INTERNATIONAL DEVICES & DIAGNOSTICS MONITOR

Vol. 4, No. 38
Sept. 24, 2018

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FDA to Rely More on 510(k) Reviews Conducted by Third Parties

The FDA released a comprehensive new plan that proposes to rely more on reviews conducted by third parties to streamline its review process and avoid re-reviews of 510(k) applications.

The plan is aimed at improving efficiency and consistency of the premarket notification process, with a goal to have 85 percent of third-party submissions not re-reviewed by the agency by 2021.

FDA Commissioner Scott Gottlieb said the third-party reviews "must be equivalent in rigor and completeness to the kinds of reviews that we'd conduct."

Gottlieb said the agency is "taking new steps to better leverage reviews provided by experts in FDA-recognized third party review organizations," as part of its efforts to expedite patient access to lower-risk devices.

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Australia Rolls Out Work Plan To Engage With International Regulators

Australia's Therapeutic Goods Administration released a new work plan spelling out how it will engage with overseas regulators to increase information sharing and regulatory convergence.

The agency noted it will be working this year to establish policies and guidelines for work-sharing processes with the EU, Canada, Japan and the U.S.

The agency also plans on working with counterpart s in the International Medical Device Regulators Forum (IMDRF) to develop a common "Table of Contents" to establish a standard format to support electronic device submissions.

Australia is also heading up an IMDRF working group to develop guidance that establishes definitions and regulatory pathways for

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Under the plan, the FDA would streamline its review of device premarket submissions that have already undergone a review by qualified, expert third parties. For eligible submissions, the FDA would review third-party recommendations to make its final decision and generally would not re-review the submission itself.

Leveraging outside reviews for lower-risk products could improve productivity by allowing FDA reviewers to focus on evaluating applications for higher-risk and more complex devices, the agency said.

The agency issued draft guidance alongside the plan to provide clarity and transparency for industry and FDA-recognized third-party review organizations (3PROs). The guidance outlines factors used to determine which device types are most appropriate for the program, the process the agency would follow when deciding whether to recognize third party review organizations, and specific commitments Congress authorized to strengthen the program.

Faster Reviews

Because much of the reviews will be conducted by outside experts, the program is expected to reduce agency review times to 30 days or less by eliminating duplicative re-reviews of certain information by FDA staff. The guidance replaces 2016 draft guidance and reflects statutory changes under the FDA Reauthorization Act (FDARA).

FDARA provides FDA with the authority to tailor the list of eligible devices and directs the FDA to provide guidance that states how a device type, or subset of a device type, is eligible for review by 3PROs.

The FDA will also consider the extent to which 3PROs have access to the information needed to make well-informed recommendations, the extent to which a review requires multi-faceted interdisciplinary expertise and the extent of postmarket safety data that would be required, the guidance says.

The agency is developing web-based training and other resources to help guide 3PRO reviews and make it easier for them to ask FDA questions. One such tool includes a guided tailored template to ensure that review memos include all the information required for specific devices types.

The agency will also establish an early interaction process that allows 3PRO reviewers to ask FDA questions at any stage of the review process. In addition, it will develop device-specific training by FDA subject matter experts. A pilot program is underway that will provide a training development toolkit focused on radiography devices.

The draft guidance describes scenarios where 3PROs should contact the FDA's Ask the Expert service before beginning a review. The agency will also establish a channel to notify 3PROs of adjustments in FDA review practices as technology changes.

Although the framework seeks to improve the efficiency of the review of 510(k) submissions for certain lower-risk devices, the final authority to decide which devices may by marketed remains with the FDA.

The agency also plans to carry out routine or for-cause audits of 3PROs and it will suspend or withdraw a 3PRO's recognition status if it is found to be non-compliant.

Read the new plan here: www.fdanews.com/09-18-18-FDA3rdpartyplan.pdf.

Read the guidance here: www.fdanews.com/09-18-18-FDA3rdpartyguidance.pdf.

FDA Warns ITG-Medev For Validations, Other Failures

ITG-Medev failed to follow up on its promised solutions to nonconforming process validations and documentation of acceptance activities, the FDA said in a warning letter to the devicemaker.

The FDA inspected the firm's San Francisco facility in June and found that the company failed to conduct proper sterilization validation. In its response, the company said it would have a third-party contract laboratory conduct the sterilization validation and provide the FDA with validation results.

The FDA noted the firm had not provided the agency with any additional response or corrective action information. It also failed to say how it plans to ensure the contract lab will be able to validate sterilizations conducted at a different facility. "For example, your response does not indicate whether the third-party laboratory will conduct the validation at the contract sterilizer, or if the third-party laboratory will simply be reviewing the results of the testing," the agency said.

In response to failures to document acceptance of finished devices, the company created a new form for documenting acceptance. However, according to the FDA, the new form did not include information such as the date and signature of the approver.

Additionally, the firm promised to develop a new CAPA procedure, but claimed to have always followed existing CAPA procedures "without the paperwork," although all CAPA activities are required to be documented.

ITG-Medev also failed to properly document either an investigation it claimed it would undertake for a product non-conformance or an evaluation of suppliers and contractors. The company also said it would establish a complaint form but it did not provide evidence that it created one.

Lastly, despite telling the FDA it would complete missing quality audits noted in the first inspection by August, the firm had not submitted additional evidence of corrections to the FDA, according to the warning letter.

Read the full warning letter here: www.fdanews.com/09-20-18-ITGMedevInc.pdf. — Zack Budryk

Stakeholders Ask FDA to Clarify CGMP Guidance on Combination Products

AdvaMed and other industry groups asked the FDA to provide more details on the agency's proposed list of alternative mechanisms for compliance with CGMP requirements for combination products.

The agency issued a June 13 notice proposing a list of alternative or streamlined mechanisms for complying with CGMP requirements.

In written comments on the proposal, AdvaMed asked the FDA to give more examples of combination product types and manufacturing processes for which good manufacturing practices diverge from standard combination product CGMPs and to clarify what alternate approaches sponsors can use to comply with CGMPs.

"This information would allow sponsors to better understand the varying and alternative or streamlined mechanisms available to meet combination product CGMP requirements," AdvaMed said. "In turn, this information would position sponsors to apply these mechanisms or propose new mechanisms."

PhRMA asked the agency to clarify the scope of the guidance's exemption of combination products from device quality systems regulation. Specifically, the trade group said, the agency should clarify that the exemption applies to combination products co-packaged with a Class I device intended to be used for delivery of the drug. "PhRMA previously iterated our concerns with the current combination product regulations with respect to drug products co-packaged in convenience kits with low-risk delivery devices (such

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as dosing cups, syringes, spoons, etc.), which may subject the drug manufacturer to the full QSR when such devices are included with a drug in a convenience kit," the trade group said.

"Requiring drug manufacturers to comply with the full scope of the QSR for combination products incorporating these device constituent parts increases the complexity and cost of manufacturing drugs and providing these convenience kits," PhRMA said.

Read the comments here: www.fdanews.com/09-20-18-Comments.pdf. — Zack Budryk

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personalized medical devices. The work will promote global harmonization in terminology and premarket requirements for these devices.

"Consistency helps when sharing information between participating regulators, industry and others," the agency said. The agency also plans to work with IMDRF to harmonize terminology relating to adverse event types, evaluation, patient injury and device components. Broad consultations with stakeholders are planned to craft adverse event standardization guidance, the agency said.

Other ongoing work with IMDRF includes developing a common set of competency, training and conduct requirements for reviewers to build confidence in the consistency of regulatory reviews across jurisdictions.

The TGA will also participate in ISO technical committees to develop standards for devices, including standards that underpin quality management, sterilization of devices, administration of products such as catheters, lung ventilators and related equipment.

Standards Australia is Australia's nominating body to ISO, and local committees serve to make sure that ISO standards are suitable for use in Australia before they are adopted. This year, standards and guidance documents devices will be developed with the ISO Technical Committee 198 for:

- Radiation sterilization;
- Moist heat sterilization;
- Packaging;
- Reprocessing of resterilizable devices;
- Washer-disinfectors; and
- Assurance of sterility.

The TGA is an active member in the Medical Device Single Audit Program along with Brazil, Canada, Japan and the U.S. The agency said it plans to support MDSAP assessments performed in the Western Pacific region.

The TGA is also stepping up its involvement in the Indo-Pacific region to help regulators address capacity gaps for products to combat potential health threats — such as diagnostics to detect infectious diseases.

Read the TGA work plan here: www.fdanews.com/09-18-18-TGA.pdf.

South Korea's Mi Gwang Contact Lens Short-Sighted on Quality

Numerous quality system failures were uncovered at South Korea's Mi Gwang Contact Lens Company during a March 2018 FDA inspection.

The firm's plant in Gyeongsan-si had not identified quality data sources to be analyzed to minimize the impact of internal and external failures when it came to taking corrective and preventive action, according to the eight-item Form 483.

Manufacturing processes were not developed to ensure that devices conformed to specifications, and device history records were incomplete and lacked vital data.

Inspectors found that procedures for receiving, reviewing and evaluating complaints by a formally designated unit were not established. A number of complaints lacked product evaluations and inspection results, and document control procedures were not established.

Medical device reporting procedures didn't include internal systems to determine when an event meets MDR reporting criteria.

In addition, procedures for management reviews were not established, and senior management didn't participate in management review meetings.

Read the Mi Gwang Contact Lens Form 483 here: www.fdanews.com/09-20-18-migwangcontactlenscoltd483.pdf.

Buffalo's Graphic Controls Acquisition Fails to Control Product

Devicemaker Graphic Controls Acquisition lacked numerous procedures to ensure that products conformed to specifications, according to a 483 the firm received following a May 8 -14 inspection of its Buffalo, New York facility.

Numerous CAPAs reviewed didn't include an adequate investigation and many didn't include validation of the effectiveness of the corrective actions taken. The agency investigators noted that complaints describe corrective actions that "are taking place or have taken place," but CAPAs were not created for the issues identified in the complaints.

The 483 said the firm had not established procedures to control products that don't conform to specified requirements. For example, a number of nonconformances reviewed didn't include documented evaluation of the need for an investigation and there was no justification for control of nonconforming material.

The inspection revealed that sampling sizes used for in-process inspections and functional testing of electrodes was not based on valid statistical rationale.

Also, preventive maintenance for machines being used was either performed late or missed altogether, and the firm lacked procedures for periodic inspections.

In addition, rework and re-evaluation activities were not documented in the device history record and personnel training was not documented.

Read the Graphic Controls Acquisition Form 483 here: www.fdanews.com/09-20-18-graphiccontrolsacquisitioncorp483.pdf.

Validation, CAPA Failures Plague Canadian Devicemaker Pega Medical

Validation and CAPA failures were among quality system failures uncovered during a Feb. 26 to March 1 FDA inspection of Pega Medical's Quebec facility.

Process validation activities failed to include acceptance activities or documented evidence of manufacturing conditions representative of routine production activities, the five-item Form 483 said.

The heavily redacted 483 noted that no acceptance criteria were established and no product testing was conducted for a product as part of the validation exercises for the company's pediatric orthopedic devices, including 3D-printed orthopedic implants.

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GAO: VA Hospitals Struggle With Reusable Medical Equipment

Many VA Medical Centers are unable to effectively reprocess reusable medical equipment, leading some to opt for disposable instruments instead, according to a new report from the Government Accountability Office.

The Veterans Health Administration, which oversees the centers, is facing ongoing challenges with reprocessing. In 2009, 10,000 veterans found out they might have been exposed to hepatitis B, hepatitis C and HIV because of improperly reprocessed endoscopes.

In 2011, the GAO found the VHA had not provided enough guidance to ensure reusable medical equipment was being reprocessed properly. And in 2018, the VHA Office of the Medical Inspector determined veterans were experiencing procedure delays and cancellations because of an instrument shortage related to improper reprocessing.

As medical instruments have become more complex, "reprocessing has become more complicated and time consuming," said Sharon Silas, acting director of the GAO's health care team.

The centers have been hampered by the increasingly complex sterilization process, insufficient staffing at Sterile Processing Services (SPS) programs and by communication breakdowns between the VHA Veterans Integrated Service Networks responsible for inspecting the reprocessing programs.

Timely transporting of contaminated reusable medical equipment is an issue for centers that don't have an on-site SPS program.

Contaminated reusable medical equipment must be transported to the location where it will be reprocessed within four hours of use. That timeframe extends to 12 hours if the medical center uses a pre-cleaning solution spray before transporting. But the timeframe is still challenging for many centers because of the distance to the nearest SPS department — so some are using disposable medical equipment.

Although this seems like a costly workaround, VHA officials said it can be cheaper than reusable medical equipment "depending on the situation."

The GAO's review mainly focused on the VA's oversight and found that for fiscal year 2017, the VHA lacked more than 25 percent of the VISN reports on inspections of SPS departments.

The GAO's 2018 audit did not address the manufacturer's role in the reprocessing process, though Silas believes companies can take steps to help ensure patient safety.

She said manufacturers should develop reprocessing guidelines for reusable medical equipment that are easy to follow and should "promptly notify customers of changes to these guidelines or any safety issues involving their equipment."

As manufacturers develop new instruments, "they should also conduct thorough testing to ensure the items can be effectively reprocessed," she said.

Read the full GAO report here: www.fdanews.com/09-11-18-ReusableMedicalEquipment.pdf. — Tiffany Winters

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Medical, *from Page 5*

CAPA procedures did not include an evaluation of the validation of related manufacturing processes after changes in respective manufacturing processes were implemented. The 483 notes that the impact of confirmed product failures was not evaluated as part of CAPA investigations.

Process control procedures were found to be lacking because they didn't describe controls necessary to ensure conformance to specifications. For example, production and process controls don't ensure that processing parameters were monitored or verified during routine production activities, the 483 said.

Finally, the FDA inspector found that changes in product inspection instruction plans were not documented or evaluated on related production change documents.

Read the Pega Medical Form 483 here: www.fdanews.com/09-20-18-pegamedicalinc483.pdf.

FDA Finalizes Guidance for Labeling, Testing of Heparin Devices

The FDA issued guidance on labeling and safety testing for heparin-containing medical devices, finalizing the agency's 2015 draft.

Heparin-containing combination products and medical devices should comply with the contaminant safety testing recommendations in the USP monograph on Heparin Sodium and follow CDER's guidance on detection of oversulfated chondroitin sulfate (OSCS) contamination, the guidance says.

The FDA recommends that manufacturers receiving a heparin sodium drug substance or API represented as "USP" for use in a combination product should document that the substance has been tested according to the current USP drug substance monograph and that it was manufactured and tested in keeping with current heparin guidance. They must also comply with the elements of safety testing required for compliance with quality system regulations and GMPs for combination products.

Read the final guidance here: www.fdanews.com/09-19-18-Heparin.pdf. — Zack Budryk

APPROVALS

InBios Cleared for Dengue Detection Kit

The FDA granted 510(k) clearance to InBios' DENV Detect NS1 Elisa Kit, used for detection of the dengue virus in patients.

The antigen detection assay is used for presumptive clinical laboratory diagnosis of the Dengue virus and has not been cleared for testing blood or plasma donors.

The kit uses samples collected from patients within the first week of showing symptoms of dengue fever or dengue hemorrhagic fever to detect the presence of the dengue virus.

Micro Ultrasound Device Gains Further Canadian Approval

Exact Imaging's FusionVu application, a feature of its ExactVu micro-ultrasound system, received regulatory approval from Health Canada.

The ExactVu micro-ultrasound platform provides real-time high resolution for targeted prostate biopsies.

The newly approved feature can be used to assist in analysis of a patient's MRI by aligning it with the live micro-ultrasound image.

OptraScan's Whole-Slide Scanners Receive CE Mark

OptraScan's on-demand desktop scanning devices have been approved for marketing in the EU.

The small-sized devices, which are used to scan slides and come in 20x and 40x magnification, fit in small workspaces and have cloud capabilities, as well as low and high throughput and a small footprint.

The slide scanners, which come in four different models, allow flexible storage, archiving and management of the metadata and digital images produced from scanning, as well as different features depending on the model.

Xact Robotics Earns CE Mark For Robotic Navigation System

Xact Robotics gained CE Mark approval for its robotic navigation and steering system used for image-guided percutaneous procedures.

The system has been cleared for use in planning and accessing areas in the abdomen during percutaneous procedures that are led by X-rays or ultrasound.

After the physician selects a target and entry point using the system, the robotic navigation system suggests a trajectory, along with verification checkpoints along the recommended path.

Motus GI Cleared to Market Slim Sleeve for Colonoscopes

The FDA granted 510(k) clearance for Motus GI to market its Pure-Vu Slim Sleeve for use with slim colonoscopes.

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The company's Pure-Vu Slim Sleeve device performs cleansing the same way as the standard Pure-Vu Sleeve device, and both are compatible with the Pure-Vu workstation.

The sleeve fits over the colonoscope during a colonoscopy, allowing physician to safely clean matter during the procedure and gain clear visualization of the colon mucosa.

Illuminoss Receives Additional Clearance for Bone Stabilization System

The system can be used to create an implant that conforms to the patient, providing strength and stability across the implant supporting the weakened bone.

The FDA has granted Illuminoss additional clearance for its photodynamic bone stabilization system.

The device can now be used by skeletally mature patients to treat traumatic, fragility, pathological and impending pathological fractures of the humerus, radius and ulna.

FDA Approves Device for Treatment Of Acute Coronary Artery Perforations

The FDA approved Biotronik's PK Papyrus Covered Coronary Stent System for treating acute coronary artery perforations or tears in the blood vessels of the heart — the first device approved by the agency for the indication in 17 years.

The device is advanced into the perforated coronary artery vessel using a balloon catheter. Once the stent is implanted, it provides a physical barrier to seal the tear in the artery wall while still allowing blood to flow through the device to the heart muscle.

The agency granted the approval through its humanitarian device exemption pathway. It reviewed real-world survey data from 80 patients who received stents.

Philips Gains CE Mark for Beltless Maternal Monitoring Device

Philips received CE Mark approval for its Avalon system, a fetal and maternal monitoring device that updates a patient's electronic medical record.

The beltless device is based on electrode technology and is used to stream patient data, such as fetal and maternal heart rate and uterine activity, to the electronic record via Philips' obstetrical information management system.

The device features a single patch and reusable pod that are placed on the mother's belly to capture critical parameters.

Contego Cleared for Carotid PTA Balloon System

The FDA granted 510(k) clearance for Contego's Paladin Carotid percutaneous transluminal angioplasty (PTA) balloon device for removing embolic material.

The device, which is used in carotid stent procedures, pairs an angioplasty balloon with an integrated 40-micron filter, giving it enhanced procedural flexibility and an extra level of protection.

Its embolic protection filter can be adjusted in vivo to account for differing patient anatomies.

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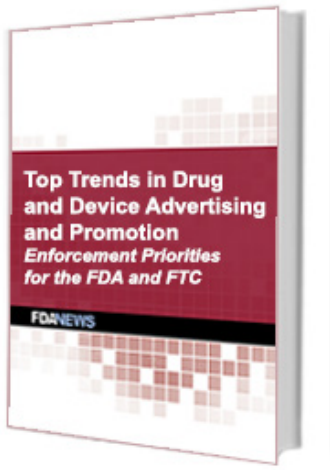

Top Trends in Drug and Device Advertising and Promotion: *Enforcement Priorities for the FDA and FTC*

As drug and device companies develop new and innovative ways of promoting their products — such as targeting new markets, influencer marketing and using social media and reality television — it's important to understand the regulatory priorities of the FDA and the FTC to avoid running afoul of those agencies.

Top Trends in Drug and Device Advertising and Promotion takes a deep dive into six areas regulators give the most attention:

1. **Consistent Communication:** Three factors that ensure communications are consistent with a product's approved labeling
2. **Direct-to-Consumer Advertising:** Use of distracting visuals, competing superimposed images and lively music that can minimize the required presentation of risk information
3. **Risk Disclosure:** How much information needs to be presented and how
4. **Payer Communications:** Disseminating healthcare economic information, or HCEI, to payers postapproval
5. **Preapproval Promotion:** A new safe harbor for communicating information about investigational products to payers
6. **Transparency:** Making it clear that a communication is sponsored advertising

Order your copy of **Top Trends in Drug and Device Advertising and Promotion: *Enforcement Priorities for the FDA and FTC*** and know how to handle hot spots in advertising and promotion while avoiding warning letters and other enforcement actions.

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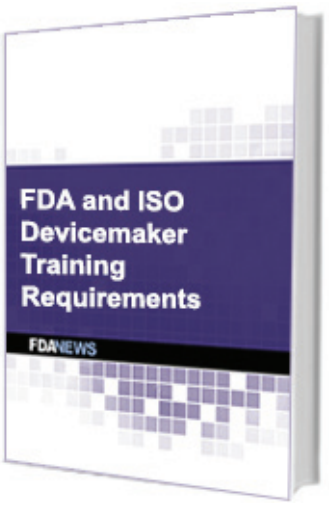

FDA and ISO Devicemaker Training Requirements

Device manufacture is a complicated business, but few areas are more rulebound than QMS. Many a devicemaker has come up short trying to stay abreast of the FDA's QSR, ISO 13485:2016, and other ISOs while trying to comply with competence, training and awareness rules.

It takes more than teaching simple skills to achieve the state of job readiness and performance required of devicemakers' workforces. Regulators agree that a comprehensive training program should consider employee education, experience, background and skills. What they don't agree on is what those concepts mean and how to incorporate them into training.

FDA and ISO Devicemaker Training Requirements breaks down training requirements in both the FDA's QSR and international standards ISO 13485, 9001 and 10018 — among others — shows where they overlap and where they differ and provides a plan for developing a training program that fills in all the gaps. You will learn:

- The four elements of competency
- Definitions of key terms and requirements
- The concept of a "designated individual" and the qualifications for the role
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