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FDA Launches Initiative to Accelerate Opioid-Oriented Device Development

In a move to combat the opioid crisis, the FDA launched an "innovation challenge" to stimulate the development of medical devices that could provide novel pain treatments and help prevent, detect and treat opioid addiction.

The agency is encouraging developers to submit proposals from June 1 to September 30, including for products such as treatments for pain that do not require opioid analgesics, treatments for opioid withdrawal or opioid use disorder, diagnostics for detecting patients at increased risk for addiction, and technologies that can prevent diversion of prescription opioids.

The challenge is open to products in any stage of development and extends to developers of currently marketed devices who want

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Singapore Eases Registration Process for Some Devices

Singapore's Health Science Authority announced changes to legislation that will allow faster access to certain low-risk medical devices and stand-alone mobile applications.

The authority is also updating its policies with more detail on requirements for telehealth devices and high-risk devices that modify appearance or anatomy.

Beginning June 1, about 75 percent of Class B medical device applications will be granted immediate market access, HSA said. Currently, Class B registration takes about 60 days for a product to be registered.

Under the new regulations, Class B products and Class C standalone products that are approved by at least one reference regulatory agency — including Health Canada, Japan's Ministry of Health, Labor and Welfare, the U.S. FDA, Australia's Therapeutic Goods

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FDA Approves First Artificial Iris

In its first approval of an artificial iris, the FDA approved HumanOptics' CustomFlex, a surgically implanted device to treat adults and children whose iris is completely missing or damaged.

The device is indicated to treat defects due to aniridia — a congenital condition that affects approximately 1 in 50,000 to 100,000 people in the U.S. — as well as other conditions such as albinism, traumatic injury or surgical removal due to melanoma.

The implant is made of thin, foldable silicone and is custom-sized and colored for each patient. Safety and effectiveness was demonstrated in a clinical trial of 389 adult and pediatric patients with aniridia or other iris defects. More than 70 percent of patients reported significant decreases in light sensitivity and glare as well as an improvement in health-related quality of life following the procedure.

The product received a breakthrough device designation and was approved through a premarket approval application.

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to demonstrate that their device has an improved benefit-risk profile for pain management compared to opioids.

Applicants chosen by the FDA — to be announced in November — will work with the agency through "enhanced interactions" to accelerate the development and review of their innovative devices, giving developers more incentives to invest in products that can help address the opioid crisis and advance promising technologies.

"Medical devices, including health devices like mobile medical apps, have the potential to play a unique and important role in tackling the opioid crisis," said FDA Commissioner Scott Gottlieb. "We must advance new ways to find tools to help address the human and financial toll of opioid addiction." — James Miessler

FDA Seeks Comment On Medical Device Software

The FDA invited stakeholder comments on how it should craft rules governing medical device software under the 21st Century Cures Act.

The act exempted certain software from regulations for medical devices if the software is intended for administrative support of health care centers, is "for maintaining or encouraging a healthy lifestyle," is designed to serve as a patient's electronic health records, if it is used for "transferring, storing, converting formats, or displaying data" or it is designed to "provide limited clinical decision support."

The FDA issued two draft guides last December and now wants public input on "any risks and benefits to health associated with these non-device software functions."

The agency said it is "developing a report to summarize the impact of such software functions on patient safety, including best practices to promote safety, education and competency related to such functions."

Comments can be submitted under docket number FDA-2018-N-1910.

No Regulatory Changes for Australia's Personalized and 3D Printed Devices

Australia's Therapeutic Goods Administration (TGA) released findings from a public consultation on proposed regulatory changes for personalized and 3D printed medical devices and said, based on the stakeholder feedback, it has decided not to implement regulatory changes for the devices at this time.

The agency received a total of 24 submissions, including 15 from industry stakeholders such as AdvaMed, Stryker and Johnson & Johnson, six from health care practitioners and organizations, two from universities and government organizations and one from a consumer representative.

In its November 2017 consultation paper, the TGA noted the increasing use of 3D printing for medical applications "is raising questions globally about the adequacy of the current medical device regulatory frameworks to mitigate risks to patients, and to meet requirements for health care providers and manufacturers."

Consistent Comments

Stakeholders did not agree on all of the proposals, but "consistent throughout the submissions was a recognition of the need for the TGA to take action to improve the current arrangements for custom-made medical device regulation, which are too broad," the agency said.

The first proposal suggested "tightening" the definition of a custom-made device and introducing new definitions for personalized devices. The TGA said the current regulatory framework "does not include an adequate vocabulary for devices that are intended for a particular patient."

The agency proposed redefining the term to ensure that 3D printed patient-specific implants are not included in this category. Most respondents recognized the need to add new definitions, however many said the proposed definitions did not provide sufficient clarity.

The TGA's proposal to exclude 3D printed patient-specific devices from the custom-made definition would mean that such devices could be regulated under the existing framework for medical devices.

A spokesperson for the Medical Technology Association of Australia (MTAA) told FDAnews that "the proposed revised definition for custom-made medical devices, with its narrowed-down scope, is in our opinion appropriate and aligns with [the] current EU and U.S. overall approach to custom-made devices."

As part of the proposal, the TGA asked respondents to consider whether it should set a limit on the number of custom-made devices that can be produced by one manufacturer in a year, as is done in the United States. Most respondents were not in favor of this proposed change. Cook Medical argued that an arbitrary cap could "limit access for patients who require custom-made devices." AdvaMed concurred, saying that any limit set would be "necessarily arbitrary," potentially preventing patients from accessing needed technology. The company also argued that "the custom-made pathway provides the value of reduced regulatory burden for medically needed products under very limited circumstances."

The third TGA proposal, which suggested changing the definition of a manufacturer, also generated a debate, with half of the respondents agreeing on the proposed changes and the other half calling for further clarification.

Definition Change

Under the current definition of manufacturer, a person is not considered the manufacturer of a medical device if the person assembles or adapts the device for an individual patient but the device has already been supplied by someone else. The widespread use of 3D printers requires a change in this definition in order to determine liability in cases where a health care provider creates 3D printed medical devices, such as dental crowns, using a product that was supplied by a third party.

The third proposal also called for the creation of a new category of devices called a "medical device production system," which would be defined under

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Administration, and EU notified bodies — without safety issues will be eligible for immediate market access. In addition, the device should have three years of marketing history.

Class A sterile devices, such as examination gloves and sterile intravenous sets, will no longer need to be registered with HSA. Previously, these devices had to be registered to ensure they complied with sterility requirements.

Under the new regulations, manufacturers will need to list all their these Class A medical devices on the public online Class A database to ensure safety and to facilitate post-market surveillance.

"HSA constantly reviews our regulatory framework to ensure that it stays relevant and forward looking," said Chan Cheng Leng, director of the authority's Health Products Regulation Group. Allowing immediate entry of these lower risk devices "would enable us to focus our attention on newer and higher risk devices," he said.

More Clarity for High-Risk Products

HSA has also provided more clarity on existing regulations covering high-risk devices. For example, high risk devices used to modify the appearance or the anatomy are subjected to additional regulatory controls. These products include implants, injectable dermal or mucous membrane fillers and invasive devices for fat removal or fat degradation purposes. The agency has developed a Positive List to help devicemakers identify if their products are regulated.

HSA will require manufacturers to provide training for the users of more complex devices such as implantable devices.

Telehealth devices intended for medical purposes will be regulated as medical devices, the agency said. Devices intended solely for well-being or lifestyle purposes, such as smart watches to track heart rate and heart rate measuring devices not intended for medical purposes, will not be subject to regulatory controls. However, a statement needs to be included on labels and in advertisements that the products are not meant for medical purposes.

HSA said it would continue to strengthen post-market surveillance activities, including inspections and compliance monitoring. The agency believes the changes will enable it to detect safety signals early and to promptly investigate adverse events.

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the proposal as a "collection of products, including specified raw materials, that is intended to be used by a health care practitioner to produce a finished medical device." The proposed change would clarify that producers of these customized devices, such as 3D printed dental crowns, are not manufacturers, and are therefore not required to meet the regulatory requirements of a manufacturer.

In its comments, Stryker said it supports updating the current legislative definition of a manufacturer of medical devices, but that attempting to create a new category of devices "has the potential to create confusion between manufacturing and a marketed product."

Johnson & Johnson also expressed concern that the proposal to create a new category of medical devices would blur or even eliminate the line between manufacturing and marketed product.

In general, proposed changes to the custom-made medical device conformity assessment procedure, which would allow the TGA to enter and inspect manufacturing sites for custom-made devices, were viewed positively, as was a proposal to re-classify software and anatomical models used for recording diagnostic images. A fifth proposal, which suggested regulating devices that contain human origin material under a devices framework rather than a biological framework, also drew favorable responses.

The TGA said it will "further explore " other areas identified as requiring additional clarity prior to any regulatory change.
— Donna Scaramastra Gorman

483 Roundup: FDA Flags Device Firms For Design Controls, Data Integrity

The FDA issued 483s to three device facilities for a variety of deficiencies including design control procedures, data integrity, CAPAs and complaint handling.

Elite Medical Supply of New York: The FDA cited Elite Medical Supply of New York for problems with its design control procedures and handling of CAPAs and complaints.

Investigators issued the Form 483 after a December 2017 inspection of the device specification developer's West Seneca, New York facility. They found the design for the company's Elite Medical Multi-Mode Stimulator was bought from another company but that Elite Medical did not document a review or approval of the design history file to ensure completeness and accuracy. Moreover, the company had no procedures for introducing outside designs.

Investigators also found that procedures for design validation did not include any requirement to demonstrate equivalency to the production units.

The agency also found that several complaints were reviewed for units identified as "dead on arrival" due to batteries not being charged ahead of shipment. The firm's quality assurance manager said a corrective action was taken to prevent the problem, but this was not documented in a CAPA.

The company's complaint-handling procedures also did not require documenting the complainant's address or phone number, replies to the complainant or dates of the subsequent investigation. At least one of the complaint reports also lacked complainant information.

Ivoclar Vivadent: The FDA issued a Form 483 to Ivoclar Vivadent for noncompliant process control procedures, CAPA procedures and test/measurement equipment.

The agency issued the form after a January 2018 inspection of the company's Amherst, NY, facility.

Investigators found the company's soldering, press operation and foil production facilities, did not comply with procedures requiring operators to use the correct stamp for the alloy or solder being cut and stamped. The document identifying the approved stamps for each alloy and solder was retired on July 14, 2017 and an approved list was not put back in place until January 9, 2018, the agency said.

The FDA also found that several CAPAs reviewed did not include documentation for

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Personnel Requirements for CAPA Teams

Companies putting together CAPA teams will need to assign the following individuals:

- CAPA manager: This is the person in the company who is responsible for the overall CAPA system, including coordinating all CAPA activities and taking a role in investigations of nonconformances and other quality problems;
- Process owner: For each of the processes and data elements/sources that the company tracks, the company will need a process owner. Having process owners from the departments that actually conduct those processes will improve the quality of the data received and increase buy in to the CAPA process. This is important because one of the keys to CAPA success is breaking down "silos" and expanding participation beyond the quality team using a collaborative, cross-functional approach. The company should set regular planning, strategy and review meetings involving owners, team members and management;
- CAPA owner: Once a nonconformity or other problem is found, the company must assign it to a CAPA owner. This person will be responsible for coordinating a team to investigate the problem and then develop and implement a plan to correct the problem and prevent it from recurring; and
- CAPA monitor: The company should designate someone, such as the CAPA owner, to use trending techniques to catch — and address — quality problems early and to monitor ongoing process performance and the effectiveness of the CAPA plan.

Excerpted from the *FDAnews* management report: *Creating QSR-Compliant CAPA Systems: A Practical Guide for Devicemakers*.

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corrective actions addressing the identified root causes. Some corrective actions only documented the effectiveness check submitted to close the CAPA. Some corrective actions did not properly document review and acceptance ahead of implementation.

The investigators also observed that the company did not properly evaluate whether problems with accuracy in its test/measurement equipment had any negative impact on the quality of the devices.

Veran Medical Technologies: The FDA hit Veran Medical Technologies on handling of CAPAs and complaints as well as its documentation of acceptance activities.

The agency issued a Form 483 after a March 2018 inspection of the device manufacturer's Saint Louis, Missouri facility. It found the facility did not properly document that the corrective actions it took did not adversely affect products and that it failed to adequately document that the corrective actions eliminated the problem.

The company also failed to follow its complaint review procedures and did not log at least five calls that should have been documented as potential complaints.

Moreover, the company's receiving inspection report for at least one lot did not have the required signatures of personnel responsible for the inspections.

The FDA investigators also found device history records for Veran's SPiNView System did not include primary identification labels and labeling used for each production units, and that the facility did not conduct onsite audits to evaluate its critical suppliers.

The company also improperly labeled class IV accessible laser radiation devices and did not submit product reports prior to introduction of the SPiNView System. It also failed to submit an annual report for the system.

Read the three Form 483s here: www.fdanews.com/05-30-18-ThreeForm483s.pdf.
— Zack Budryk

TGA Issues Recommendations For In-House IVD Compliance

Australia's Therapeutic Goods Administration (TGA) released guidance outlining its latest thinking on how laboratories can meet the country's regulatory requirements for *in-house in vitro* diagnostics.

The TGA defines an in-house IVD as a pathology test that has been developed or modified within a laboratory to carry out testing on human samples in order to assist in clinical diagnosis and decision making.

The agency established the new IVD regulatory framework in July 2010 and the transition period for compliance ended on June 30, 2017.

Laboratory networks that use IVDs must operate under a single quality management system (QMS) that is centrally managed and applied at all work locations that manufacture or use in-house IVDs. Management review, internal quality audits, corrective and preventative action, complaints and changes to documentation must all be managed centrally under the QMS.

In order to comply, a laboratory or manufacturer must be accredited by Australia's National Association of Testing Authorities (NATA) and meet National Pathology Accreditation Advisory Council (NPAAC) standards.

Once these requirements are met — including the NATA corporate accreditation — the laboratory can manufacture and distribute in-house IVDs within its network.

The guidelines also outline the three situations in which a laboratory is considered to have created an in-house IVD: devices developed de novo, where the laboratory designed, developed, assembled and packaged the device, which they will use for its intended purpose; devices developed using design specifications of another laboratory or assembled from commercially supplied components; and commercial IVDs that are physically modified or are used for something other than the purpose specified by the manufacturer.

Read the full IVD guidance here: www.fdanews.com/06-01-18-IVDs.pdf.
— Donna Scaramastra Gorman

Parliament Proposes EU-Wide Health Technology Assessments

Draft legislation from the European Parliament calls for joint assessments of new health technologies including medical devices rather than the current system of individual assessments by EU member states.

Although the EU's member states are each responsible for healthcare delivery, joint findings on HTA outcomes could help inform those decisions, according to a draft report from the parliaments' Committee on the Environment, Public Health and Food Safety.

By cooperating in assessments through early "horizon scanning" to pinpoint technologies that will have major impacts, early dialog could ensure better study designs. In addition, assessments can help with divestment decisions when more suitable technologies are developed, the report said.

Several joint assessments were conducted in early pilot projects and a successful framework has been established that would allow for more joint HTAs moving forward, the committee said.

The proposal suggests that HTAs should be conducted for all products that receive marketing authorization. But it stresses that the joint work should not delay or interfere with the CE marking of medical devices.

Twenty EU member states, together with Norway, currently have HTAs in place for medical devices.

Read the committee's draft report here: www.fdanews.com/05-30-18-ECHTA.pdf.

APPROVALS

Zimmer Biomet's 3D Printed Titanium Spinal Implant Receives 510(k) Clearance

The FDA gave 510(k) clearance to Zimmer Biomet's Zyston Strut open titanium interbody spacer system, a titanium implant manufactured through a 3D printing process.

The system consists of a group of lumbar cages designed to enhance the graft capacity, strength and visualization of interbody spacers in spinal fusion cases, and includes a variety of sizes to work with different patient anatomies and surgical procedures.

The system, available in straight and curved profiles, includes surgical tools to insert, move and remove the implants.

FDA Clears Synedgen's Wound Hydrogel

Synedgen's Catasyn advanced technology wound hydrogel was given 510(k) clearance by the FDA for advanced physician administration and over-the-counter use.

Used by patients, the hydrogel can dress and manage minor burns, cuts, lacerations, abrasions and abrasions of the skin.

Under the care of a physician, the hydrogel can be used to treat second degree burns, post-operative sites and partial to full thickness dermal ulcers including pressure sores, arterial ulcers, diabetic ulcers and venous stasis ulcers.

BioGX Launches Six CE-Mark Tests For Antibiotic Resistance and Meningitis

BioGX expanded its BD Max molecular diagnostics platform with six CE Mark diagnosis tests for meningitis and antibiotic resistance.

The six new tests can diagnose viral meningitis HSV/VZV, bacterial meningitis NSH, bacterial meningitis ELGBS, carbapenem resistance KNO, carbapenem/colistin resistance VGM and vancomycin resistance.

With the expansion, the BD Max system now comprises eleven tests, with an additional ten planned for the second half of 2018.

Avinger Gains 510(k) Clearance for Pantheris

Avinger received 510(k) clearance from the FDA for its lumivascular atherectomy system, Pantheris, an image-guided device for treatment of peripheral artery disease.

The system includes a single balloon designed to allow blood flow occlusion and to treat blocked peripheral blood vessels using optical coherence tomography.

An in-process clinical trial is examining the device's use for treating in-stent restenosis in lower extremity arteries.

Attune Medical Receives 510(k) Clearance for New EnsoETM Models

Attune Medical received 510(k) clearance for new models of its EnsoETM temperature management device to raise or maintain patient temperature with Cincinnati Sub-Zero's Norm-O-Temp hyperthermia system.

The device manages patient temperature through the esophagus. The clearance includes EnsoETM with ENFit, which allows for enteral fluid administration through the device, and the original EnsoETM.

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Supplier Quality Metrics for Devicemakers: *Predicting and Selecting the Best*

Regulators are watching your supplier management practices closely. The FDA's Quality System Regulation (QSR), ISO 13485 and the international Medical Device Single Audit Program (MDSAP) all have specific requirements for purchasing controls and acceptance activities. They expect your suppliers to function as an extension of your quality system. So how do you choose the ones most likely to meet your standards?

An effective supplier evaluation system includes determining your expectations, converting them into measurable characteristics/metrics, defining the measurement method and setting the target you expect suppliers to hit.

In the **Supplier Quality Metrics for Devicemakers** management report you'll learn how to use predictive analysis of such metrics as delivery time, management efficiency and lot acceptance rate to identify suppliers you can count on and spot potential problems in the future. You'll learn:

- Requirements for receiving acceptance
- The difference between a contract manufacturer and a specifications developer and why it matters
- What aspects of your purchasing controls will be evaluated in an MDSAP audit
- How to create a supplier scorecard
- How to evaluate what you receive from suppliers
- Issues to look for in a supplier's complaint records
- How to analyze performance metrics to predict if a supplier is likely to create a problem.

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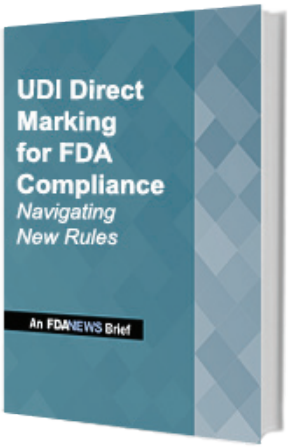

UDI Direct Marking for FDA Compliance: *Navigating New Rules*

Confused by the FDA's UDI direct marking regulations? What information should go on the label and the device itself? What methods of marking are acceptable? What's the difference between a device identifier and a production identifier? What additional requirements are placed on reprocessed devices?

The FDA's final guidance on UDI (unique device identification) raises as many questions as it answers. With full compliance for Class I, II and unclassified devices looming, lawyers are hard at work parsing the FDA's language.

Jay Crowley was the architect of UDI while at the FDA. Now a consultant advising devicemakers, he remains the go-to expert on UDI compliance. In the FDAnewsBrief, **UDI Direct Marking for FDA Compliance**, Crowley lays out a path to compliance. He explains:

- The technology necessary for creating and verifying bar codes
- The difference between direct marking and direct part marking
- How the rules apply to device components and accessories
- Exceptions to the direct marking requirements
- Record-keeping requirements
- Testing to make sure any direct mark doesn't affect the safety or performance of the device
- UDI requirements in the premarket submission stage.

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