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IN THIS ISSUE

FDA Updates Guidance on 510(k)s For Expandable Biliary Stents

The FDA released new draft guidance for devicemakers on submitting premarket notifications for metal expandable biliary stents and their delivery systems.

When the original 1998 guidance was drafted, the FDA had concerns about biliary stents being used off-label for vascular systems, which could cause harm due to lack of safety and efficacy data.

Metallic stents have since been approved for cardiovascular indications, but the agency still has concerns about use of the biliary stents for cardiovascular indications unless they have also been cleared for the indications through a PMA.

The agency continues to place limitations on substantial equivalence determinations for biliary stents and it limits the guidance to biliary stents indicated for palliation of malignant strictures in the biliary tree.

(See **Stent***, Page 2)*

FDA Extends Comment Period for Inhaler Guidance Criticized by Industry Groups

The FDA reopened the comment period for its guidance on metered dose inhaler and dry powder inhaler drug products after receiving comments questioning the agency's thinking in the draft.

The Association for Accessible Medicines called on the agency to allow a transition period to comply with the new guidance because the revisions were so significant.

AAM said sponsors have based their development plans and budget allocations on requirements outlined in the agency's 1998 guidance, "making it difficult to retrospectively change course," adding that the FDA "should provide clarity around its expectations for companies to comply with the new guidance and consider a suitable transition period, for example 2 years."

(See **Inhaler***, Page 2)*

Stent, *from Page 1*

Many recommendations for 510(k) submissions remain the same, but the guidance includes new sections for sterility testing, shelf life and packaging, magnetic resonance compatibility and stent delivery systems. The guidance also provides more detailed examples such as an example of a device and predicate comparison.

One addition to biocompatibility testing includes material-mediated pyrogenecity, as well as suggested details on specific stent processing steps, including heat treatment and any subsequent surface finishing steps. Differences in formulation, processing, sterilization, or device surface properties that could affect biocompatibility of the final product.

For sterility testing, the FDA refers device-makers to updated guidance issued in January 2016 on submission and review of sterility information in premarket notification submissions for sterile devices. The guidance requires much more detail on sterilization methods.

For shelf life and packaging, the guidance recommends evaluating package integrity for maintaining device sterility and for evaluating changes to device performance or functionality. Recommended package integrity test methods include simulated distribution and associated package integrity as well as simulated aging and associated seal strength testing to validate package integrity and shelf life claims.

For evaluating the effects of aging on device performance, the FDA said that shelf-life studies should evaluate critical device properties to ensure it will perform consistently during the proposed shelf life. The agency describes specific bench tests to evaluate device functionality to evaluate design components.

The guidance includes new recommendations for magnetic resonance compatibility for passive implants, noting that MR imaging of patients with biliary stents poses the following potential hazards:

- Movement of the stent, resulting in tissue damage or displacement of the stent;
- Heating of the tissue surrounding the stent, resulting in damage to the biliary duct and surrounding tissue; and
- Image artifacts near the stent that may render MR images of nearby anatomy uninterpretable or misleading.

The updated guidance recommends a number of new bench tests, including galvanic corrosion, stent integrity, radial compression force, radial outward force and radioparity.

There is also a new section on stent delivery systems, and the guidance recommends that device-makers validate the accuracy and repeatability of the delivery system. It suggests testing to ensure the stent is not adversely affected by the delivery system both during deployment and withdrawal.

Read the draft guidance here: www.fdanews.com/07-19-18-BiliaryStents.pdf.

Inhaler, *from Page 1*

Secondly, the AAM wrote, the FDA should clarify the distinction between its expectations for NDAs and ANDAs. To avoid confusion, the final guidance should make clear when specific requirements are only appropriate for NDAs.

Lastly, the group wrote, the agency should be more precise in outlining the new stability requirements in the draft.

The International Pharmaceutical Aerosol Consortium on Regulation and Science, meanwhile, urged the FDA to clarify the guidance's risk management principles to make clear that the principles are to be documented within the context of a design controls process established by the sponsoring company.

The current draft, the consortium said, often describes its examples as "typical" or "general relationships," although there is "an infinite number of delivery system design and formulations that could be developed as combination products."

Read the comments here: www.fdanews.com/07-19-18-Inhaler.pdf. — Zack Budryk

Industry Questions FDA's Draft Guidance on Abbreviated 510(k)s

Stakeholders asked the FDA to clarify its proposal to expand the Abbreviated 510(k) program by allowing the use of performance criteria for demonstrating substantial equivalence.

Most comments on the agency's draft guidance asked for clarity on how the program would be different from the existing 510(k) process.

One industry group, the Bringing Real-World Insight for Device Governance and Evaluation (BRIDGE) Coalition, said more public input is needed to decide which products should be eligible for the program.

The FDA should expand on the definitions and processes within the guidance, such as when additional data is required and how criteria will be established, it said in its comments on the draft guidance, the coalition said.

It urged the agency to explain how the expanded abbreviated 510(k) pathway differs from the existing system and whether there are expectations for the number of submissions the FDA expects to see.

The coalition also expressed concern over the flexibility of performance criteria and asked for clarity on how the criteria would be kept current.

(See **510(k)***, Page 4)*

BRIEFS

Indian Devicemakers Push for Early Implementation of Packaging Rules

Indian devicemakers have urged the government not to extend a deadline for implementing new packaging rules.

The new rules, which were originally scheduled to be implemented in January 2018, require manufacturers to declare country of origin, date of manufacture, quantity and expiration dates for all pre-packaged devices.

The Association of Indian Medical Device Industry said Indian devicemakers were ready to comply with the new rules and they should be implemented as soon as possible. An AiMED spokesperson said the government was hurting Indian devicemakers by delaying implementation because other international companies were able to put products on the market that may not comply with the new requirements.

MHRA Recalls Novaline Hemodialysis Bloodlines

The UK's Medicines and Healthcare products Regulatory Agency issued a massive recall of NovaLine bloodlines used with Baxter/Gambro dialysis machines.

Manufactured by Vital Healthcare, the recall affects all lots of NovaLine tubing sets for hemodialysis that were manufactured in 2017. Specific product codes manufactured in 2017 have functional and assembly issues that may lead to air entering the system, blood loss, clotting and delays in treatment, the manufacturer said in the field safety notice.

The agency listed seven possible failures of the devices and actions customers should take to mitigate the risks. The manufacturer said all affected products should be removed from inventories.

Switzerland Overhauls Device Manufacturing Certificate Process

Swiss Medic will overhaul the way it issues export certificates and manufacturing certificates for devices in the fall and introduce new fees that take effect on Jan. 1, 2019.

Export certificates and manufacturing certificates are issued for countries that don't recognize European CE marking, and the increased demand was becoming unsustainable, the agency said.

Upcoming changes include clear requirements for submitting documents and product lists, electronic submissions, fee adjustments, and new service agreements that outline the scope of services Swiss Medic will provide, as well as the entitlements and obligations of the companies.

510(k), *from Page 3*

It said it was "looking for information on why this new approach will be of use to FDA and stakeholders," and it questioned whether there could be a performance standard in situations where there is no predicate device.

The Medical Imaging & Technology Alliance raised similar questions in its comments, saying it was concerned about the clinical and scientific evidence standards for validating equivalent analytical and clinical performance "despite the lack of direct comparisons with the predicate device."

It said the benefit of using the program is unclear in that the Special 510(k) program is 30 days while both the abbreviated 510(k) and the traditional 510(k) program are 90 days. "A clearly stated reduction in review time would be helpful," MITA said.

In addition, the association stressed that many devicemakers sell their products in global markets, and the FDA should approach proposed performance criteria and standards with "global harmonization in mind," to reduce the burden on industry to comply with multiple regulatory requirements across different jurisdictions.

The Alliance for Quality Medical Device Servicing, which is comprised of independent service organizations that provide third party services to device manufacturers, said specific language should be added to include service and maintenance procedures, methodologies, tools and documentation that would be made available to all servicers, including end users and third-party service organizations.

The alliance said it "believes that by doing so the FDA will help address restrictive and anti-competitive practices that are deliberately limiting or preventing access to these materials."

It stressed that providing such access would help ensure safety through the total product lifecycle of medical devices, adding that collaboration between independent service organizations and original equipment manufacturers is "paramount to providing safe, high quality and cost-effective service."

To that end, the FDA should state in the guidance that OEMs submit service and maintenance materials as part of the device description in the 510(k) and make them available. This would not increase the burden on OEMs but "reinforces the need to make available these outputs which are already required as part of existing regulations."

Read the full comments here: www.fdanews.com/07-19-18-Comments.pdf.

FDA Flags Neo Innovations For Complaint-Handling, MDRs

The FDA issued a Form 483 to class II device manufacturer Neo Innovations over design controls, medical device reporting and complaint procedures.

The agency issued the 11-observation 483 following an April inspection of the firm's Pueblo, Colorado facility. The investigator found the firm had no design control procedures in place for control of its class II IPL/Xenon Tattoo Removal Device and it had no design history file for the product. Investigators also found the firm had no procedures in place for medical device adverse events or for handling evaluating complaints related to the NEO IXL tattoo removal kit.

The company also had no procedures in place for control of corrective and preventive actions relating to the NEO IXL and it lacked procedures to evaluate raw material suppliers for the products or to document any changes to the materials they supplied.

The facility also had no device master record for documents associated with specifications and manufacturing requirements for the product.

In addition, the company had no procedures for management reviews. The facility also lacked procedures for quality audits and failed to conduct audits at least annually.

Lastly, the agency official found the company lacked training records and had no procedures in place for training on SOPs or quality system regulations.

Read the Neo Innovations Form 483 here: www.fdanews.com/07-20-18-neoinnovations483.pdf. — Zack Budryk

Tennessee Devicemaker Cited For Risk Analysis, Labeling

The FDA hit Nashville-based CNMC Company with a Form 483 over inadequate risk analysis and device labeling procedures observed by an agency investigator during a March inspection.

The firm's procedures for controlling and inspecting device labeling did not document label release. The facility did not document any label inspections or releases for its EquiDose II Diode Detector dose monitors.

The company performed an incomplete risk analysis for its Model 206 Electrometer device, failing to address possible hazards related to functional failures, energy and maintenance. The analysis did not fully address potential environmental hazards, such as using the device outside its intended environment, or possible usage related hazards, such as usage by untrained personnel or inadequate labeling.

In addition, the device's hazard of incorrect measurement is considered negligible "although resulting measurements may have a direct relationship to the accuracy of the radiation therapy dose delivered," the agency said.

The firm also failed to analyze service reports to identify and predict quality issues. Between January 2017 and February 2018, it did not analyze receiving and service records that it initiated. Some service reports were missing required information, such as the date of service, the test and inspection data and the personnel servicing the device.

(See **483***, Page 6)*

Common Root Cause Analysis Investigation Mistakes

The investigation process can often fall victim to a number of common mistakes. The most frequently cited of these is the tendency of teams to jump to conclusions in their haste to find the root causes of an incident. They allow the conclusion to drive the data, rather than allowing the data to drive them to the appropriate conclusion. Other common mistakes include:

- Allowing individuals and departments eager for answers to rush the investigation;
- Using training as a scapegoat or easy fix when a problem occurs; and
- Failing to test assumptions.

While training will usually form part of a CAPA response, companies should not use training, or the lack thereof, as an easy root cause without looking deeper into a problem. This is why a multidisciplinary team approach should be taken while investigating. Doing so relies on the knowledge of the entire team of investigators. Instead of reflexively zeroing in on training, a designer may detect a flaw in the design of a device — something another team member might have missed.

It's critical in an RCA to keep an open mind and focus on the facts. It may be tempting to rely on expertise and opinion. While both remain important, in the end only the facts of a given case will provide the objective evidence that leads to the successful conclusion of an investigation.

At its conclusion, the investigation lays out root causes and proposed corrective (if not already implemented) and preventive actions. This will feed into the CAPA plan that must be developed, which spells out how and when preventive actions will be implemented.

Q: *How does a company proceed when a nonconformity has been identified in the field?*

A: When a nonconformity is identified in the field, a company should have procedures detailing how to assess the impact of that nonconformity. First of all, what is the risk to the product and the safety of the customer, the end user? Then the company has to identify where this product is in the field, who has it, and decide what action to take based on the risk to patient safety.

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

LED Technologies Hit for Complaint Handling, Trend Analysis

The FDA issued Greenwood Village, Colorado-based company LED Technologies a 483, after observing poor complaint handling, an inadequate design history file and a failure to conduct trend analyses.

One of the firm's corrective and preventive action procedures required the firm to conduct trend analyses in order to evaluate reported complaints, non-conformities, quality records, audit reports, documentation and production processes. The agency discovered that the firm had only conducted the analyses as required for reported complaints.

The firm also did not use appropriate statistical methodology when performing a trend analysis for reported complaints. Specifically, it did not provide a mechanism for identifying existing and potential causes of non-conforming product or other quality problems, the agency said.

Read the LED Technologies Form 483 here: www.fdanews.com/07-19-18-ledtechnologiesllc483.pdf. — James Miessler

483, *from Page 5*

The investigator cited the firm's failure to document the results of corrective and preventive actions. Out of seven closed CAPA request forms that were initiated since January 2016, five had no documentation of the results of planned corrective actions and they all lacked documentation of the results of proposed verification activities.

In another observation, the agency official noted that the firm's rework and reevaluation activities were not fully recorded in the device history record. Specifically, the firm did not document the details of rework performed on a Model 206 feedback module assembly. The nature of the rework performed should have been documented on a product rework record and an engineer needed to approve it first.

The device history record contained no documentation of the type of rework and/or repair activities performed, or any engineering approval of repairs, the agency said.

Read the Form 483 here: www.fdanews.com/07-19-18-cnmccompanyinc483.pdf. — James Miessler

FDA Urges Sponsors to Ensure Data is 'Interoperable or Integrated'

Medical product sponsors and researchers should work with electronic health record keepers to help improve clinical trial accuracy and efficiency, the FDA said in a new guidance.

In a final guidance, the FDA encourages sponsors and investigators to use approved EHR or electronic capture data capture (EDC) systems to exchange key information, noting that doing so can dramatically speed up information sharing and precision.

Sponsors and investigators should use EHR systems endorsed by the Office of the National Coordinator for Health Information Technology (ONC). If they lack access to ONC-certified systems, they should make sure security measures are in place to protect study data, the agency said.

Study monitors should have easy access to "all relevant information" detailed in signed consent forms, including how long identifying records will be kept.

Records relating to medical devices must be retained for at least two years after an investigation wraps up or the date that the records are no longer required to support a premarket approval application or a notice of completion, whichever is later.

Read the FDA's July 18 guidance here: www.fdanews.com/07-18-18-HealthRecordData.pdf.
— Bill Myers

APPROVALS

Zebra Medical Vision Cleared For Brain Bleed Algorithm

The FDA granted 510(k) clearance to Zebra Medical Vision's AI imaging algorithm for intracranial hemorrhaging detection.

The algorithm will be included in the company's Deep Learning Imaging Analytics platform, which can analyze CT data for signs of fatty liver, emphysema, low bone density and other conditions.

The algorithm is intended to be used for point of care detection and worklist prioritization, allowing physicians to more accurately and speedily detect brain bleeds.

FDA Clears Cutting Edge Spine's Cervical Spine Interbody Implant

Cutting Edge Spine announced that the FDA granted 510(k) clearance for its EVOL ha-C cervical interbody system.

The company also plans to release anterior lumbar interbody fusion, oblique lateral interbody fusion and direct lateral interbody fusion systems later in the year.

The system is made of PEEK-OPTIMA HA enhanced material that is used in the creation of implants. Implants made from the material have shown to cause early onset bone formation and bony apposition to the implant during fusion.

Angiodroid Earns CE Mark For Intra-Aortic Balloon Pump

Angiodroid received a CE Mark for its Angiopulse, an intra-aortic balloon pump (IABP) device that utilizes pressure regulation.

The device is designed specifically for weaning situations and is suited for all types of patients in need of IABP therapy.

The device offers the user touch screen, wireless interface with remote control, therapy monitoring and interactive user guide capabilities.

EchoNous Receives Approval For Catheter Placement Tool

EchoNous was given 510(k) approval for its Vein device, a tool that uses ultrasound to assist in the placement of peripheral IV catheters.

The device is intended to be used by nurses to improve their placement of catheters and can be used for both children and adults.

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

Approvals, *from Page 7*

The tool, which uses a two-button control, visualizes superficial and deep veins and gives clear images at depths from 1 to 5 centimeters.

French Company Receives CE Mark For Laparoscopic Applicator

Surgical hemostasis specialist Biom'Up received the CE Mark for its laparoscopic applicator, extending its indication.

The extended indication allows surgeons to use HemoBlast Bellows hemostatic powder for both open and laparoscopic surgery.

The device's additional indication allows the device to be used for hemostasis when controlling bleeding in classical procedures is impractical, ineffective or impossible during laparoscopic procedures for vascular, abdominal, urology, gynecology, neck and head surgery.

Medtronic's Less-Invasive Implant Approach For HeartWare Device Gains Approval

The FDA approved Medtronic's less-invasive implant approach for its HeartWare left ventricular assist device used to treat patients with advanced heart failure.

The device helps increase blood flow throughout the body by helping the heart to pump. It is typically implanted via a surgical procedure, median sternotomy, in which a vertical incision is made down the chest and the breastbone is divided.

The new approval allows implantation via thoracotomy, a procedure that makes a small incision between the patient's ribs on the left side of the chest.

SuperSonic Imagine's Ultrasound System Receives Approval

Supersonic Imagine's new ultrasound system, the Aixplorer Mach 30, received 510(k) clearance and the CE Mark.

The device offers enhanced imaging modes developed by the company, as well as a functional design and touchpad designed to simplify use.

The Mach 30 uses an elastography solution that allows users to conduct real-time 2D and 3D evaluation and visualization of tissue stiffness.

FDA Approves Stryker's Flow Diverter For Treating Brain Aneurysms

Stryker received FDA approval for its Surpass Streamline flow diverter, used in treating certain types of brain aneurysm.

The Kalamazoo, Michigan based company's device treats unruptured large and giant wide-neck aneurysms. The device is placed in the patient's artery to divert blood flow.

The unruptured aneurysms are harder to treat because of their location and the surrounding anatomy.

Medtronic Gains Expanded FDA Nod for Pacing Leads

The FDA granted expanded labeling for Medtronic's SelectSecure magnetic resonance imaging SureScan model 3830 cardiac leads for pacing of the muscle fibers that conduct the electrical impulses that regulate heartbeat.

The bipolar, steroid-eluting leads attach to a single or dual chamber pacemaker and now have approval for sensing and pacing in the atrium or right ventricle.

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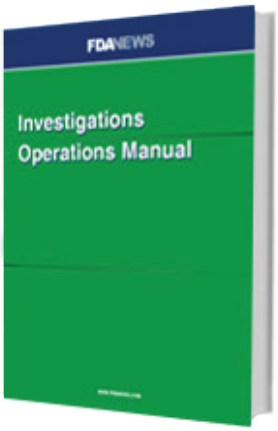

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FDA and ISO Devicemaker Training Requirements

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
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