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Senators Question Digital Health Pre-Cert Program

Three Democratic senators raised concerns about the FDA's digital health pre-certification program and called for more details from the agency.

In the Oct. 10 letter, Sens. Elizabeth Warren (D-Mass.), Patty Murray (D-Wash.) and Tina Smith (D-Minn.) included more than 20 questions on the agency's proposed framework for the program, including the FDA's legal framework, the qualification process, monitoring and postmarket surveillance, and the agency's ability to oversee digital health products.

"The agency should be focused on ensuring it has the tools and capacity to guarantee that software products that perform medical device functions are safe and effective and to hold companies that skirt the rules accountable," the letter states. "Instead, the Pre-Cert Pilot focuses heavily on the potential of standards for design, validation, and maintenance of software and the ability to capture post-market data

(See **Senators**, *Page 2)*

Australia Rolls Out New Advertising Regulations for Devices

Australia has updated its regulations covering advertising for medical devices and the changes will take effect in January 2019.

The biggest change is that certain advertisements will no longer require pre-approval beginning in July 2020. However, sanctions and penalties will be much tougher for device manufacturers that fail to comply with the new advertising code.

"The broadened sanctions and penalties will complement the TGA's education and compliance tools to allow us to take a graduated approach to achieve advertising compliance," the Therapeutic Goods Administration said.

The TGA earlier issued draft guidance on a new Therapeutic Goods Advertising Code, which ensures that marketing and

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to reduce premarket review time or eliminate the need for premarket review altogether."

The senators said more detail is needed about the FDA's timeline for deploying a more tailored precertification framework. It's unclear from FDA's working model what specific statutory and regulatory authorities the agency is using for the precertification program or whether the agency will need new statutory authority to precertify entities outside of a pilot, they said.

They also expressed concern about the "challenge questions" that accompany the working models, which are intended to help CDRH and the nine companies participating in the pilot (*IDDM*, Feb. 5).

As part of the set of questions, the FDA asked for feedback on whether there should be "phased market authorization" for Software as a Medical Device (SaMD) in which different elements are reviewed both premarket and postmarket using real world evidence to support full market authorization.

The pilot proposal is ambiguous about what legal authority the agency would draw on to establish an authorization under which SaMDs hit the market before sponsors provide sufficient evidence to justify full market approval, the senators said.

They also questioned the potential overreliance on the National Evaluation System for Health Technology (NEST) and expressed concerns about NEST's capacity "to support the type of hands-off approval and clearance process FDA is proposing for SaMDs."

Read the full letter here: www.fdanews.com/10-11-18-Letter.pdf. — Zack Budryk

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Australia, *from Page 1*

advertising of devices promotes quality use while not misleading consumers.

The new code provides more objective tests for breaches of the code and addresses inconsistencies between drugs and devices. Some new definitions have been included in the new code to give devicemakers more clarity on the new requirements. For example, the definition of a "health warning" clarifies that a warning should only include statements that are critical to a consumer's assessment of a product.

Stakeholders had asked the agency to extend the deadline for compliance to the new code. In response, TGA said it will take a risk-based approach in handling compliance during the transition period and will apply the principles set out in its framework on complaints handling for device advertising.

The agency said it would focus on working with sponsors and manufacturers to correct advertising, with a focus on mandatory statements. Sections 11 to 14 of the code includes required information and statements that manufacturers must include in advertisements.

The agency clarified that the date on which an application for pre-approval is decided will determine the version of the code that the advertising must comply with. For example, if an application decision is made on or after Jan. 1, 2019, advertising will be assessed against the 2018 advertising code. The 2015 advertising code will be used to assess advertising for decisions on goods made on or before Dec. 31, 2018.

Another component of the new regulations is a single platform for online complaints relating to medical device advertising. Under the new system, introduced in July, the TGA has sole responsibility for handling complaints about device advertising directed at the public.

Advertisers can learn how to prepare compliant ads through e-learning modules. The first module on the basics of therapeutic goods advertising regulation is now available, with future modules planned for the coming months. The agency said advertisers can check whether a particular therapeutic good can be advertised to the public by using a simple online decision tool (*IDDM*, July 9).

FDA Warns BD for Contaminated Water, Environmental Conditions

In a warning letter to Becton Dickinson Medical System, the FDA said the devicemaker must further document its corrections to problems with environmental conditions and safeguards against contamination.

The FDA inspected the facility earlier this year and found it had used municipal tap water, which has been found to be a potential source of microbial contamination, in cleaning and disinfecting solutions. In response, the company promised to discontinue its use, temporarily shut down manufacturing operations and permanently remove faucets and sinks from the janitor's closet. The facility also pledged to validate and establish a revised, risk-based cleaning program based on a broader assessment of potential microbiological contaminants.

The inspection also found failure to establish procedures for cleaning or controlling operator practice in the facility's cleanrooms where aseptic filling of saline/heparin syringes took place. Operators in the cleanrooms were observed touching gowns without sanitizing the entire surface of gloved hands and making rapid movements in the cleanrooms despite procedures requiring slow, deliberate movement. In response, the facility committed to only using sterile spray bottles to hold cleaning and disinfecting solutions, as well as to retraining employees on cleaning behavior and practices.

The FDA further faulted the company on its sterility testing for syringes. In response, the company pledged to revise its sampling SOPs, increase the minimum number of syringes required for lot sampling, and add a statistical method for establishing viable alert and action limits.

The company also did not validate either the unidirectional airflow of the laminar flow hoods used for aseptic filling of syringes or the removal of residue of disinfecting and cleaning solutions in the flow hoods, according to the FDA. The facility promised to perform unidirectional smoke studies for the flow hoods.

Lastly, the company did not integrate alarm systems into the laminar flow hoods/cleanrooms to alert employees of a loss in HEPA filtered air, and its environmental monitoring program did not require daily monitoring of the gloved fingers of all cleanroom operators engaged in aseptic syringe filling. The company said it would install and validate continuous monitoring equipment on all flow hoods and cleanrooms.

While all of the firm's responses appear to be satisfactory, the FDA noted that several are ongoing and the agency would conduct a follow-up inspection to verify compliance.

Read the full warning letter here: www.fdanews.com/10-11-18-BDMedicalSystems.pdf.
— Zack Budryk

Allergan Recalls Implant in EU For Loose Silicone Particle

Allergan recalled its Ozurdex 700 mg intravitreal implant because a single loose silicone particle may become detached from the needle sleeve during administration of the implant and may be delivered into the eye along with the implant.

The defect was discovered during a routine manufacturing inspection. The 300 micron silicone particle originated from the needle sleeve. Additional testing by Allergan found two to four percent of defective units, but defect rates as high as 22 percent have been reported.

Although the root cause of the defect has not yet been determined, Allergan identified a corrective action that eliminates creation of the particle and is implementing the correction before releasing additional stock.

"The risks associated with the injection of the silicone along with the Ozurdex implant cannot be precisely ascertained due to a lack of adequate information," Allergan said in an Oct. 5 recall

(See **Allergan***, Page 4)*

Canada's MEDEC Supports Government's Digital Health Strategy

Canada's Medical Technology Companies association said it strongly supports the Canadian government's plans to change the country's complex regulatory, reimbursement and procurement process for medtech.

The government's newly unveiled roadmap to grow Canada's medical technology provides an "unparalleled opportunity for national leadership in addressing barriers that are currently impeding the adoption of health innovation and the growth of the medtech industry," said MEDEC's CEO Brian Lewis.

The roadmap focuses on five areas to grow the nation's medtech industry:

1. Accelerate innovation adoption;
2. Design agile regulations;
3. Harness digital technology;
4. Develop and attract talent; and
5. Create anchor firms.

A primary barrier to adopting innovative devices is the "traditional cost-focused bulk-buy procurement approach" favored by health systems in Canada. What's needed is a procurement approach that moves "beyond price to value," the report said.

It recommends moving toward a value-based system similar to EU models, and it cites the example of Norway, which examined purchase price as well as failure rates and patient-reported pain in its procurement of IV catheters.

Similarly, the Netherlands established a foundation for value-based procurement in the form of a network of hospitals that is measuring patient outcomes, as well as a national registries platform for patient-reported outcomes.

Pre-market notification for devices such as is overseen by the FDA should be adopted in Canada, the report said, stressing that Canada's "multi-tiered system" poses significant hurdles to devicemakers.

The report recommends using more joint reviews and foreign reviews for approval of devices in Canada and calls for more collaboration among provinces and territories to coordinate health technology assessments and streamline reimbursement and procurement decisions.

The government hopes to implement a national digital strategy to guide federal investments in digital health to unify provincial and territorial partners to leverage digital technology to improve care.

Canada's single-payer health system has a number of strengths in implementing such a system, including the ability to collect patient outcome data and to facilitate information sharing among hospitals.

Although Canada has developed some electronic health record systems, what's missing is an interoperable set of systems, a harmonized data and privacy framework and a single accessible electronic record for every Canadian patient, the report said.

Read the full report here: www.fdanews.com/10-11-18-EconomicStrategyTables.pdf.

Allergan, *from Page 3*

notice. The silicone particle "is not expected to degrade, and it will remain permanently in the vitreous cavity unless removed."

The company also warned that a corneal adverse reaction could not be ruled out.

The Ozurdex implant is a combination product indicated to treat macular edema following branch retinal vein occlusion or central retinal vein occlusion. Allergan said that for some patients the benefit of the product might outweigh the risk.

The Class II recall affected 17 batches of products distributed between May 2016 and July 2018 in the EU, the UK's Medicines and Healthcare products Regulatory Agency reported.

FDA Issues Cybersecurity Warning for Medtronic Cardiac Device Programmers

The FDA flagged cybersecurity vulnerabilities in two implantable cardiac device programmers manufactured by Medtronic and approved a software update that will allow providers to continue using the programmers without connecting to the internet.

The Carelink and Carelink Encore programmers are used during implantation and follow-up visits for Medtronic's implantable cardiac devices, including pacemakers, defibrillators, cardiac resynchronization devices and insertable cardiac monitors. The programmer software can be updated either through an internet connection to the Medtronic Software Distribution Network or by a Medtronic representative plugging directly into the device.

The FDA confirmed that an internet connection to the Medtronic network could be exploited and allow an unauthorized user to alter either the programmer or the implanted device. The agency said it considers the company's corrective action to be a voluntary recall.

"While we are not aware of patients who may have been harmed by this particular cyber vulnerability, the risk to patient harm of leaving such a vulnerability unaddressed is too great," said Suzanne Schwartz, associate director for science and strategic partnerships at CDRH.
— Zack Budryk

What to Expect From a MDSAP Audit

With the Medical Device Single Audit Program (MDSAP) being implemented as an inspection standard in five countries — Canada, the United States, Brazil, Australia and Japan — now is the time for devicemakers to learn the ins and outs of this unique audit model.

Companies selling products in Canada will need to be MDSAP certified by the end of 2018. In the U.S., devicemakers can — and, in most cases, probably should — use MDSAP audits as a substitute for regular FDA inspections.

The MDSAP framework generally follows ISO 13485 – Medical Devices, Quality Management Systems and incorporates specific regulatory requirements from each of the countries participating in the program. MDSAP also was modeled on the FDA's Quality System Regulation (QSR), so its focus areas should be familiar to devicemakers inspected by that agency.

There are two key differences between how MDSAP and FDA inspections are conducted. The first is that MDSAP takes a process-based approach and emphasizes linkages between different processes, rather than the traditional "silo" approach FDA inspections tend to take. A MDSAP audit has a much wider scope, breaking down the auditing activities into a series of processes, each of which are allotted a given amount of time. Auditors also look at how these processes feed into one another and the larger quality system the devicemaker has in place.

The second key difference is that MDSAP audits are conducted by approved third-party auditing organizations rather than employees of the FDA or other regulatory bodies.

There are two key documents that form the backbone of MDSAP. The first outlines the actual audit program, laying out the seven processes that make up all MDSAP audits. The second is the MDSAP Companion Document, which contains more details about each of those seven processes, including key goals and outcomes auditors should look for when investigating these areas.

MDSAP audits are based on three-year cycles, which essentially follow the standard audit cycle prescribed by ISO 13485. First, a devicemaker will be subjected to an initial certification audit of its entire quality management system (QMS). That initial audit will take place in two stages. Stage one is a preparation review, or "desk review," while stage two is the on-site audit.

Following the certification audit, a devicemaker can expect surveillance audits every two years and a recertification audit in the third year.

Excerpted from the FDAnews management report: *Surviving an MDSAP Inspection — A Guide for Devicemakers*.

MHRA Seeks Industry Input On No-Deal Brexit Provisions

The UK's Medicines and Healthcare products Regulatory Agency (MHRA) is seeking industry feedback on a potential no-deal Brexit scenario in which the agency would function as a medical device and medicine regulator on its own.

The agency said it would assume its own regulatory responsibilities if post-Brexit negotiations with the EU go sour, including handling new licensing routes, possible new global partnerships, a competitive fee structure and pharmacovigilance duties.

The MHRA called for input from industry, healthcare professionals and the public on the proposed changes in its technical notice, titled "How medicines, medical devices and clinical trials would be regulated if there's no Brexit deal." The comment period closes Nov. 1.

The survey developed by the agency asks stakeholders if they agree with MHRA proposals for various situations. For example, it asks if they support a new plan to incentivize marketing application submissions for rare diseases, as well as a proposal that would see the UK continue to recognize prescriptions from countries on a post-exit country list that will initially include EU and European Economic Area countries.

The agency also called for industry input to help measure costs, such as the administrative and manufacturing costs for altering packaging to include UK information, and labor costs for staff time spent providing baseline data for Centrally Authorized Products.

"Should we not achieve our desired relationship with the EU, the government will ensure that patients are not disadvantaged by the future regulatory regime," MHRA said. "We will establish a regulatory system that continues to protect the interests of patients and strengthens the UK life sciences industry."

Read the MHRA's request for comment here: www.fdanews.com/10-08-18-consultationprintout.pdf. — James Miessler

BRIEFS

UK Extends Expiration Dates For EpiPens to Cope With Shortages

The UK's Medicines and Healthcare products Regulatory Agency extended the expiration dates on Mylan's EpiPen to deal with looming shortages due to ongoing supply issues with Mylan's contract manufacturer, Meridian Medical Technologies.

The EpiPen and EpiPen Junior adrenaline auto-injector pens are expected to be in limited supply for the remainder of 2018. To deal with the shortage, MHRA has allowed the company to extend the expiration dates by four months.

Mylan is out of stock of the EpiPen Junior 150 mcg, and a limited supply is expected in October, with additional deliveries in November. The UK notes that children over 30 kg should use the EpiPen Junior 300 mcg pen.

There are two alternative adrenaline auto-injector devices available: Bausch & Lomb's Emerade and ALK's Jext. Both companies are aware of the supply disruptions and are working with their supply chains to increase supply to the UK for the remainder of the year, the MHRA said.

MHRA Recalls Digital Pregnancy Tests

The UK's Medicines and Healthcare products Regulatory Agency Issued a recall for Wondfo Clear & Simple digital pregnancy tests due to a number of false positive results from the tests manufactured by the Guangzhou, China-based company.

Wondfo reported that some of the test kits could deliver false readings, attributing the problem to a large gap between the test strip bracket and the plastic enclosure of the test kit that allowed a change in light to affect the tests.

The recall affected one lot involving 58,000 tests distributed in the UK, according to the MHRA.

APPROVALS

Eximo Medical's Atherectomy Laser Cleared by FDA

The FDA granted 510(k) clearance for Eximo Medical's B-Laser atherectomy system, used for treating patients with peripheral artery disease, including in-stent restenosis.

The device — the first 355nm laser system cleared in the U.S. — is used in atherectomy procedures, minimally invasive procedures that remove atherosclerosis from a patient's blood vessels.

Atherectomies offer an alternative to angioplasties, which involve inflating temporary balloons to widen and unclog arteries.

FDA Approves Zeiss Treatment for Astigmatisms

Zeiss' ReLex Smile received premarket approval from the FDA, expanding its myopia treatment options to include patients with astigmatism.

The approval allows for a small incision lenticule extraction (Smile) procedure that is less abrasive on corneal surface tissue.

The procedure uses Zeiss' VisuMax femtosecond laser to create a lenticule and incision inside the cornea in a single step.

Bioneer Gains CE Mark for HIV-1 Kit

Bioneer earned CE-IVD marking for its HIV-1 quantitative analysis kit that uses a reverse transcription polymerase chain reaction technique to detect RNA expression.

The kit runs on the South Korea molecular diagnostics firm's ExiStation automated molecular diagnostics system.

The kit is used to count the presence of HIV-1 RNA in patient blood samples.

Mighty Oak Medical's Midline Navigation Guide Cleared

The FDA granted Mighty Oak Medical 510(k) clearance for its Firefly midline navigation guide, a 3D-printed and patient-specific device designed for cortical bone trajectory for pedicle screws.

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

Approvals, *from Page 7*

The Firefly, which is used for bone fixation, is compatible with every pedicle screw system.

The guide mechanically follows a predetermined trajectory and can eliminate the need for an O-arm imaging system or robot.

FDA Clears RightEye's Vision System

RightEye's vision system — also called RightEye — received 510(k) clearance from the FDA for recording, analyzing and viewing patient eye movements.

The portable system is used to support the identification of visual tracking impairments and perform vision-derived health screening.

The system comes with multiple applications, including functional vision screening, reading proficiency assessments and sports-related vision assessment and training.

FDA Clears Bose's Hearing Aid for Marketing

The FDA granted marketing authorization to the Bose Hearing Aid for patients 18 and older with mild to moderate hearing loss.

Patients can adjust the hearing aid using a mobile application on their phone. The wireless device is the first hearing aid that can be programmed and controlled by patients without any interaction with a health care provider.

The FDA cleared the device under the De Novo premarket review pathway based on data from clinical studies of 125 patients that showed self-fitting by patients was comparable to fittings by professionals.

SpineEX Interbody Fusion Device Gets 510(k) Clearance

The FDA cleared SpineEX's Sagittae lateral lumbar interbody fusion (LLIF) device for use in spinal fusion surgeries.

The minimally invasive fusion procedure causes less disruption to lower back muscles because it approaches from the patient's side, resulting in faster recovery and less blood loss.

The personalized device is expandable and offers a large graft space ideal for lumbar fusion procedures.

FibriCheck's Heart Monitor App Cleared by FDA

The FDA granted 510(k) clearance for FibriCheck's heart monitor smartphone application, which is used to detect issues with the user's heart rhythms.

FibriCheck's app — which is expected to be launched on the U.S. market in 2019 — uses the phone's camera and software to monitor patients for heart rhythm disorders.

FDA Clears DDC Technique For K2M's Mesa Platform

K2M's dual differential correction (DDC) technique was granted 510(k) clearance by the FDA for use with the company's Mesa Platform.

The platform is used for treating patients with, front-to-back imbalances in the spine that occur when one of the natural curves of the spine becomes under- or overly-pronounced.

The DDC technique uses patient-specific rods and rails, as well as rod rigidity and degree of bend, to correct spinal imbalances in the patient.

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Regulating Digital Health Tools: *Understanding the FDA's New Guidances*

Clinical decision support software … software as a medical device … artificial intelligence and machine learning – rapid developments in digital technology are blurring the line between FDA-regulated medical devices and unregulated "lifestyle apps."

To keep pace, the FDA has issued a slew of guidances to explain what and how it will regulate software-driven devices. The final guidance *Software as a Medical Device* and two draft guidances, *Clinical and Patient Decision Support Software* and *Multiple Function Device Products*, aim to clear up the confusion, but devicemakers still need a map for navigating the regulatory maze.

Regulating Digital Health Tools — based on a presentation by noted regulatory expert Bradley Merrill Thompson — combs through the guidances and sets out the rules devicemakers must follow. You'll learn:

- How the FDA's new policy allows sponsors to comply with postmarket surveillance requirements
- How the FDA is working with industry to promote innovation in the development of digital health functions, as well as how these novel products can be integrated into advanced therapeutic options for patients
- The status of the FDA's precertification pilot program and how it may determine future regulation
- Industry reaction to the FDA's efforts

Regulating Digital Health Tools: *Understanding the FDA's New Guidances* gives readers a complete understanding of how the FDA is regulating software applications and digital health devices — and where a device falls on the spectrum from unregulated "lifestyle" apps to high-risk regulated medical devices.

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EU MDR Compliance: *A Checklist for Meeting Manufacturing, Safety and Performance Requirements*

The new EU Medical Device Regulation is massive… complex… and confusing… and you must be ready to comply by May 26, 2020.

When the European Union revised its system of rules for medical device manufacturers in 2017, it replaced a longstanding set of directives on specific topics with one large document that covers all aspects of making devices in EU countries.

Not only did they consolidate all the rules, they gave them greater weight. Previously, medical device directives provided guidance but did not have the force of law. The new MDR, however, contains mandates that are legally enforceable by EU member countries.

The FDAnews report **EU MDR Compliance** can help. Our editors have combed through the regulations, picking out the most minute compliance points and building them into a checklist of 200+ requirements you can use to confirm that you are satisfying all the EU mandates for device manufacturing. The report provides:

- Definitions of key terms in the EU MDR
- Knowing where to find specific requirements in the 150+ page regulation
- Checklists that walk you through every aspect of manufacturing, safety and performance requirements
- A training tool for employees new to the regulations

EU MDR Compliance: *A Checklist for Meeting Manufacturing, Safety and Performance Requirements* is the tool that collects all the requirements, explains them and itemized them in an easy-to-use form to ensure compliance.

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