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FDA Pilot Will Use Third-Party Certification To Speed Digital Devices to Market

A new FDA pilot program will streamline the review process for high-risk digital devices while allowing low-risk devices onto the market without FDA review.

FDA Commissioner Scott Gottlieb announced the program as part of a broader effort within the agency to develop a framework for regulating digital health tools. As part of the pilot, Gottlieb said, the FDA is exploring creating a third-party certification pathway for lower-risk devices that would help assess the quality and reliability of a company's software design, testing and maintenance.

That certification program could allow lower-risk digital medical devices to enter the market without FDA premarket review and streamline the premarket review for higher-risk devices.

Gottlieb framed this approach as part of a broader shift in how the FDA handles the review process, moving away from

(See **Pilot***, Page 8)*

FDA Credits Device Trial Redesign For First-in-the-World Valve Approval

A more practical, streamlined approach to device regulations by the FDA is credited with helping make the agency the first in the world to approve a new heart valve.

When the agency approved the first transcatheter heart valve, the Edwards Sapien THV, nearly six years ago, the United States was the 42nd nation in the world to do so, according to Jeffrey Shuren, M.D., Director, CDRH and Bram Zuckerman, M.D., Director, Divi-sion of Cardiovascular Devices, CDRH.

Since then, the FDA has refocused its device priorities, emphasizing patient access, real-world evidence and transparency in agency expectations. Shuren and Zuckerman credit these improvements for the FDA's recent approval of the latest Sapien valve, the

(See **Valve***, Page 4)*

South Africa New Device Regs Are Now Live

As of June 1, South Africa has its first regulatory system for medical devices and in vitro diagnostics.

The new independent state-owned regulatory entity is called the South African Health Products Regulatory Authority (SAHPRA) and will regulate both drugs and devices.

This completes a process begun in September 2015 when South Africa's Department of Health and Medicines Control Council announced the proposed regulations (*IDDM*, Oct. 16, 2015).

The agency began grandfathering devices and IVDs into the new system in February, and that implementation period will end on Aug. 24, according to the South African Medical Device Industry Association (SAMED). After the implementation ends, companies wanting to sell their devices in South Africa will need to license their products.

ISO 13485 Certification

The country will begin to implement a quality management system, and devicemakers will need to have ISO 13485 certification. But that process is expected to take a few years to implement, and for now, companies will need to certify in their applications that their processes include the essential elements of a quality management system.

SAMED formed a working group to help its member companies "understand the steps required to allow companies to become certified locally to the ISO 13485 standard," the association said.

Similar to the EU, the regs require that foreign devicemakers have an authorized representative in South Africa. One representative will be required for each manufacturing site.

The new regs are covered in four separate documents that cover licensing and importing medical devices and IVDs, classification of devices and IVDs, good manufacturing practices, and general safety principles.

The updated regs lay out a risk-based classification system based on good manufacturing practices. Under the risk-based classification system, there are four classes of devices or diagnostics:

- Class A – low risk;
- Class B – low to moderate risk;
- Class C – moderate to high risk; and
- Class D – high risk.

For licensing a Class C or Class D device or IVD in South Africa, manufacturers will need to show proof of premarket approval or registration from at least one regulatory authority in Australia, Brazil, Canada, the European Union, Japan, U.S. or the World Health Organization Prequalification status (*IDDM*, Aug. 26, 2016).

Mode of Action

Combination products that were previously covered under the Medicines Control Council will be regulated as devices if the primary mode of action is a medical device.

SAMED has actively been pursuing relationships with global regulators and agencies to forge international ties to bring South African standards in line with other global regulators. The organization participated in the Asian Harmonization Working party, and the global Medical Technology Aliance, which gives input to the International Medical Device Regualtors Form (IMDRF).

The association's Health Economics and Reimbursement Committee is focusing on reimbursement and health technology assessment in the private and public sectors as well. The association noted that the National Treasury has implemented a centralized procurement mechanism that will procure essential devices for government hospitals.

SAMED said it hopes the new system will improve procurement outcomes in the country, because one of the biggest issues for its members is outstanding payments by provincial health departments.

Device Industry Should Strive for Quality And Compliance in Parallel, Experts Say

Simply being FDA compliant — even if you're following every regulation as closely as it can be followed — may not be enough to make your medical device one of high quality, and it is high quality devices that will not result in recalls or adverse events.

That's according to Michelle Boucher, vice president for research for Tech-Clarity, and David Wolf, program director of Medical Device Strategy for PTC, who together led an *FDAnews* webinar, *Making the Right Choice—Your Case for Quality.*

During the presentation, Boucher said it's the recognition of this reality that led to the launch for the FDA's Case for Quality, an initiative that calls together industry, healthcare providers, patients, payers, and investors to foster medical device quality via identifying and promoting practices that result in high-quality devices and adapting FDA regulatory approaches to align with those practices. The Case for Quality is part of CDRH's 2016-2017 strategic priority to promote a culture of quality and organizational excellence

Better, Safer Devices

A robust focus on quality will of course be good for patients in the form of better, safer devices, said Boucher, but it also will lead to greater return on investment, which is good for medical device manufacturers who now have to spend, on average, $400,000 to clear a warning letter when one occurs.

Indeed, the medical device industry spends between $2.5 billion and $5 billion annually to rectify nonroutine quality events such as major observations, recalls, warning letters, consent decrees, associated warranties and lawsuits. The growth of those costs is outpacing the growth of the industry, said Boucher.

A new push for high quality could also pay off in different ways. The FDA is evaluating rewarding companies for high quality by potentially eliminating a PMA or 510(k) prerelease inspection, which, said Wolf, definitely could shorten the NPI. "The more you can shift the prevention, [the more] you're going to significantly reduce that cost of poor quality," he added.

Boucher added that research done by McKinsey & Co. shows that the focus on quality can really drive significant opportunities and can potentially increase profits by 3 percent to 4 percent.

Focus on Quality

How to approach a new focus on quality over simple compliance?

Being small helps, said Wolf. He has worked for a large company and a small company, and said the smaller one was able to be more nimble when it came to product-centric design quality. In the smaller company, Wolf said, "we had full design controls, the CAD, we harmonized our manufacturing software with our CAD software, so we didn't have to IGES and put that out and have a lot of rework and scrap and downtime transferring from engineering to manufacturing. And then also being able to test everything in kind of a product-centric fashion, we actually produced higher quality products than the larger company that I worked for that was doc-centric and really compliant."

Try to be less document-centric and more design centric, Wolf said. When you have a document-centric process in place, you have to shift all the design over in a document-centric way, and it really takes away from the resources, away from innovation.

"As you make that shift, think about your entire lifecycle, because quality issues can really occur at any point along the entire lifecycle of your product development process," said Boucher.

To thrive in the high-growth period that's expected in the medical device industry, Boucher

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Valve, *from Page 1*

Sapien 3—this time, the first national regulatory agency to do so.

The first step in the process was rethinking the agency's non-clinical testing requirements. The FDA improved transparency, predictability and consistency during the process and as a result, trimmed the time before devicemakers could initiate clinical studies. The agency also stepped up its collaboration with industry stakeholders on trial design to ensure the design produced data that applied to the device's intended patient population.

Since the first valve's FDA approval in 2011, more than 600 patients have engaged in off-label, valve-in-valve use, which allows for use of the device without open heart surgery through either a small cut in the patient's chest or a blood vessel; during the approval process for the Sapien 3, the FDA incorporated real-world evidence to evaluate the safety and effectiveness of this use.

Cause for Optimism

This methodology is cause for optimism in the device industry, Zuckerman and Shuren write, and could lead to further expansion of approved uses for other devices, but only if "robust registries" are available.

The agency's creation of the National Evaluation System for Health Technology (NEST) will also be key to creating more opportunities to incorporate real-world evidence into the device approval process, according to the post; NEST will weigh device safety and effectiveness based on a combination of clinical registry, electronic health record and medical bill data.

CDRH has also launched a program to incentivize early feasibility studies for new devices, according to the blog post. Through these efforts, the FDA hopes to reverse the trend of outsourcing during the trial and feasibility study process. Device manufacturers have increasingly conducted feasibility studies overseas in recent years, according to Zuckerman and Shuren, securing their marketing authorizations overseas first and returning to the United States for clinical trials and final FDA approval.

However, many manufacturers have already committed to remaining in the United States as a result of the program, which will give device makers the option to conduct early clinical testing of devices to provide initial clinical safety data, an important option in scenarios where nonclinical testing methods are not available or appropriate.

By giving device makers an alternative to outsourcing, the program will save travel costs, streamline communications and allow for more early interactions with FDA officials, according to the blog post.

The blog post can be read here: www.fdanews.com/06-15-17-FDABlog.pdf. — Zack Budryk

483 Roundup: Curbell, Carestream, Dynarex, Hard Corporation

The FDA issued Form 483s to four New York-based device manufacturers, primarily for issues with procedures and record-keeping.

Curbell Medical Products: The FDA issued a Form 483 to Curbell Medical Products, citing inadequate procedures for nonconforming products and corrective/preventive actions.

The agency issued the form after a March inspection of Curbell's Orchard Park, NY, facility. According to the FDA, the company did not include cleaning board switches as part of its rework procedures for non-conforming products even though the rework for one product order included board switch cleaning. Employees conducted rework procedures that were not part of their documented training, according to the form.

The FDA further found that in several cases between October 2014 and March 2017, corrective and preventive actions did not validate that the action did not adversely affect the finished devices. Curbell promised to correct both observations.

Carestream Health: Device manufacturer Carestream Health landed a Form 483 from the FDA due to issues with its testing, validation and complaint procedures.

The agency issued the form following a March inspection of Carestream's Canandaigua, NY, facility. FDA officials found performance qualification activities for several of the facility's devices are inadequate, and in many cases were not conducted with the appropriate job element. Similarly, performance qualification activities for the manufacture of those devices took place before the validation plan was approved.

The company also failed to document review and evaluation for corrective actions it took; the records for such actions do not address the potential impact of the problem in future units or document when certain corrections occurred.

The agency also faulted Carestream's complaint procedures, noting that it did not create complaint tickets for certain events and for others took nearly two months to create them. There were similar problems with records of changes to documents, with inspectors finding document change requests for not always maintained.

Dynarex Corporation: The FDA issued a Form 483 to Dynarex, citing its design validation records, document control procedures and document approval processes.

The agency issued the form following a February/March inspection of the company's Orangeburg, NY facility. Not only were Dynarex's design validation records incomplete, the company also lacks a laboratory for analysis and to issue Certificates of Analysis, simply copies and pastes information to their letterhead. The firm lacks established procedures for issuing certificates, according to the form.

Lastly, the firm changed at least one complaint form without completing a Change Authorization Notice, according to the form.

Hard Manufacturing: The FDA hit pediatric device maker Hard Manufacturing for its procedures for design control, complaints and nonconforming products.

Following a February/March inspection of the company's Buffalo, NY facility, the FDA issued a Form 483. According to inspectors, the company has not implemented its design control procedure as written, and has no design history file.

The agency also found that three of 15 complaints in 2016 were not properly investigated and included either no or insufficient justification for the lack of investigation. Lastly, of 11 non-conformance reports over a 13-month period, several did not document an investigation or the rationale for lack of one.

None of the companies responded to a request for comment.

The four Form 483s can be read here: www.fdanews.com/06-17-17-FourForm483s.pdf.
— Zack Budryk

Quality, *from Page 3*

said, one needs to be able to manage the high cost of compliance while keeping in mind that the cost of noncompliance is even higher. To do that, companies should look to implement processes and technology that are going to help lower the cost of compliance.

Also recommended, said Wolf, is connected remote service. "We have publicly available information on companies that have implemented remote service and diagnostics and are seeing tremendous gains, sometimes up to 20 percent of their revenue on connected and remote service," he said.

In addition, Wolf says the Internet of Things remains an exciting and promising realm that medical device companies are getting into. "It is important to get data back and not be reliant on the customer to deliver that data and get through several channels in a timely fashion back to the people that need it internal to the company," he said of IoT.

But a key cornerstone to improving quality and thus increasing profit is software.

"What I'm seeing a lot of companies getting value out of is software, lifecycle management — specifically being able to, on the service side, have connected service and remote service with IoT," said Wolf, who added that PTC has acquired a company called Exeda that allows one to get that information back real time.

"Trying to take advantage of the technology — without doing massive rip and replace — to me is key," said Wolf.

APPROVALS

OrbusNeich Gains FDA Clearance For Coronary Dilatation Catheters

The FDA has awarded marketing clearance to OrbusNeich's Sapphire PTCA balloon dilatation catheters — the Sapphire II PRO and the Sapphire NC Plus.

The Sapphire II Pro has a tapered tip and an ultra-low profile, which allows insertion through tight lesions.

Sapphire NC Plus is indicated for dilatation of in-stent restenosis and post-delivery expansion of balloon expandable coronary stents.

3M'S Tegaderm CHG I.V. Gets FDA Clearance for Expanded Indication of Securement Dressing

The FDA has expanded the indication of 3M's Tegaderm CHG Chlorhexidine Gluconate I.V. securement dressing to include catheter-related bloodstream infections.

The dressing is a translucent, gel pad applied to the area where an I.V. is placed to allow healthcare professionals to monitor the insertion site for early identification of complications and to minimize catheter movement and dislodgement.

Bayer Wins FDA Clearance of myBETAapp And Betaconnect Navigator

The FDA has approved Bayer's supplemental Biologics License Application for myBETAapp and the Betaconnect navigator.

The autoinjector is used to administer Betaseron (interferon beta-1b) which uses Bluetooth to connect the autoinjector to the new myBETAapp on a mobile device or computer.

Betaseron is a prescription medicine used to reduce relapses in individuals with relapsing forms of multiple sclerosis.

SpaceOAR System Acquires Approval in Japan

Augmenix has received approval from the Japanese Ministry of Health, Labor and Welfare to market its SpaceOAR system in Japan. The device is an absorbable prostate-rectum spacer that reduces rectal injury during prostate radiotherapy.

The SpaceOAR system is CE marked, FDA cleared, approved in Australia and licensed in Canada.

FDA Warns See Clear Company For Record Keeping Problems

The FDA issued a warning letter to contact lens manufacturer The See Clear Company, citing problems with its complaint and corrective action procedures.

The agency conducted an inspection of the company's Norcross, Ga., facility during October and November and issued a Form 483. Although See Clear promised to correct these problems, the agency has no way to determine whether the company's efforts have been effective, and the company response did not include documentation of corrections it made.

The initial inspection found the company's corrective and preventive action procedure does not include verifying and validating corrective actions or recording changes in the procedure. The FDA also faulted the company's complaint procedure, noting that it does not cover how to determine when investigations are necessary or appropriate methods of handling customer complaints or maintaining complaint files.

The firm also had no established procedures for accepting incoming products or documenting acceptance or rejection, according to the warning letter, and the facility could not provide complete distribution records or define the firm's control over contractors.

The company's written procedures for nonconforming products do not reflect current practices, and the firm could not provide complete device history records for one lot of its Diamond Brand soft contact lenses.

The company also failed to document personnel training as well as the dates of both quality audits and approval documents, and the company's management was unable to provide dates, agendas and attendance records for 2014 and 2015 review meetings, according to the FDA.

The full letter can be read here: www.fdanews.com/06-13-17-SeeClear.pdf. — Zack Budryk

Malaysia Issues New Mandatory Device Reporting Requirements

Companies will need to report within 48 hours from discovery if a medical device sold in Malaysia presents a serious threat to the public health according to new requirements released by Malaysia's Medical Device Authority.

The new reporting criteria were designed to better delineate the seriousness of problems associated with medical devices, and include different reporting requirements depending on circumstances.

If a device leads to the death or serious deterioration in health to a patient, "or could do so were the incident to recur," the adverse event must be reported within 10 days of discovery.

Finally, a failure of the device or "a deterioration in its effectiveness" or inadequacy in labeling must be reported within 30 days.

The reporting requirements also include a new mandatory reporting form, which device manufacturers, distributors or authorized representatives must submit to the MDA when reporting adverse events. It may be mailed, faxed or emailed.

The MDA defines an adverse event as:

- A malfunction or deterioration in the performance of a device according to its intended purpose;
- An inadequate design or manufacture;
- An inaccuracy in labeling or instructions for use; and
- A significant public health concern.

The MDA defines an adverse event as reportable if it meets all three of the following criteria:

- An event has occurred or a potential adverse event is recognized through information available;
- The manufacturer's device is a contributing factor to the event;

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Pilot, *from Page 1*

product-by-product review and toward a more company-based approach.

FDA officials believe a focus on real-world evidence will create a friendlier climate for investment in digital health technology and devices. This, in turn, would help developers implement new or updated software more quickly and allow the FDA to focus its resources on top priorities, he said.

Granting more regulatory leeway to lower-risk devices has long been floated within the agency as a way to free up FDA resources and create a less burdensome industry environment. Earlier in June, the agency granted certain low-risk Class I and unclassified devices, such as mechanical wheelchairs and manual surgical tools, a deadline extension for compliance with universal device identification rules.

The agency also will take concrete steps to implement the 21st Century Cures Act's digital health provisions as well as publishing guidance to clarify the scope of FDA jurisdiction concerning digital health, according to Gottlieb. These documents will clarify the agency's position on which devices and apps that combine software functions fall under FDA jurisdiction and those that do not.

These initiatives, Gottlieb writes, fall under the broader umbrella of FDA efforts to promote and take advantage of the recent growth in medical technology.

The ultimate aim, he writes, is to ensure the agency addresses new medical technology in the most modern, efficient way possible.

Gottlieb's blog post can be read here: www.fdanews.com/06-16-17-Gottlieb.pdf.
— Zack Budryk

Malaysia, *from Page 7*

- The event led to death or serious injury or the event could lead to death or serious injury.

Foreign device manufacturers wanting to market a product in Malaysia must have an authorized representative in the country to manage device registration and postmarketing issues with the regulator.

Medical devices marketed in Malaysia are classified according to risk, similar to the European Union. Class A devices represent little risk, Class B devices are associated with low to moderate risk, Class C device are considered moderate to high risk, and Class D devices represent the highest-risk devices.

Before April 2016, Class A devices were exempt from the registration process, but they now require registration.

Companies whose devices are sold in the U.S., EU, Australia, Japan or Canada, can take advantage of a simplified registration process in Malaysia. The timeline to review a product depends on a product's risk classification.

Read the MDA notice here: www.fdanews.com/06-13-17-Malyasia.pdf.

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