare spring and covered proximal configurations, to give physicians more flexibility and control for simple and complex anatomies.

Most patients with thoracic aortic disease are treated using minimally invasive endovascular stent grafts.

FDA Approves Tusker Medical's Ear Tube Delivery Device

The FDA granted Tusker Medical approval for its Tubes Under Local Anesthesia (Tula) system, a tympanostomy tube delivery device for treating recurrent ear infections, also known as otitis media.

The device is the first ear tube delivery system that can be used in young children using local anesthesia in the doctor's office, enabling treatment without the use of general anesthesia, the agency said.

The system uses Tusker Medical's ear tubes, its anesthetic Tymbion, and several devices used to deliver the ear tubes and anesthetic into the ear drum.

Venus Concept Nabs CE Mark, Canadian OK for Laser Hair Removal System

Venus Concept has received both the CE Mark and a Health Canada medical device license for its Venus Epileve product, a portable laser hair removal device.

The device is intended as a treatment for male-pattern hair growth in women, permanent hair reduction and razor bumps in Europe, and for hair removal and permanent hair reduction in Canada.

The product features a real-time cooling system for patient safety and comfort. A limited launch is planned in the second quarter of 2020, followed by a full launch in the second half of the year.

Renovia Earns 510(k) Clearance For Urinary Incontinence Treatment

Renovia has received 510(k) clearance from the FDA for its Ieva Pelvic Digital Therapeutic, a device used to strengthen the pelvic floor muscles and treat mild to moderate urinary incontinence in women.

The device offers real-time feedback to women performing pelvic floor muscle exercises by using a movement-based sensor.

The company plans to publish the results of its recently completed multi-center trial "in the coming months," noting that the study found statistically better results for users of the UI treatment. A larger multi-center trial is planned to kick off in the first half of 2020, Renovia said.

FDA Clears Disposable Sheath For Hysteroscopy System

UVision360 has received 510(k) clearance for a rotatable disposable sheath attachment for its Luminelle DTx hysteroscopy system.

The system uses a wide-angle lens, long depth of view and an algorithm that automatically adjusts focus and lighting during hysteroscopy and cystoscopy procedures.

The newly cleared attachment measures 3mm in diameter, reducing the need for anesthesia due to its small size, the company said.

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Customer Service
888.838.5578 • +1 703.538.7600
customerservice@fdanews.com

Editorial: Declan Conroy
+1 703.538.7644
dconroy@fdanews.com

Ad Sales: Jim Desborough
+1 703.538.7647
jdesborough@fdanews.com

Multi-User Sales: Bailey Sterrett
+1 703.538.7637
bsterrett@fdanews.com

300 N. Washington St., Suite 200 • Falls Church, VA 22046-3431 • www.fdanews.com

Reporters: James Miessler, Jordan Williams, Colin Stoecker

President: Cynthia Carter

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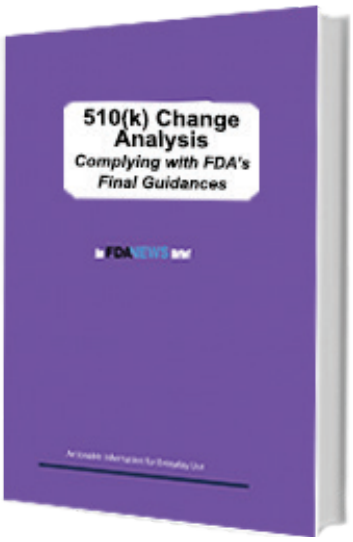

510(k) Change Analysis: *Complying with FDA's Final Guidances*

510(k) Change Analysis: *Complying with FDA's Final Guidances* breaks down the guidances finalized in October, 2017 — *Deciding When to Submit a 510(k) for a Change to an Existing Device* and *Deciding When to Submit a 510(k) for a Software Change to an Existing Device* — and provides a step-by-step method for making the right call for submitting a new 510(k) application. Expert-developed spreadsheets walk you through the questions you must ask and lead you to the proper conclusion.

After reading this book, you'll understand:

- What kinds of changes trigger the need for a new 510(k) application and which don't
- How to evaluate the effect of the change on the device's safety and effectiveness
- How to assess the risk the change may introduce
- The components of risk as described in ISO 14971
- How to follow the complex flowcharts the guidances present
- How to develop a risk matrix
- How to document the decision-making process, including justifying a decision not to file a new 510(k)

In addition to the decision-making spreadsheets that all but do the work for you, the report includes copies of both guidances and an example of a change analysis effort.

Order your copy of the **510(k) Change Analysis** brief for step-by-step instruction on deciding whether you need to submit a new 510(k) if you change an existing device.

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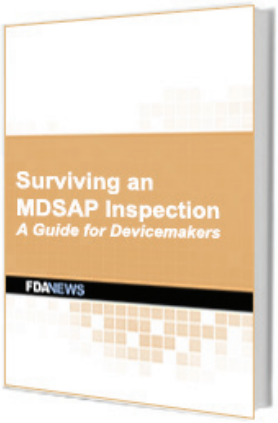

Surviving an MDSAP Inspection: *A Guide for Devicemakers*

Currently, Australia, Brazil, Canada, Japan and the United States are participating in the MDSAP program. If you pass one MDSAP inspection you'll be ready to pursue marketing authorization in five separate countries.

But, if you're going through MDSAP for the first time your experience will be very different from regulatory inspections you've gone through in the past.

- You'll know exactly when and how often to expect an audit
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- You'll know exactly what questions the auditor will ask

The prescriptive nature of the MDSAP model makes it relatively easy to prepare for an audit — if you know what to expect. **Surviving an MDSAP Inspection** provides all the information you'll need to understand the MDSAP model. You'll learn:

- The standard schedule for and duration of audits
- Specific areas auditors will examine and questions they will ask
- Different types of audits involved, such as initial certification, surveillance, desk and site audits
- How to create a checklist to make sure all your bases are covered
- The MDSAP grading system and how nonconformance issues can be escalated — and consequences of getting a bad grade

The management report also includes a copy of the MDSAP Companion document — the official guide — auditors will follow.

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