INTERNATIONAL DEVICES & DIAGNOSTICS MONITOR

Vol. 4, No. 32
Aug. 13, 2018

IN THIS ISSUE

FDA Seeks Innovative Devices To Treat Opioid Use Disorder

The FDA is moving ahead with its plan to speed reviews of medical devices and diagnostics that prevent or treat opioid use disorder. The agency invited applications by Sept. 30 and said it will announce the "innovation challenge" winners in November.

Applicants selected for the challenge will work directly with the agency to accelerate development and premarket review. The agency said it will evaluate proposals based on the feasibility, potential public health impact and novelty.

The challenge is part of the FDA's ongoing work to reduce the scope of the opioid crisis and supports several of those overarching goals, said Michelle Tarver, CDRH's director of patient science and engagement, during a recent FDA webinar outlining the challenge and its application process.

(See **Innovation***, Page 2)*

UK Brexit Implementation Period Would Mean Business As Usual

The UK's Medicines and Healthcare products Regulatory Agency released guidance on how EU mutual recognition agreements would affect devicemakers during the Brexit implementation period.

For the purposes of international agreements, the UK will be treated as an EU member state during the implementation period and there will be no disruption to existing relationships, the MHRA said.

Under the proposed implementation periods, CE marking would continue to be used and recognized for both the UK and EU markets, and UK-based device manufacturers would not require an authorized representative based in the EU.

UK notified bodies would continue to conduct third-party conformity assessments in the UK, and the results of the tests would be used and recognized in both the UK and EU markets.

(See **Brexit***, Page 6)*

Innovation, *from Page 2*

"We want to encourage development of non-opioid treatments for both acute and chronic pain," said Jonathan Jarow, the FDA's chief medical officer for the Office of Device Evaluation. "And we want to expedite both the development and review of innovative, safe, and effective medical devices that either help prevent or treat opioid use disorder."

Although the statutory requirements for device marketing won't change for products in the program, the agency will "make every attempt, particularly for breakthrough devices" to shepherd it through to market "as long as we have reasonable assurance of safety and effectiveness of the product for its intended use at the time of marketing approval," Jarow said.

The FDA is looking for technology that shows potential for the greatest public health impact and that would most benefit from FDA involvement in the development phase, Jarow added. The agency is accepting applications for medical devices including software, therapeutic devices, digital health technologies and combination products at any stage of development from concept to those that are already on the market. Breakthrough Device designation will be granted to devices that meet the statutory criteria for the designation without submission of a separate application.

Funding for a product doesn't affect eligibility and won't affect the likelihood of an application getting the green light. In fact, "our hope is that potentially being in the challenge would increase your avenues for fundraising," Jarow said.

Applications should describe the anticipated benefit of the device and its impact on public health—particularly on vulnerable populations—compared to alternative therapies, based on concept or clinical evidence.

The application should also include descriptions of the following:

- The intended use and a brief description of the device, including target patient populations;
- How the device technology is novel in design and concept and how it's better than currently available therapies, medical apps or diagnostics;
- The development plan for the medical device, including proposed clinical study design and planned marketing application;
- The development team and prior device development experience of essential team members;
- Manufacturing plans and capabilities, including any prior FDA inspection history; and
- How increased FDA participation will benefit the development program for the device.

The challenge application has a seven-page limit. To save space, Jarow suggested applicants could use links to supplemental information, such as videos or schematics, but he said the application needs to stand on its own without them.

The FDA's 2018 Strategic Policy Roadmap prioritizes policies to combat the opioid crisis, including support for cutting-edge research and improving access to treatment and recovery services. — Gienna Shaw

DITTA Urges FDA to Help Fix MDSAP's Inconsistencies

The Global Diagnostic Imaging Healthcare IT & Radiation Therapy Trade Association is calling on the FDA and the Medical Device Single Audit Program consortium to review the program's inconsistencies and revise companion documents so devicemakers and auditing organizations are clear on expectations.

DITTA said its members continue to experience long wait times to schedule MDSAP audits and there is a need for more guidance to deal with inconsistencies among auditing organizations.

The association sent a letter to the FDA to enlist the agency's help in improving the program ahead of next month's International Medical Device Regulators Forum meeting in Beijing.

DITTA surveyed its members and found that many devicemakers have to wait several months to get audit date confirmations and certificates from auditing organizations.

The association also said there were wide discrepancies among audits at different manufacturing plants, making it difficult for manufacturers to ensure they receive MDSAP certification, due to different interpretations of findings that effect costs and planning.

For example, the association said some auditing organizations "believe that all activities that are conducted by resources outside of the four walls of a site should be treated as outsourced processes, even if conducted under the same quality management system. This was clarified in the ISO handbook but it is not widely known by AOs."

There are also inconsistent audit time calculations and audit response criteria where multiple certification schemes are audited at the same time. For example, MDSAP nonconformance response timeframes and the evidence required do not align with ISO, DITTA said.

In addition, inconsistencies in the scoring methodologies among different AOs are causing confusion, with some manufacturers noting inconsistencies within individual AOs.

Manufacturers said that each AO "seems to have a different interpretation of what is considered a 'repeat' finding," and the inconsistences are creating problems for devicemakers as repeats can impact on the failure or success or their audits.

Duplications Not Part of the Plan

Devicemakers also questioned why audits for the EU Medical Devices Directive are being conducted as part of MDSAP audits when the EU is not a participating MDSAP member.

AOs are also requesting to review premarket applications that have already been reviewed and approved by regulators and some AOs are auditing against the requirements of all five MDSAP countries even if the audited site is not required to be audited by a certain jurisdiction.

The association urged the FDA to work with the MDSAP consortium to draft additional documents to address the inconsistencies.

South Korea Moves To Deregulate Device Industry

The South Korean government announced some deregulatory measures to accelerate device market access to boost the country's medical device industry.

The move is part of an effort to ease market entry for lower risk devices and boost the country's innovative device industry, particularly for artificial intelligence, 3D printing and robotics technologies, according to a new report by Fitch-Solutions, formerly BMI Research.

The government established a $28 million venture fund to finance commercialization of innovative technologies and it plans to support new R&D units in research hospitals to encourage collaboration between the device industry and the hospital sector to create new technologies.

(See **Korea***, Page 4)*

Korea, *from Page 3*

The government had previously tagged 3D printing, artificial intelligence and robotics as key areas in which the country could develop manufacturing capability and competitiveness.

Korea's Ministry of Food and Drug Safety released new guidelines for assessing devices using AI, big data and robotics.

In May, Korea approved its first AI-based diagnostic tool. The Med BoneAge device, sponsored by Korean devicemaker Vuno, uses software developed in collaboration with the Seoul Medical Centre to identify the age of a patient's bone through comparative X-rays. The company is working with the ministry to approve its AI-based image analysis software, including CT and X-ray chest analysis for detecting lung diseases and ophthalmoscopic image analysis for detecting eye diseases.

Korea's MFDS will conduct separate reviews for advanced medical devices to allow for preferential market access for innovative devices and they will go through a much shorter regulatory approval process to accelerate introduction, while the approval process for lower risk devices will move from a positive system to a negative system.

MFDS said this will cut approval times from more than one year to just 80 days by allowing evaluations to take place after the market release.

The MFDS is also implementing an integrated assessment process involving the National Evidence-based Healthcare Collaborating Agency and the Health Insurance Review and Assessment Service to allow simultaneous technical evaluation and health insurance reimbursement review. This should cut the overall process from nearly 500 days to less than 400 days.

To further boost its device sector, the Korean government is aligning its regulatory framework with international standards. For example, the Ministry of Science and ICT and the Korea Internet Security Agency published new guidelines for medical device cybersecurity risk management. The Smart Medical Cyber Security Guide references the UL 2900 cybersecurity standard.

FDA Hits Tennessee Firm for Missing Procedures, Other Deficiencies

The FDA cited Reliance Mobility in a Form 483 with 13 observations after an April inspection of the company's Columbia, Tennessee, facility.

The agency investigator found the facility had no design history files for two speech generating devices and it lacked procedures for design control. The company also lacked adequate device history records and procedures for quality audits, acceptance activities and document control.

In addition, the facility had inadequate procedures for control of labeling. For example, the procedure did not "ensure labeling is not released until a designated individual has examined the labeling for accuracy and the release, including the date and signature of the individual perfo1ming the inspection, is documented," the agency said.

The company's device history records for the two devices did not include the labeling for each production unit, manufacture dates, final acceptance records, or documentation of the software version downloaded into each device.

The agency also faulted the company on its complaint-handling procedure, finding that it did not properly ensure all complaints were evaluated to determine if medical device reporting was necessary or ensure that complaints received by customer support were actually logged as complaints.

The company's procedures for reporting adverse events did not ensure completed MDRs were submitted in a timely manner or address how all information reasonably known would be submitted and it had no established CAPA procedures, the agency said.

The company also lacked procedures for control of nonconforming product or for evaluation of suppliers, contractors and consultants.

Read the Reliance Mobility Form 483 here: www.fdanews.com/08-09-18-reliancemobilityllc483.pdf. — Zack Budryk

Three Practical Keys to an Effective QCU

The quality control unit must be designed in a way that enables it to see and react to issues as they arise or, better yet, preemptively. The unit must touch all of the quality systems regulated by the FDA or other regulatory bodies.

First and foremost, the QCU must be fully independent of other operations in the facility. Just like the internal audit teams, QCU staff must be independent of all quality systems so that their oversight of these systems can be unbiased. Even the perception of bias in favor of a particular process or system can render a QCU ineffective.

The second characteristic is value; that is, the QCU must be valued throughout the company, from upper management all the way down through production line staff. If the unit is not seen as valuable to the company, its operations and its products, it will not be given the resources it needs to properly oversee the quality systems throughout the corporation.

Third, the entire company must understand that responsibility for quality — the QCU's function — is different from the responsibility for quality assurance. QA steps are taken at each stage of production. A wide range of employees and departments will have certain QA responsibilities involving personnel, training, documentation, equipment maintenance and myriad other activities and materials that go into device manufacture.

On the other hand, quality control, the QCU's purview, refers more to an overarching philosophy. This is mirrored, for instance, in the FDA's own Quality System Inspection technique, which focuses on key systems that are specifically designed for quality control on a corporate-wide scale, and which are supported by the various quality assurance activities that go on during day-to-day operations.

"I like to use the phrase that everybody is responsible for quality, but not everybody is responsible for quality assurance," says Crystal Mersh, executive partner with quality control unit consultancy QxP.

Excerpted from the FDAnews management report: *Effective Internal Audits and Quality Control Units for Devicemakers*.

FDA Flags Hand Biomechanics Over MDRs, CAPAs

Hand Biomechanics failed to complete package integrity validations and had incomplete medical device reporting procedures, the FDA said in a Form 483 issued after a March/April inspection of its Sacramento, California, facility.

Investigators found the company did not complete a package integrity validation for three products labeled as sterile.

The company also failed to initiate CAPA files for failures identified in a 2017 warning letter or to properly investigate the cause of loss in production control which led to non-conforming seal packaging.

The facility also lacked complaint procedures to determine whether a complaint represents an event required to be reported to the FDA.

The FDA also found the company's complaint-handling procedures included an evaluation for MDR reportability but did not treat death or serious injury as a reportable event.

Read the Hand Biomechanics Form 483 here: www.fdanews.com/08-09-18-handbiomechanics-labinc483.pdf. — Zack Budryk

FDA Cites Quasar Bio-Tech For Design Changes, Complaints

The FDA rapped Quasar Bio-Tech for inadequate design changes, complaint-handling and risk analysis in a Form 483 after an April 2018 inspection of the company's Sarasota, Florida, facility.

Investigators found the company did not properly document design changes to product labeling to its Baby Quasar Plus and Quasar MD Plus, and the changes were not verified or validated for regulatory impact as required by the company's written procedures.

The inspection also found a complaint received in October 2016 and internally identified as an adverse reaction was not properly investigated for MDR reportability. The customer in question said use of the device caused them to follow up with a "specialist," but the company kept no records of follow-up with the customer to determine whether medical intervention was necessary.

In addition, the company's procedures for customer complaints did not include requirements to identify the most likely underlying cause.

The facility's failure mode analysis documents did not identify risks associated with manufacturing and supplier-obtained components, and CAPA procedures did not include how to analyze quality data.

The company also failed to move printed circuit boards from inventory to assembly in a way that ensured environmental protection, the agency said.

Read the Quasar Bio-Tech Form 483 here: www.fdanews.com/08-09-18-quasarbiotechinc483.pdf. — Zack Budryk

Brexit, *from Page 1*

"To give businesses, organizations and citizens certainty, common rules will remain in place until the end of the implementation period," MHRA said, which would mean that businesses will be able to trade on the current terms until the end of 2020.

This means that a centrally authorized product will be valid for the EU and the UK during the implementation period.

During the implementation period, the MHRA may continue to attend EMA meetings and EU committee meetings, and it may continue to participate in all discussions but it will not be able to vote. In addition, the UK will continue to have access to all EU databases and systems currently in use.

The EU Medical Devices Regulations will apply from May 2020 during the implementation period. The new EU IVD regulations will not apply until May 2022.

"However, elements of both new device regulations have applied directly in UK law since May 2017, meaning medical devices, including IVDs, can now be legally placed on the UK market if they are in conformity with the new regulations," the agency said.

FDA Pushes Back UDI Compliance Date for Combination Products

The FDA extended the compliance date for Global Unique Identification Database (GUDID) submission requirements for combination products, giving devicemakers another year to comply.

The compliance date, which the agency extended to Sept. 24, 2019, applies to manufacturers of co-packaged and cross-labeled combination products that are subject to CDER premarket review.

The agency said it is pushing back the deadline because it is "deploying enhancements to GUDID to better accommodate data submissions of combination products that are reviewed by CDER and contain device constituents."

The agency cautioned manufacturers that its compliance date extension has no effect on the UDI label requirements compliance date for co-packaged and cross-labeled combination product manufacturers. That date remains Sept. 24, 2018. — James Miessler

APPROVALS

NuVasive's Surgical Automation Platform Cleared by FDA

The FDA granted 510(k) clearance for Pulse, NuVasive's surgical automation platform, which combines 2D and 3D navigation and smart imaging capabilities.

Used for spinal surgery, the device includes multiple technologies with features that allow wifi and independent device access.

Pulse addresses visualization problems during surgery by using multiple high-resolution cameras to allow surgeons an uninterrupted line of sight.

CarboFix Spine Screw Systems Cleared by FDA

CarboFix's CarboClear carbon fiber pedicle screw system was granted 510(k) clearance by the FDA for three different sized screws.

The three screw types, which come in diameters of 5.5, 6.5 and 7.5 mms and lengths of 30-45 and 35-55 mms, are marked by an ultra-thin titanium shell to allow visualization with a fluoroscope.

The device can be used temporarily in patients with advanced stage thoracic and lumbar spine tumors who cannot undergo fusion.

FDA Clears Sekisui's Diabetes Assay

The FDA granted 510(k) clearance for Sekisui Diagnostics' Sekure Hemoglobin A1C (HbA1c) assay for diagnosing diabetes mellitus.

The assay eliminates manual preparation prior to testing. It is now available on the company's SK 500 clinical chemistry system.

The HbA1c assay has also been cleared for identification of patients at risk for developing the disease and monitoring long-term blood glucose controls in individuals that have the disease.

FDA Approves Roche's HPV Test For Cervical Cancer Screening

The FDA approved Roche's cobas HPV test for first-line screening of cervical cancer in women 25 years and older.

The cobas HPV test is now approved for all cervical cancer screening indications included in professional society guidelines.

The test assists healthcare providers in identifying women at risk for cervical cancer by identifying the DNA of the HPV genotypes most responsible for causing cervical cancer, as well as high-risk genotypes.

TGA Approves Baxter's Infusion System

Australia's Therapeutic Goods Administration approved Baxter's Evo IQ infusion pump system.

The infusion system comes with an advanced drug library and software that reduces dose errors to improve patient safety.

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

Approvals, *from Page 7*

It also features technology that allows physicians to switch easily between gravity and pump applications without changing sets, which may reduce the chance of touch contamination.

Medtronic's Spinal Cord Stimulator Approved in Canada

Health Canada approved Medtronic's Intellis spinal cord stimulator for treating chronic pain.

Commonly used for treating pain caused by failed back syndrome, the device sends mild electrical signals to nerves in the epidural space.

Spinal cord stimulators are also used for treating complex regional pain syndrome, intractable angina, pain from nerve damage and visceral abdominal and perineal pain.

FDA Clears Modulated Imaging's Clarifi Imaging System

The FDA granted 510(k) clearance to Modulated Imaging's Clarifi imaging system, used for noninvasively assessing tissue function.

The device quantifies and displays hemoglobin concentration and its distribution and reveals individual biomarkers for physician use.

The imaging system measures oxygenation and hemoglobin levels in order to treat burns, foot ulcers, chronic wounds, peripheral vascular diseases and other conditions.

Hologic Gains Approval For Group B Strep Assay

The FDA granted approval for Hologic's group B streptococcus (GBS) assay for its Panther Fusion system.

The approval comes after July's GBS awareness month, an initiative to improve knowledge and prevention methods for GBS during pregnancy.

The nucleic acid amplification test is used to identify pregnant women that carry the bacterium, which can lead to life-threatening complications in their children.

Strata's Tip Accessory for Excimer Laser Receives Clearance

The FDA granted 510(k) clearance to Strata Skin Sciences for its Multi-Micro Dose tip accessory, which is used with its Xtrac 308nm excimer laser.

The tip accessory is used in conjunction with the excimer laser, which is used to treat psoriasis. It can be used on areas that are difficult to treat and have not responded to other types of treatment.

The accessory is designed to filter narrow band UVB light to deliver the maximum dose for patients without causing blisters.

FDA Expands Indication For Savi Scout Reflector

Cianna Medical received 510(k) clearance to expand the indication for its Savi Scout reflector.

The expanded indication allows the Scout device — which is used for wireless breast tumor localization — to be used for localization of soft tissue, including axillary lymph nodes.

The reflector is used for breast tumor treatment procedures, such as targeted lymph node dissection, marking tissue before neoadjuvant chemotherapy and breast tumor localization.

FDANEWS

Customer Service
(888) 838-5578 • +1 (703) 538-7600
customerservice@fdanews.com

Editorial: Declan Conroy
+1 (703) 538-7644
dconroy@fdanews.com

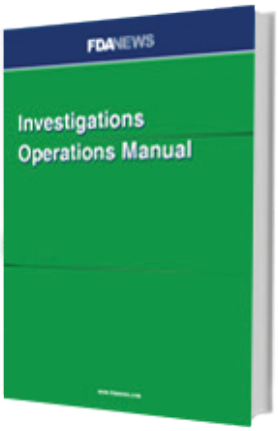
Ad Sales: Jim Desborough
+1 (703) 538-7647
jdesborough@fdanews.com

Multi-User Sales: Jeff Grizzel
+1 (703) 538-7669
jgrizzel@fdanews.com

300 N. Washington St., Suite 200 • Falls Church, VA 22046-3431 • Phone: (888) 838-5578 • +1 (703) 538-7600 • www.fdanews.com

Reporters: Zack Budryk, James Miessler, Bill Myers

President: Cynthia Carter



Investigations Operations Manual 2018

The **Investigations Operations Manual** is the primary policy guide for FDA investigations and directs the conduct of all fundamental field investigational activities. Adherence to the manual is required.

Now you can have the same investigation manual for 2018 that the FDA investigators use.

Know what the investigators look for — before they even get there. Know the investigators' expectations and rights. Find and fix problems *before* they end up on a Form 483 or warning letter.

There is no better way to prepare for an inspection than studying the actual procedures the FDA teaches its investigators.

Available directly from FDAnews, the newly updated edition of the **Investigations Operations Manual 2018** is the primary source FDA investigators use to conduct field inspections.

Order today.

Get insider information on:

- Sampling techniques
- Import hold procedures
- Recalls
- Types of investigations
- And more…

Make sure you've got the *latest* version before the FDA knocks on your door.

FOUR EASY WAYS TO ORDER

1. **PHONE:** Toll free (888) 838-5578
   or +1 (703) 538-7600
2. **WEB:** www.fdanews.com/55983
3. **FAX:** +1 (703) 538-7676
4. **MAIL:** FDAnews
   300 N. Washington St., Suite 200
   Falls Church, VA 22046-3431

☑**Yes!** Please send me ____ copy(ies) of **Investigations Operations Manual 2018** at the price of $377 for each PDF.

Name _____

Title _____

Company _____

Address _____

City_____ State _____ Zip code _____

Country _____

Telephone _____

Fax _____

Email _____

METHOD OF PAYMENT

❑ Check enclosed (payable to FDAnews)

❑ Bill me/my company. Our P.O.# _____

❑ Charge my credit card:
❑ Visa ❑ MasterCard ❑ American Express

Credit card no. _____

Expiration date _____

Signature _____
(Signature required on credit card and bill-me orders)

Virginia customers add 6% sales tax.

18FLYR-N