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Health Canada Expects Some Devicemakers to Opt Out of MDSAP

Health Canada said some devicemakers may cancel their licenses and discontinue selling their products in Canada rather than conform to the new Medical Device Single Audit Program requirements.

Manufacturers had asked the agency to push back the deadline because they were having difficulty scheduling MDSAP audits. All Class II, Class III and Class IV device manufacturers are required to comply with the program requirements by Jan. 1, 2019.

Although the agency said it would stick to the deadline, it said in an earlier notice that it would not take enforcement action if manufacturers have undergone a MDSAP audit by Dec. 31. It also is allowing shorter audits for smaller companies with lower-risk products (*IDDM*, May 14).

(See **MDSAP**, *Page 2)*

European Commission Issues EU MDR/IDVR Implementation Plan

The European Commission issued a new work plan for implementation of EU regulations on medical devices and in vitro diagnostics.

The plan outlines the status and projected timelines for 12 implementing acts for the EU's Medical Devices Regulation (MDR) and In Vitro Diagnostics Regulation (IVDR) as well as 12 other initiatives. The first implementing act was completed last November, defining the scope of notified body designations, which the Commission described as essential for the launch of the NB designation procedure.

According to the working plan, 33 NB designation applications were received as of mid-September and 22 joint assessments have been scheduled.

Other implementing acts will address reprocessing of single-use medical devices and common specifications for products without a medical purpose, both slated for November 2019, and the setting up

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Even so, Health Canada said it expects some manufacturers to discontinue selling their products as early as Nov. 1.

Manufacturers must submit documented evidence of their transition to MDSAP by Dec. 31 to maintain their device licenses, the regulator said. "Medical device licenses may be suspended if manufacturers are not able to demonstrate that they have undertaken the transition to [MDSAP]," the agency said in a new document that responds to frequently asked questions.

The FAQ document also describes transition options. For example, if a manufacturer is completing the audit in 2019, it must provide a completed F202 form as well as an ISO 13485 certificate and documented evidence that it has made arrangements to undergo a MDSAP audit.

Devicemakers choosing to transition to the MDSAP program during a surveillance audit will be required to submit a Canadian medical devices conformity assessment certificate with their transition documentation in lieu of a MDSAP certificate, the agency said.

Companies that hold a Canadian conformity assessment certificate that doesn't expire until after Jan. 1., 2019, should contact their auditing organization to transition to MDSAP. Both recognized and authorized auditing organizations are approved to issue MDSAP certificates.

Devicemakers that only sell products in Canada will be required to transition to MDSAP, but they will not be audited for requirements in Australia, Brazil, Japan and the U.S., the agency said.

The regulator said that distributors, retailers and private label manufacturers don't need a MDSAP certificate. However, original equipment manufacturers are subject to MDSAP requirements, and if the OEM does not plan to transition, the product may not be able to be sold or advertised in Canada. It clarified that stockpiling of products will not be allowed.

The MDSAP program allows a single regulatory audit of a manufacturer's quality system to satisfy requirements in multiple regulatory agencies. Health Canada stressed that the program was announced three years ago to give manufacturers time to comply.

Read the FAQ document here: www.fdanews.com/10-18-18-MDSAPFAQ.pdf.

EU, *from Page 1*

of expert panels, scheduled for the third quarter of 2019. The schedule also includes the setting up of expert laboratories. The timing is still to be determined but will be in 2020 at the earliest.

Rules to facilitate fulfilment of tasks by EU reference labs and to ensure their compliance are scheduled for the fourth quarter of 2019 or the first quarter of 2020, as well as the setting up of new structures under the IVDR for EU reference laboratories. Surveys with Medical Device Coordination Group members and stakeholders are ongoing, the Commission said.

MedTech Europe has expressed concern that only two of the 18 mandatory implementing acts have been completed so far. The MDR is scheduled to take effect on May 26, 2020, followed by the IVDR on May 26, 2022.

Read the Commission's work plan here: www.fdanews.com/10-18-18-EC.pdf. — Zack Budryk

FDA Issues Premarket Guidance For Devices With Cybersecurity Risks

The FDA has released guidance for sponsors of devices with cybersecurity risks on what they should include in their premarket submissions, as well as considerations for device design and labeling.

The guidance defines two types of devices by level of cybersecurity risk — tier one and tier two. Tier one devices can connect, either wired or wirelessly, to other devices, a network or the Internet, and could result in harm to the patient(s) if compromised by a cybersecurity attack. Examples include pacemakers, dialysis devices and insulin pumps. Tier two devices are any devices that don't meet the criteria for tier one.

"These recommendations can facilitate an efficient premarket review process and help ensure that marketed medical devices are sufficiently resilient to cybersecurity threats," the agency said.

The device's design documentation should center around showing that the device is "trustworthy" — the device should be reasonably secure from cybersecurity misuse and intrusion and follow generally accepted security procedures.

The guidance makes many recommendations for device trustworthiness in Section V related to limiting access to trusted users, authenticating and checking authorization of safety-critical commands, ensuring content is trusted through code/data integrity and maintaining data confidentiality. For tier one devices, design documentation should address all of these recommendations; tier two devices should either do the same or include a risk-based rationale explaining why cybersecurity design controls aren't needed.

The agency includes specific recommendations for labeling. For example, it suggests that the labeling should include proper cybersecurity controls for the device — such as the use of an antivirus or firewall. Additionally, labeling should describe features that protect the device's critical functions, and should describe procedures for backup and restoration of backups.

The guidance also suggests specific design features and cybersecurity controls the agency believes should be incorporated. It recommends that the device should only allow cryptographically verified updates or firmware to be installed, and suggests that the integrity of all incoming data be verified. Design features should also detect and track any security compromises and permit routine security and antivirus scanning.

Read the full guidance here: www.fdanews.com/10-18-18-Cybersecurity.pdf. — James Miessler

FDA and DHS Expand Cooperation To Ensure Device Cybersecurity

The FDA and the Department of Homeland Security signed a memorandum of agreement that expands their collaboration for medical device cybersecurity.

The agreement formalizes a long-standing relationship. The two agencies have collaborated in the past on different aspects of medical device security, such as the coordination of vulnerability disclosures, which provides devicemakers with technical information about vulnerabilities from cybersecurity researchers and allows quick responses to potential threats.

They've also worked together on after-action reviews of cybersecurity drills led by DHS, which simulate real-world cybersecurity attacks and allow stakeholders and agencies to practice and develop responses to threats.

The FDA said that the potential for threats and vulnerabilities rises with increased medical device innovation and integration with hospital networks and technology — such as other devices. As this happens, "ensuring that devices are adequately protected against cyber intrusions [becomes] paramount to protecting patients," FDA Commissioner Scott Gottlieb said.

Gottlieb said the partnership will help the two agencies share information and work together to "stay a step ahead of constantly evolving medical device cybersecurity vulnerabilities."
— James Miessler

UK's MHRA Issues Guidance On How to Comply With EU MDR

Some medical devices that don't have an intended medical purpose — such as non-prescription colored contact lenses — will be required to comply with the EU's new regulations for medical devices by May 26, 2020, the UK's Medicines and Healthcare products Regulatory Agency said in a new guidance on Annex XVI of the EU's Medical Device Regulation.

Devices on the Annex XVI list are similar to medical devices but the manufacturer claims only an aesthetic or other non-medical purpose. The groups of products were included in the new regulation to "introduce requirements around the manufacturing and surveillance of these previously unregulated products to protect the health and safety of users," the agency says.

The products are classified into six broad groups:

1. Contact lenses or other items intended to be introduced into the eye, such as non-prescription colored contact lenses;
2. Products that modify the anatomy through invasive measures such as solid body contour modifying implants (excluding piercing and tattoos);
3. Substances used for facial or other mucous membrane filling by subcutaneous, submucous or intradermal injections such as dermal fillers;
4. Equipment used to reduce, remove or destroy adipose tissue, such as equipment for liposuction, lipolysis or lipoplasty;
5. High intensity electromagnetic radiation emitting equipment such as lasers and intense pulsed light equipment used for skin resurfacing or body hair removal; and
6. Equipment intended for brain stimulation that applies electrical currents or magnetic or electromagnetic fields that penetrate the cranium to modify neuronal activity in the brain, such as transcranial stimulation.

Manufacturers of these types of products will need to first identify which risk class the device falls under. A conformity assessment by a notified body might be required as well as a CE mark and a basic unique device identifier. The manufacturer will need to submit information to the UDI database as well as the Eudamed database.

In addition, the manufacturer will need to comply with common specifications that explain how products should be assessed to demonstrate safety and performance. The specifications must include risk management and may also cover clinical evaluation.

Other manufacturer obligations include having a responsible person for regulatory compliance in place, and ensuring that distributors and importers in the supply chain are compliant. Other post-marketing requirements will apply, including periodic safety reports.

Read the MHRA guidance here: www.fdanews.com/10-18-18-MHRA.pdf.

FDA Hits French Devicemaker for MDRs

Cair LGL, a manufacturer of medical devices and equipment for hospitals, failed to properly submit MDRs, adequately maintain complaint files or evaluate complaints, the FDA said following a February inspection of its facility in Lissieu, France.

The FDA issued a Form 483 noting the facility failed to submit an MDR report within the required 30-day window of receiving or becoming aware of information suggesting a device had malfunctioned in a way that would likely contribute to death or serious injury if it recurred.

The inspection found the firm missed the 30-day reporting deadline by up to 212 days.

In addition, some individual complaints referenced numerous device malfunctions, but the facility's complaint trending failed to account for a single received complaint referencing multiple device malfunctions.

Read the 483 here: www.fdanews.com/10-19-18-Cair.pdf. — Zack Budryk

Root Cause Analysis and Investigations

Failure to conduct adequate investigations is one of the most frequent findings of noncompliance made by U.S. and European regulators. Investigations have several objectives:

- Identifying the cause of the failure (or event);
- Determining if the item(s) affected by the unwanted event can be corrected (e.g., reprocessed or reworked in some way);
- Finding ways to prevent the problem from happening again; and
- Understanding the scope (how big the issue is, how many products might be affected) and the impact of the problem on patients, including direct impact and a secondary impact should there not be adequate supplies of a medically need product.

There are several different triggers that prompt an investigation in a pharma manufacturing and quality organization. Deviations, quality events, unusual trends, out-of-specification (OOS) results, out-of-expected (OOE) results, complaints, adverse events, failures or rejections are some of the typical initiating situations. What is done and the urgency of the response is usually determined by some type of procedure-defined risk-based assessment strategy that triages the event into "minor," "major," or "critical" events.

In some limited situations, an investigation may not be necessary. For example, if the event is immediately observed, its cause obvious, the issue can be simply and immediately corrected, it is not a GMP compliance issue or at odds with the marketing authorization, and has no patient impact, the event should be simply documented and the root cause and symptom trended. If any of these conditions are not met or if this is happening more often (i.e., a trend appears) then an investigation could commence. (Your firm should consider a risk-based strategy based on the products made and the patients served.)

Those who investigate accidents or crimes refer to "the golden hours" — typically the first 12 to 24 hours after the event during which finding clues, recovering evidence and interviewing people is most productive. After this period, memories fade, evidence deteriorates, and clues can disappear. While not always possible — for instance in the event of a customer complaint or a failed stability sample — the sooner one begins an investigation and collects "fresh" evidence, the better the chance of getting to the true root cause(s). Assuming you have 30 days to get the investigation completed, if you start on day 20, you often will be spending more total time and not have as much success in getting to root cause.

The type, size and complexity of the incident dictates, in part, the approach that is used in investigating it. For relatively straightforward situations, one lead investigator may do a suitable job. In other cases, the investigation may require a cross-functional team involving people who have particular sets of knowledge and skills. In some situations, a team may call on those with special expertise to be external, short-term resources to the investigators.

Excerpted from the FDAnews management report: *Quality Management Essentials – Expert Advice on Building a Compliant System*.

FDA Releases Fall List Of Planned Rulemakings

The FDA released its semi-annual regulatory agenda including the following proposed and final rules for medical devices and diagnostics:

- A final rule, expected in November, that implements a section of the FDA Safety and Innovation Act requiring the agency to use administrative orders to announce or change device classifications — instead of doing so through regulation;
- A final rule that will reclassify in vitro diagnostic devices for Bacillus detection into class II (special controls). The agency believes the change, which is set for March 2019, is necessary to "provide a reasonable assurance" of the safety and effectiveness of IVD Bacillus diagnostic devices;
- A proposed rule that would establish procedures and criteria for the de novo process that increase its transparency and predictability to devicemakers. The agency did not include an expected action date for the rulemaking;
- A proposed rule that would make the FDA's regulations consistent with a statutory change in the FD&C Act that excludes certain medical software functions from the "device" definition and thereby takes them out of the agency's jurisdiction. The agency did not include an anticipated action date; and
- A proposed rule meant to revise the quality system regulation of medical devices for harmonization. The revisions will replace existing requirements with specifications that reached an international consensus standard — ISO 13485:2016. The revisions are intended to lessen regulatory and compliance burdens on devicemakers.

The agency said it no longer plans to finalize some rules including:

- A proposed rule that would have modified the laser product performance standard to be closer to the amended International Electrotechnical Commission (IEC) standard for laser and medical laser devices; and
- A proposed rule that would have required medical device establishments listing certain home-use devices to electronically submit the label and package inserts of FDA-listed devices.

Read the full rule list here: https://bit.ly/2yLmRXG. — James Miessler

BRIEFS

Health Canada Designates Devices That Deliver Drugs Via Smoking as Class II

Health Canada has ruled that a medical device that delivers a drug to a patient via smoking (including medical cannabis) is a Class II device.

The regulator notes that a device used for smoking drugs for therapeutic use is considered an active device, because the operation of the device depends on a source of energy other than energy generated by the human body or gravity.

As an active device, a medical license is required to sell such a product in Canada.

UK Coroner Blames Teenager's Death on Inadequate EpiPen

A UK coroner who examined the body of a 15-year old girl who died of anaphylaxis attributed her death to an inadequate dose of adrenaline delivered by an EpiPen needle that was too short.

Natasha Ednan-Laperouse had an anaphylactic attack on an airplane to Nice, France after consuming a bagel that contained sesame. The coroner's report noted the EpiPen needle that delivered the adrenaline was 16 mm, but said the preferred length is 25 mm for adrenaline injectors to access muscle in most individuals.

"I heard during expert evidence that EpiPen needle length was 16 mm — suitable according to the UK Resuscitation Council for pre-term or very small infants," the coroner said. "The combination of what my expert told me was an inadequate dose of adrenaline for anaphylaxis and an inadequate length needle raises serious safety concerns," he added.

CDRH Issues Final Orders On Six Device Classifications

CDRH has issued final orders reassigning classifications for six types of medical devices.

The orders, aimed at cutting burdens associated with premarket applications, cover several categories of device, including those indicated for neurology, ophthalmology, surgery and anesthesiology.

The orders consolidate five device types under class II and one under class I. The five devices grouped into class II include the thermal vestibular for headache, the intranasal electrostimulation device for dry-eye symptoms, the positive airway pressure delivery system, the hemostatic device for intraluminal gastrointestinal use and the positive airway pressure delivery system.

The special controls established by the reclassifications include software verification and biocompatibility. Four are for prescription-only device types, which are exempt from CDRH's "adequate directions for use" rule.

The FDA developed the classification assignments based on de novo classifications CDRH received and granted in 2017 and 2018, with the exception of a 2009 submission CDRH granted in 2012. The classification requests were submitted by companies including FRESCA Medical, Pacer Therapeutics, Allergan, Wilson-Cook Medical, Scion NeuroStim and Moleculight.

Moleculight was the source of the only device assigned to class 1, the wound autofluorescence imaging device.

Read the notices here: www.fdanews.com/10-18-18-CDRH.pdf. — Zack Budryk

APPROVALS

FDA OK's 3mm Micro Instruments For Senhance's Digital Laparoscopy Device

The FDA has cleared new 3mm micro instruments for the Senhance Surgical System, a digital laparoscopy platform.

The clearance of the instruments allows the system to be used for microlaparoscopic surgeries in which surgeons can make tiny incisions in patients.

The capability of the instruments to make very small incisions mean that patients will experience virtually no scarring for many surgical procedures.

Hologic's Bordetella Assay Earns CE Mark

Hologic received a CE Mark for its Panther Fusion Bordetella assay, expanding the menu of the molecular testing device.

The real-time PCR assay can detect and differentiate between B. pertussis and B. parapertussis from samples collected from the patient's nasopharynx.

Because the assay can differentiate between the two bacteria, which are known to cause whooping cough, it enables physicians to prescribe the right antibiotic for the patient.

Transseptal Access System Cleared by FDA

The FDA granted 510(k) clearance for Transseptal Solutions' TSP Crosser, a transseptal access system used for placing cardiovascular catheters in the left heart chambers.

Transseptal punctures are used to access the left side of the heart without having to place catheters in the aorta, by puncturing the septum that separates the left and right atria.

The device is comprised of a sheath, dilator and flexible puncturing needle, with a radiopaque loop wire at the end. The sheath can turn 180 degrees in either direction.

Health Canada Gives Green Light To Medtronic's Insulin Pump

Health Canada has approved Medtronic's MiniMed 670G insulin pump system for use by Type 1 diabetes patients.

The device automatically adjusts basal insulin delivery to stabilize glucose levels and meet

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

Approvals, *from Page 7*

the patient's real-time needs. It was specifically approved for patients seven years of age or older with Type 1 diabetes.

The company said that it expects to launch the insulin pump in Canada this fall. About 300,000 Canadians have Type 1 diabetes.

FDA Shoots Down Clear TearLab Dry-Eye Test for 510(k) Clearance

The FDA determined that the 510(k) application for Clear TearLab's point-of-care TearLab Discovery MMP-9 test did not pass its criteria and the agency declined to clear it.

The platform is designed to allow eyecare professionals to analyze multiple biomarkers contained in human tears with nanoliter-volume collection.

The agency said that the dry-eye test did not adequately demonstrate substantial equivalence based on the data and information provided.

South Korea Health Regulator Clears Non-Small Cell Lung Cancer Diagnostic

South Korea's Ministry of Food and Drug Safety granted approval for AmoyDx's ROS1 fusion assay as an accompanying diagnostic for Pfizer's non-small cell lung cancer medicine Xalkori (crizotinib).

The PCR-based assay received the CE Mark in 2013 and was approved in China and Japan in 2014 and 2017, respectively.

The assay analyzes tumor messenger RNA from tissue or body fluids to identify 14 ROS1 gene fusions that can lead to cancer.

Tandem's Insulin Pump Receives Health Canada Licensing

Tandem Diabetes Care has received a medical device license from Health Canada for its t:slim X2 insulin pump.

The pump is expected to be launched province-by-province in the coming months depending on the product's registration with local health programs.

The device is up to 38 percent smaller than other insulin pumps and can hold up to 300 units of insulin.

CIVCO Radiotherapy's Immobilization System Cleared in U.S. and EU

CIVCO Radiotherapy received 510(k) clearance from the FDA and a CE Mark in Europe for its Solstice SRS immobilization system, which positions the head and neck for radiotherapy treatments.

The system is customizable to position and immobilize a patient's head and neck for radiotherapy, enabling more precise treatment.

The device includes a carbon fiber head support, thermoplastic mask and a customizable cushion.

CIVCO said the product will be available for shipment later this month.

Centric Medical's External Fixation System Cleared by FDA

The FDA granted Centric Medical 510(k) clearance for its Saturn external fixation system, a device used to stabilize the foot, ankle and long bone segments.

The device is made up of rings, struts, threaded rods, pins, wires and connectors, and can be used for fusions, fractures and deformity constructions.

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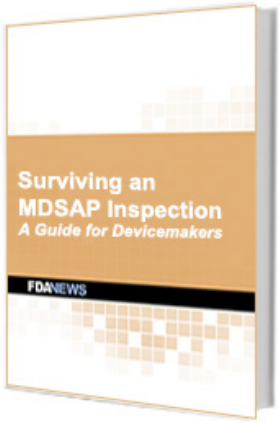

Surviving an MDSAP Inspection: *A Guide for Devicemakers*

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
- You'll know exactly how long the audit will be
- 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.

Order your copy of **Surviving an MDSAP Inspection: *A Guide for Devicemakers*** and know what to expect from an MDSAP audit and how to prepare for it.

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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.

The key is awareness — of product vulnerabilities, current threats, developments in cybersecurity protection, how to defend your company from disastrous liability litigation… and the list goes on.

Hack-Proofing Medical Devices will show you how to get — and keep — control of your devices' networked operations. The management report covers:

- Six environmental stressors that contribute to cybersecurity problems
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- How the FDA and international regulators are handling issues involving software as a medical device (SaMD)
- Types of cybersecurity threats, including ransomware and device piggybacking
- And much more!

BONUS — the report also provides a variety of tools including:

- A checklist for verifying a device's cybersecurity controls status
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