INTERNATIONAL DEVICES & DIAGNOSTICS MONITOR

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IN THIS ISSUE

Devicemakers to Pay Nearly $1 Billion Under MDUFA IV

The FDA and the medical device industry have agreed on the terms for a new medical device reauthorization package that would allow the agency to collect $999.5 million in user fees over the next five years.

Effective Oct. 1, the draft agreement marks the fourth reauthorization of the medical device user fee program. Details will be published in the next few weeks, and the final recommendations are scheduled to be delivered to Congress in January 2017.

The MDUFA IV agreement does not change user fees announced for fiscal year 2017 that were released in late July (*IDDM*, July 29). The user fee plan would begin in fiscal 2018.

The funding under MDUFA IV will go toward hiring additional full-time staff at the FDA to improve device review times as well as

(See **MDUFA**, *Page 2)*

FDA Explains Use of Risk-Benefit Factors, Patient Preference in Device Approvals

The FDA has issued guidance describing in detail how the risks and benefits of a new device should be considered when the device is up for premarket approval or de novo classification.

In its decisionmaking, the FDA will consider the types of benefits, their magnitude, the probability of the patient having one or more benefit and the duration of effects.

It will also consider the extent of the probable risks and harms, including severity, types, device-related adverse events, procedure-related complications, and the number and rates of harmful events associated with the device.

When assessing the probability of a harmful event, the FDA will consider the portion of the intended patient population likely

(See **Guidance**, *Page 4)*

MDUFA, *from Page 1*

improve efficiency. Other efforts include establishing a program to collect real-world evidence from different sources such as registries, electronic health records, and other digital sources; a third-party premarket review program and development of a submission and tracking portal.

AdvaMed said the agreement "has the potential to be a game changer to improve the efficiency and predictability of the agency's review process.

"The legislation includes a series of strong, measureable performance goals and additional resources that should help reverse the decline in performance FDA has experienced in recent years," the association said in a statement.

The agreement also includes more opportunities for interactions between FDA and sponsors before and during the review process, and an independent outside review of the agency's management review process, the association added.

AdvaMed highlighted the following key performance goals of the new agreement, which include:

- Significant improvements for total review time goals, which will lower the total time goal for 510(k)s and PMAs to historical norms;
- Greater accountability through two independent analyses of FDA's management of the review process — one at the beginning and one at the end of the MDUFA IV timeline — and implementation by the agency of a quality system management approach to the device review process; and
- Further process enhancements to increase the consistency and timeliness of the review process. These include FDA commitments to provide feedback to companies at least five days prior to a pre-submission meeting; a requirement to document the rationale for issuing a deficiency letter; implementation of a standards conformity assessment program; and a pilot to assess the effectiveness of real-world evidence to support premarket activities.

Australia's TGA Recalls ResMed Astral Ventilators

Australia's Therapeutic Goods Administration is recalling ResMed Astral 100 and Astral 150 ventilators due to an internal battery issue.

The ventilators provide support to patients with respiratory difficulties; they have an internal battery designed to deliver continuous power when AC power is disrupted or when a patient is mobile.

The internal battery is intended to provide power for up to eight hours under normal conditions. When a ventilator is being used with the internal battery as the sole power source, the 'low battery' alarm is designed to activate when there are 20 minutes of ventilation time remaining and the 'critically low battery' alarm is designed to activate when there are 10 minutes of ventilation time remaining.

ResMed has received a number of reports of the ventilation stopping without either the 'low battery' or 'critically low battery' alarms activating. The risk of this occurring is increased if the internal battery has been charged a high number of times.

ResMed will begin replacing internal batteries in all Astral 100 and Astral 150 ventilators currently in use beginning next month. The ventilators also should have a routine maintenance service every two years, the TGA said.

Read the recall notice here: www.fdanews.com/08-24-16-TGArecall.pdf. — Tamra Sami

Survey: Most Devicemakers Not Ready For Looming UDI Regs

Only about 15 percent of device manufacturers of Class II and Class III devices are currently compliant with new unique device identifier requirements that go into effect Sept. 24, according to a recent survey.

Roughly half of the 120 medical device companies polled hadn't even conducted internal audits, and 53 percent said they would need additional support for their UDI processes to meet the regulatory requirements.

The survey showed that 93 percent reported that UDI requirements have had a major or at least noticeable impact on their existing labeling processes.

Only half of respondents felt that their current barcode labeling software solution would be able to scale to meet long-term UDI regulations and other evolving international requirements, according to the survey conducted by Loftware and USDM Life Sciences.

"Despite adequate lead time, just 15 percent of respondents indicate that they are already compliant with the next phase of the regulation, and of those who are currently working towards compliance, nearly 40 percent will be taking it right to the due date of Sept. 24," the report said. "For regulations that they've been aware of for three years now, it's surprising that so many companies are cutting it this close with impending deadlines."

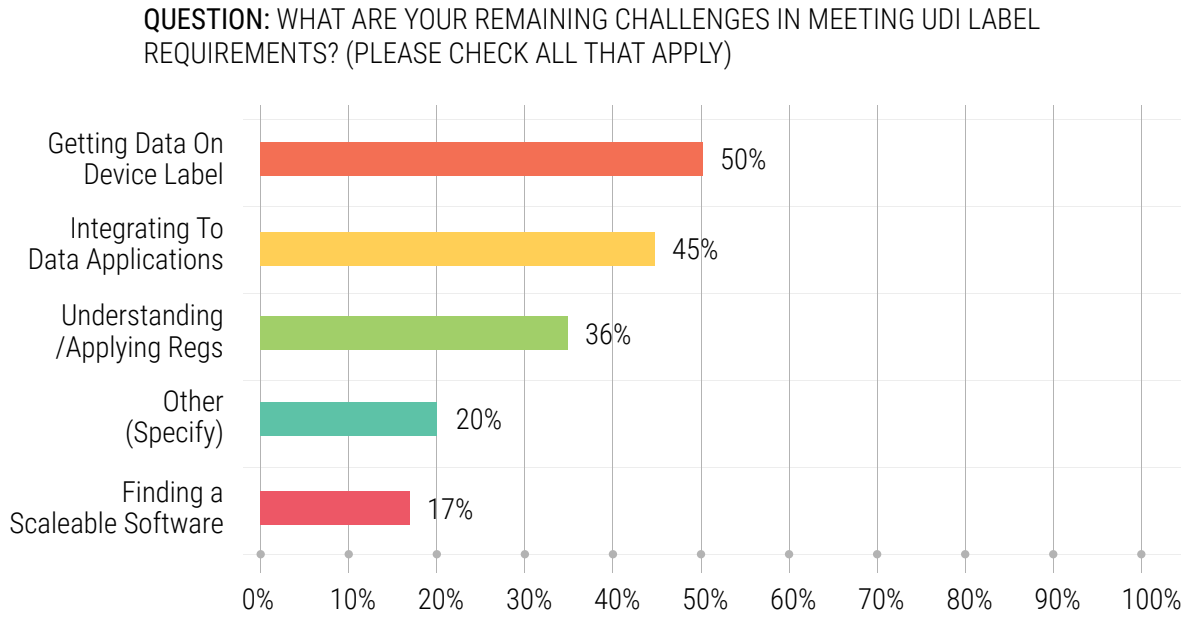
Top Challenges

Devicemakers said that getting all of the necessary data on the label is one of their top challenges (50 percent) as well as pulling labeling data from enterprise applications (45 percent). About 36 percent of companies said understanding and applying the regulation was also a challenge (see chart below).

The FDA issued draft guidance in July that clarified agency expectations for UDIs, which must appear in two forms on device labels and packages: an easily readable plain-text form and an automatic identification and data capture technology form (*IDDM*, July 29).

UDI labeling regulations are being phased in through 2020 in a concerted effort to identify and track medical devices. The Sept. 24 deadline requires labels and packages of Class

(See **UDI**, *Page 6)*



Source: Loftware

Guidance, *from Page 1*

to experience the event, factoring in whether the event occurs once or repeatedly. It will also consider duration and severity, as some adverse events may be reversible while others can cause permanent harm.

"We also consider the number of different types of harmful events that may result from using the device and the severity of their aggregate effect," the guidance says. "When multiple harmful events occur at once, they have a greater aggregate effect."

Additional factors the FDA considers include uncertainty, patient-reported outcomes, characterization of the disease, availability of alternatives, risk mitigation, postmarket data and whether the device is a novel technology addressing an unmet need.

One factor specifically related to diagnostics is the risk from false-positive or false-negative results, the guidance says.

It notes that "although a great deal of emphasis" is placed on clinical data, "nonclinical data also can be critical to understanding a device's safety and effectiveness. Medical devices often have attributes that cannot be tested during clinical methods alone and that play a major role in the safety or effectiveness of the device."

For example, with some implants, better long-term evidence has come from engineering tests that challenge the device in worst-case conditions and simulate years of use.

The guidance includes a worksheet that reviewers use to make risk-benefit determinations. However, the weighting of factors for a certain device type can change over time, making the weighting different for a similar type of device in the future.

The FDA hopes that by clarifying its decisionmaking process, it can improve predictability, consistency and transparency for sponsors, it says.

Factoring in Patient Preferences

A second FDA guidance outlines how to incorporate patient preference information into the medical device development and approval process.

Sponsors and other stakeholders should meet early with their review division if they are thinking of submitting patient preference information, the guidance advises.

Additionally, "the agency may also consider obtaining its own PPI to further understand the benefit-risk factors affecting patients with diseases or conditions who may be considering using a specific device type," the guidance says.

It recommends certain qualities for patient preference studies, including patient centeredness; representativeness of the sample and generalizability of results; capturing heterogeneity of patients' preferences; minimal cognitive bias; robustness of analysis of results; study conduct; and comprehension by study participants.

In some cases, patient preference studies can help the FDA and companies find patient subsets for whom the benefits of a device outweigh the risks, leading to approval in a limited population. In such cases, the agency may require approval conditions such as specialized labeling.

The guidance also gives recommendations on collecting and submitting patient preference information to the agency and discusses the inclusion of that information in decision summaries and device labeling.

For example, whenever possible, "the likelihood of risks and benefits should be expressed in absolute terms rather than relative terms that may be confusing," it says. "Doubling a risk means very different things if that entails an increase from 10 percent to 20 percent rather than an increase from 0.001 percent to 0.002 percent."

The risk-benefit guidance is available at www.fdanews.com/08-24-16-Denovoguidance.pdf. The guidance on patient preference information is available at www.fdanews.com/08-24-16-patientpreferenceguidance.pdf. — April Hollis

Assay Importer Warned Over Supplier Controls, Complaints

Tosoh Bioscience, an importer of assays and high performance liquid chromatographs, failed to properly manage its suppliers and handle complaints, according to an FDA warning letter.

The company's Grove City, Ohio, facility didn't describe quality requirements for its three supplier risk levels in its procedures for supplier quality system reviews and on-site audits, according to the Aug. 5 letter.

Its 2016 supplier review did not ensure that suppliers were adequately evaluated and monitored, the letter adds. "Tosoh has received complaints on two of the 11 suppliers reviewed by the FDA investigator." However, its "2016 review of these two suppliers stated 'no recorded complaints.'"

Meanwhile, its procedure for quality system audits and auditor training did not discuss re-audits of deficient areas. Tosoh's manager of regulatory affairs and quality assurance told the FDA investigator that it does not perform re-audits.

Outside Audit Needed

The FDA requested the company submit an audit certification from an outside expert, along with a copy of the consultant's report and assurance that Tosoh has initiated or completed any recommendations. The agency also asked the company to schedule a regulatory meeting to discuss the issues and a corrective action plan.

In addition to supplier control and audit problems, Tosoh was chided on its complaint handling. For example, it didn't treat service calls for analyzers under warranty as complaints, despite being defined as such by its procedures. Complaints on "consumable" products such as needles, cups, and analyzer accessory kits were not analyzed to identify existing and potential causes of quality problems.

The company's complaint-handling procedure did not ensure that all complaints are reviewed and investigated, the letter notes. The FDA investigator looked at more than 15 non-routine service reports related to possible failures of analyzers, but the complaint section in the company's database was not filled out for these issues. No investigation form was initiated.

Failure to analyze trends and nonconformances was also cited, with the investigator noting that not all sources of quality data are being analyzed. For example, leaking bottles found during manufacturing and service complaint ticket reports opened as "warranty" were not analyzed to identify existing and potential causes of quality problems.

Inappropriate Methodology

"You have not identified appropriate statistical methodology ... to detect recurring quality problems," the letter says. It points out that Tosoh's trending procedure only applies to devices with an installed base of 100 or more units. Service and complaints received on some analyzers were not analyzed because there were less than 100 units in distribution.

Additionally, information in certain sections of one of Tosoh's databases is not standardized and the "type" is not always entered, so the failure rate per part cannot be calculated accurately, the letter says. "As a result, you are not identifying failure rates per part that are above your thresholds for initiating a CAPA."

One citation noted that Tosoh found a problem exceeded its failure rate tolerance for a product but it did not initiate a corrective action request form. It also failed to verify and validate CAPAs to ensure they are effective and do not negatively affect the device.

The warning letter goes on to cite preventive maintenance issues, noting that Tosoh's schedule requires the main warehouse refrigerator to be inspected quarterly, but there were no forms/records of inspections for 2016, it says.

The company did not respond to a request for comment by press time. The warning letter is available at www.fdanews.com/08-24-16-Tosoh.pdf. — April Hollis

UDI, *from Page 3*

II devices to bear UDI barcode labels with correctly formatted dates, and the data must also be submitted to FDA's Global Unique Device Identification Database (GUDID). Class III devices that are intended for reuse must also bear a UDI as a permanent marking on the device itself.

"Many device manufacturers are struggling to meet the FDA UDI compliance timelines – however, the overriding issue to UDI compliance is in developing and implementing a sustainable, extendable UDI program and understanding that UDI is and will be a constantly growing and evolving process," the report says.

The FDA likely saw the writing on the wall that devicemakers would need more time to comply, because it released a notice on Aug. 19 reminding manufacturers that they could apply for extensions. The notice also listed exemptions for certain devices as well as the process to request an exemption or extension.

In addition, the agency provided advice for labelers struggling with fitting all the information on the label. It said that labelers could:

1. Remove or minimize information on the label that is not required under 21 CFR 801 (or 21 CFR 809.10 for IVDs);
2. Increase the size of the label or modify the label, such as moving the label to a flatter location on the immediate container to accommodate the UDI; or
3. Use a smaller form of AIDC technology or split the AIDC form into multiple segments. The easily readable plain-text UDI may also be split into multiple segments.

The agency noted that if those solutions don't address labelers' concerns, the company could submit a request for an alternative to add an overwrap that would bear the UDI or place another label bearing the UDI elsewhere on the packaging.

Read the FDA notice here: www.fdanews.com/08-24-16-UDIexceptions.pdf and the industry survey here: www.fdanews.com/08-24-16-UDIsurvey.pdf. — Tamra Sami

Senators Turn Heat Up on Mylan to Explain Price Hikes for EpiPen Device

Four U.S. senators are turning up the heat on Mylan, requesting information on the company's prike hikes for its emergency allergy auto-injector EpiPen.

Senators Susan Collins (R-Maine) and Claire McCaskill (D-Mo.), chairman and ranking member, respectively, of the Senate Special Committee on Aging, sent an Aug. 24 letter to Mylan CEO Heather Bresch summoning her to appear before the committee "no later than two weeks from today."

The senators questioned the price of the "relatively old product" and the impact of the 400 percent price increase since 2007.

Mylan came under the spotlight when Senator Amy Klobuchar (D-Minn.) urged the FTC to open an investigation into Mylan's pricing of the emergency allergy treatment.

Klobuchar, ranking member of the Subcommittee on Antitrust, Competition Policy and Consumer Rights, is asking the FTC to probe the company's sales of the epinephrine auto-injector to determine whether Mylan violated antitrust laws and incentivized contracts with insurers, distributors or pharmacies.

The recall of Sanofi's competing product Auvi-Q last year due to dosing errors left Mylan's EpiPen dominating the market as the only epinephrine auto injector product on the market.

In a letter to the FTC released Aug. 22, Klobuchar compares the price of the drug in 2008, when a two-pack of EpiPens cost $100, to the therapy's current price of $500. The 400-percent increase outpaces "stable manufacturing costs," she said.

In a separate letter released Aug. 22, Senate Judiciary Committee Chairman Charles Grassley (R-Iowa) asked Mylan to explain the rise in price, questioning the company on its price analyses, advertising budget and patient-assistance programs

In a statement, Mylan tried to deflect the negative attention, focusing instead on its efforts to raise awareness for the epinephrine auto injector, and its patient assistance program.

Read Collins' and McCaskill's letter here: www.fdanews.com/08-25-16-Senatorsletter.pdf, and Senator Grassley's letter here: www.fdanews.com/08-24-16-Grassleyletter.pdf. — Tamra Sami, Jose Vasquez

South Africa Unveils New Regs Covering Devices, Diagnostics

South Africa's Department of Health and Medicines Control Council is gearing up to implement the country's first regulatory system covering medical devices and in vitro diagnostics.

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

South Africa's Medicines Control Council released the proposed regulations in September 2015, and sought public comments (*IDDM*, Oct. 16, 2015).

The updated regs lay out a risk-based classification system based on good manufacturing practices. The updated document provides additional information on postmarketing safety requirements and reporting adverse events.

Under the risk-based classification system, there are four classes of devices or diagnostics:

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

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

Read the final licensing guidelines here: www.fdanews.com/08-24-16-SouthAfricaguidelines.pdf and here: www.fdanews.com/08-26-16-SouthAfricaClassification.pdf, www.fdanews.com/08-26-16-SouthAfricasafetyprinciples.pdf, www.fdanews.com/08-26-16-SouthAfricageneralprinciples.pdf. — Tamra Sami

FDA Proposes Quality Standards For Nonclinical Studies

The FDA is proposing that nonclinical studies intended to support submissions to the agency meet higher quality management standards.

The proposed rule, published Aug. 24, would amend good laboratory practices for nonclinical studies to require facilities to undertake a comprehensive quality system approach to oversee these studies.

Nonclinical trials are conducted under laboratory conditions to evaluate the safety and toxicity of products and serve as a precursor to initial human studies.

The proposed rule takes into account current practices as well, such as multisite studies, offering industry flexibility in meeting the proposed standards.

The purpose of the rule is to improve and embed quality management into the planning, testing and reporting phases of nonclinical trials that support medical device applications. The holistic approach is designed to help maintain data quality and integrity, the FDA said.

The FDA seeks to increase accountability under the proposed rule, requiring additional standard operating procedures and management roles.

Under the proposed rule, management must document personnel compliance with the written procedures. The FDA does not, however, prescribe specific procedures to facilities in the rule, offering management the opportunity to design standards that best suit their facilities.

Comments are due within 90 days of publication in the *Federal Register*.

Read the proposed rule here: www.fdanews.com/08-23-16-ProposedRuleNonclinicalStudies.pdf. — José Vasquez

FDA Asks Manufacturers of Syringe Pumps to Update Labeling, Warnings

Manufacturers of syringe pumps are being asked to update their labels to address flow continuity concerns that the FDA has identified as a serious risk to health.

The agency issued an Aug. 25 safety notice warning that programmable syringe pumps used to infuse therapies at low infusion rates can result in serious consequences such as delay of therapy, over-infusion or under-infusion. Reports of serious adverse events such as abnormal or unstable blood pressure, anxiety from loss of sedation, and increased pain indicators in critically ill infants have been associated with a lack of flow continuity.

The agency is asking manufacturers to voluntarily update their labeling to include warnings and precautions to clarify the use of the devices at low infusion rates. The notice said the FDA is working with manufacturers to ensure the appropriate information is conveyed.

The notice said that the problem is not specific to any manufacturer or model, and it may in fact extend to all programmable syringe pumps while infusing at low rates.

The FDA has received more than 300 medical device reports since March 1, 2013, associated with programmable syringe pump use. The reports highlight over- and under-infusion of high risk or life-sustaining medications, occlusion detection failures, boluses caused by inconsistent fluid delivery and other malfunctions. The majority of the reports noted infusions at rates of 5 mL per hour or less, the notice says.

The agency said it believed that the benefits of the devices still outweigh the risks, and it provided recommendations for healthcare professionals to help mitigate some of that risk. Those recommendations covered syringe size and selection, use of accessory devices, starting an infusion or changing a syringe, height and location of the syringe pump system and occlusion considerations.

Read the FDA safety notice here: www.fdanews.com/08-25-16-pumpsafetynotice.pdf. — Tamra Sami

Alere Pulls INRatio Monitor From Market Following Class I Recall

Alere plans to remove its INRatio and INRatio2 PT/INR monitoring system from the market and to discontinue manufacturing the product line following a Class I recall due to inaccurate test results.

The INRatio system measures blood clotting time for people taking blood thinner warfarin.

According to the Aug. 25 FDA notice, the INRatio system may generate an incorrect low result using a plasma-based INR method. If an incorrect result is acted upon, such as lowering the warfarin dose, patients could be at risk for fatal bleeding.

Alere was not able to develop an adequate modification and is thus halting manufacturing the product line, the FDA said.

Healthcare providers were advised to transition patients to an alternate method of PT/INR testing as soon as possible. Alere will continue to manufacture and distribute the test strips for a period of time to allow patients to safely transition to another monitoring method.

In a July 26 urgent recall notice to customers, Alere announced that it was voluntarily removing the product line from the market. The company noted that it issued a voluntary correction in December 2014, informing healthcare providers that the monitoring system should not be used for patients with certain medical conditions.

Australia's TGA announced earlier this month that it was withdrawing the monitoring system from the market (*IDDM*, Aug. 15).

Advocacy group Public Citizen raised the red flag on the blood testing devices in December 2015. At that time, the advocacy group said its analysis of the FDA's Manufacturer and User Facility Device Experience database showed 9,469 malfunction reports and 1,445 injury reports from 2002 through November 2015 with INRatio devices (*IDDM*, Dec. 11, 2015).

A Class I recall is the most serious type of recall, because use can result in serious injury or death. Read the FDA notice here for the full list of affected products: www.fdanews.com/08-25-16-Alertrecall.pdf. — Tamra Sami

UK Provides Guidance on Determining If Apps May Be Devices

The UK's Medicines and Healthcare products Regulatory Agency is providing guidance to manufacturers about when stand-alone software may be considered a medical device.

In the UK and Europe, stand-alone software and applications that meet the definition of a medical device are still required to be CE marked, the agency said in guidance released Aug. 25.

The guidance is provided in the form of an interactive slide presentation that directs manufacturers and users to a decision tree to help inform them about whether the app would be considered a device or not.

For software developers, the guidance includes information on classification of devices as well as suggestions on how to address the main aspects of the CE marking process.

For users, the agency offers tips on how to decide if the app or software is a medical device as well as how to ensure it is CE marked and how to report problems. — Tamra Sami

FDA Adcom Recommends OTC Diagnostics But Not for Flu

An FDA advisory committee unanimously recommended over-the-counter diagnostic assays for Chlamydia trachomatis/Neisseria gonorrhea and group A streptococcus, but said the risk outweighed the benefit for OTC flu diagnostics.

The Microbiology Devices Panel expressed concern that the potential low positive predictive value outside of the active flu season was a high risk and that risk was difficult to mitigate.

BRIEFS

China Awards Expedited Approval to Shuwen

China FDA awarded fast-track status to Shuwen Biotech for its MammaTyper, a real-time PCR kit for breast cancer stratification.

The device is a molecular diagnostic test for breast cancer stratification with Formalin-Fixed, Paraffin-Embedded (FFPE) tumor tissue samples.

Since the fast-track program was initiated in March 2014, only 10 in vitro diagnostics devices have been granted access to the special approval process.

FDA Clears Alere's RSV Test

The FDA granted 510(k) marketing clearance for Alere's molecular test that detects respiratory syncytial virus (RSV) in children and adults.

Alere i RSV is significantly faster than conventional polymerase chain reaction (PCR) tests delivering results in 13 minutes or less.

Court Consolidates Theranos Suits

A federal judge in California consolidated six class action suits that accuse Theranos of fraud and false advertising into a single case.

U.S. District Judge Yvonne Gonzalez Rogers for the Northern District of California reasoned that consolidation would "save time and effort."

The suits poured in after the company rescinded two years of tests results for its Edison blood-testing diagnostics.

Oculus Cleared Post-Dermal Device

Petaluma, Calif.-based Oculus Innovative Sciences has received FDA 510(k) premarket clearance for the company's post-dermal-procedures device.

The device is intended to remove foreign material and debris after dermal procedures. Oculus plans to market the device in the U.S. in March 2017.

FDA Approves Concussion Tests

FDA has granted approval to Impact Applications' cognitive assessment devices to evaluate brain function after an injury or suspected concussion.

The Immediate Post-Concussion Assessment and Cognitive Testing as well as ImPACT Pediatric are the first devices the FDA has approved for cognitive testing after a brain injury.

The devices test cognitive skills, such as word recognition, reaction time and memory.

Dexcom Sues InSpark Technologies

Dexcom has filed a suit against InSpark Technologies, claiming it did not infringe on three patents related to glucose-monitoring technology.

InSpark Technologies holds the three patents in dispute that concern the methods for evaluating and monitoring glucose.

Dexcom is requesting a declaratory judgment of non-infringement for '703 patent, '985 patent and '425 patent concerning its Dexcom Clarity software.

Cigna To Cover 3-D Mammography

Cigna announced it will now reimburse for three-dimensional (3D) mammography for routine breast cancer screening effective immediately.

Under its previous policy, the company covered 3D mammography for diagnostic purposes, but not for routine screening.

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Pre-conference Workshops Agenda

WEDNESDAY, NOVEMBER 2

DRUGS & BIOLOGICS TRACK

12:00 p.m. – 1:00 p.m. | **REGISTRATION**

1:00 p.m. – 5:00 p.m.

Flawless FDA Inspection Handling and Response

FDA warning letters begin with a summary of the failed inspection, and then quickly dismiss a firm's effort to respond. In a very public way, FDA categorizes one company after another as "inadequate," "insufficient," "lacking" and worse.

Handling an inspection successfully requires a strategy designed to get the FDA investigator in and out as quickly as possible. The longer an FDA investigator is on site, the worse your chances are of avoiding a FDA 483.

And when the 483 arrives, do you know how to respond in less than 15 days to avoid a warning letter?

A defensible response can be hard to assemble – and get through internal review – with enough time to beat the enforcement clock at FDA.

This workshop gives you proven, practical techniques for fast, flexible and flawless inspection handling and responses that exceed FDA expectations and support your side. You'll learn how to prepare for an inspection, how to encourage the investigator to see you in a "state-of-control," and how – if the worst happens – to go from 483 observation to FDA's coveted untitled letter – and avoid the warning letter publicity.

Attendees Will Learn:

- Critical inspection preparation techniques to take – even if you get surprised by FDA
- Hidden tactics FDA investigators use to test your controls
- How to speed the inspection to minimize the risk of 483 findings
- Key elements of a realistic regulatory inspection handling SOPs
- How to write an inspection response designed to reduce warning letter likelihood
- Red flags FDA looks for in your inspection response

Attendees Will Receive:

- A sample SOP – ready for your immediate implementation
- Three inspection handling and response checklists – ready for you to use right away
- An observation-closure matrix – ready to speed you out of FDA trouble

John Avellanet, Managing Director and Principal, Cerulean Associates LLC

MEDICAL DEVICES TRACK

12:00 p.m. – 1:00 p.m. | **REGISTRATION**

1:00 p.m. – 5:00 p.m.

ISO 13485:2016 – Understand the Concepts of Risk and Their Applications

The new QMS standard, published in March, alerts manufacturers to the presence of risk in almost all operations—from design control to supplier management to software validation and more. While it does not specifically address the concept of risk management (you'll find that in ISO 14971:2007), ISO 13485:2016 makes it clear that manufacturers must be aware of the opportunity for risk in all they do.

This workshop examines the concept of risk as presented in the new standard and explains how to apply it in the quality management systems. Through examples that illustrate ISO 13485:2016's requirements, interactive exercises that help solidify understanding, and a unique set of checklists that cover all the QMS bases, attendees will learn:

- How the QMS standard integrates with the risk management standard in ISO 14971:2007
- How the implementation timeline may differ from country to country
- How inclusion in MDSAP could impact inspections of U.S. manufacturers
- How the European version differs from the international version

Quality systems expert Dan O'Leary explains ISO 13485:2016's concept of risk in clear terms that will prepare you for the changes ahead.

Dan O'Leary, President, Ombu Enterprises

What Past Attendees Have Said About the FDA Inspections Summit:

"This Summit is in the top 3 meetings I have attended. Looking forward to next year."

"I loved the ease to interact with FDA investigators and others involved in the conference."

"I really enjoyed having the opportunity to ask FDA investigators questions in a long open session."

Day 1 Agenda

THURSDAY, NOVEMBER 3

8:00 a.m. – 8:30 a.m. | **REGISTRATION & CONTINENTAL BREAKFAST**

8:30 a.m. – 8:45 a.m.

Opening Comments by Chairperson John Avellanet, Managing Director & Principal, Cerulean Associates LLC

8:45 a.m. – 9:30 a.m.

FDA Realignment Program Is In Effect: How That Impacts You

Under its recent organizational changes, FDA is developing specific action plans to align its centers and the Office of Regulatory Affairs with new strategic goals and increased demands. The plans include critical actions to fulfill the agency's mandate in training; compliance and enforcement; imports; and information technology, all of which will affect all areas of medical products inspection and poses these vexing questions:

- What impact will the transition to a commodity-based and vertically integrated regulatory program have on inspections?
- What will be the major changes in MDSAP?
- How will new training and certification requirement impact medical product inspections?

9:30 a.m. – 11:00 a.m.

FDA Inspections – A New, Modern Record Review Technique: A Panel Discussion

It is becoming more common for investigators to review your documents and data maintained in your QMS in real time. An investigator may request electronic copies of your records on a memory stick. Or request the ability to browse through your complaint management system to review documentation. Are you prepared?

This panel will discuss:

- FDAs new ability to analyze your data – by sorting it and spotting trends which they can then link to potential issues in other quality management systems.
- The lack of SME preparation – as you don't know what they will look at you can't rehearse each document and be ready when questioned.
- Increased document challenges – some documents don't stand on their own without significant explanation.

(cont.)

- The importance of writing plain, simple English – all documents need to convey what you need without interpretation. Writing clearly and consistently has never been more important.

11:00 a.m. – 11:20 a.m. | BREAK

11:20 a.m. – 3:30 p.m.

Two Concurrent Breakout Tracks

Track 1 — Drugs & Biologics

Track 2 — Medical Devices

3:30 p.m. – 3:50 p.m. | BREAK

3:50 p.m. – 5:15 p.m. | PLENARY PANEL DISCUSSION

5:15 p.m. – 6:30 p.m. | NETWORKING RECEPTION

DRUGS & BIOLOGICS TRACK

11:20 a.m. – 11:30 a.m. | MODERATOR COMMENTS

11:30 a.m. – 12:15 p.m.

Understanding OPQ's New Inspection and Reporting Plan and Organizational Structure

This session will discuss how CDER's new "super" Office of Pharmaceutical Quality plans to divvy up inspections among its three offices, and how it will incorporate pre-approval inspections into the OPQ team review to standardize quality assessments.

Attendees will learn about OPQ's new inspection protocol that will focus on expert investigator-developed questions and assessment practices and how mobile technology will be incorporated to support investigators during inspections

12:15 p.m. – 1:00 p.m.

Quality-Driven Data Integrity Approach In the EU and US Inspections

Data integrity requirements have been strongly enforced in recent years by almost every regulated agency in the pharmaceutical environment: the expectations have been clarified in a number of guidances issued by MHRA, WHO and most recently by the FDA. Therefore, the requirements for data integrity are now considered a fundamental expectation and strictly connected to the relevant predicate rules.

This presentation will provide real life case studies and examples you can use to base your control measures upon the potential impact of data on product quality and patient safety.

1:00 p.m. – 2:00 p.m. | LUNCH

2:00 p.m. – 3:30 p.m.

How to Deal with Difficult Inspections

Co-Chair Steve Niedelman will provide real-world scenarios for dealing with tense inspections. Through open discussion and feedback, the audience will work together to come to the correct conclusion for each scenario.

3:30 p.m. – 3:50 p.m. | BREAK

MEDICAL DEVICES TRACK

11:20 a.m. – 11:30 a.m. | MODERATOR COMMENTS

11:30 a.m. – 12:15 p.m.

Update from the Office of Compliance at CDRH: Priorities for 2017

This is not your father's CDRH. There's more emphasis on global activities and a greater expectation of transparency and privacy. You'll hear the director of compliance discuss and answer questions about these important issues:

- The new inspection approach/strategy for medical devices in 2017 and its practical impact on your business
- The new CDRH, ORA and the Office of Crisis Management (OCM) streamlined process for medical devices and what it all means for electronic product related consumer complaints and Allegations of Regulatory Misconduct (ARMs)
- The new CDRH and ORA process to measure, document, and report on public health outcome metrics and how it will affect inspection compliance

12:15 p.m. – 1:00 p.m.

Medical Device Single Audit Program Pilot (MDSAP) In Full Swing

Manufacturers entering the Medical Device Single Audit Program undergo an assessment performed by a single third-party inspector that proves compliance in the U.S., Canada, Australia, Brazil, the EU and Japan.

So far, one audit has been conducted and others are in the pipeline, and responses from participants have been positive.

One big advantage to the MDSAP is that because audits aren't performed by the U.S. government, their results aren't public record — and there's no Form 483 that can be requested via the Freedom of Information Act.

Attendees will hear first-hand progress on the program from the FDA's Marc-Henri Winter, who will share lessons learned from the pilot program. Devicemakers will learn what to expect from an audit and how multiple sites should be audited.

1:00 p.m. – 2:00 p.m. | LUNCH

2:00 p.m. – 3:30 p.m.

Effective Management of Front And Back Inspection Rooms — Secrets You've Never Heard and Answers To Questions You've Always Wanted To Ask: A Panel Discussion

As the FDA's field staff continues to grow, that long overdue inspection is more likely than ever to occur. Plus add the FDA's newest push to develop teams of highly qualified investigators with a deep knowledge of your device. Together, you're in for some really tough inspections. Worried? Don't be. This panel will provide you pages of great tips and tricks to designing, staffing and managing your inspectional war rooms. Our experts will also answer those questions that have been nagging at you for years. Don't miss this exciting panel!

Attendees will learn:

- Polite in the front, craziness in the back? It doesn't have to be. Understanding the synergy of the front and back rooms
- Handling data requests, particularly for electronic records — best practices from inspectional veterans

(cont.)

- Being a SME in your job doesn't make you an inspection SME. Tips for staffing your war rooms with the appropriate people to interact with the FDA

3:30 p.m. – 3:50 p.m. | BREAK

Plenary Session Panel Discussion

3:50 p.m. – 5:15 p.m.

A Day in the Life of FDA's Field Investigators — Current Field Investigators Explain What They Look For and Why: A Panel Discussion

Ever wonder what an investigator is thinking when she receives the next inspection assignment? Investigators typically create inspection plans based on a company's previous Form 483s, warning letters, responses to warning letters, consumer complaints and recalls. But they also study a company's website, including literature, products manufactured and recent press releases.

This presentation will give you a glimpse into the inner workings of an investigator's mindset before, during and after your inspections.

Attendees will learn:

- What does an investigator's prep package contain?
- What research – both internal and external – do they use to prepare themselves for your company, plant and products?
- What do they look for once inside your plant?
- How they apply QSIT and other inspectional techniques to the QSR
- Why they include items in the EIR and Form 483 and how they take into account your comments

5:15 p.m. – 6:30 p.m. | NETWORKING RECEPTION

8:00 a.m. – 8:30 a.m. | BREAKFAST

8:30 a.m. – 8:45 a.m.

Opening Comments by Chairperson

8:45 a.m. – 9:30 a.m.

FDA's Office of Regulatory Affairs: Enforcement Update

This presentation will focus on ORA's Office of Enforcement priorities for 2017, and how the office approaches the enforcement process. This session will educate attendees on how they can more proactively prepare for FDA investigators before they arrive.

Attendees will learn:

- The latest on the FDA's re-organization of the inspectional corps
- The FDA's position on recalls and the possible actions the Office of Enforcement can take in the wake of them
- Effectiveness of criminal sanctions in improving compliance among drug and device company senior management
- Whether 483s and warning letters will be produced more quickly and highlighted for the public as a deterrent to poor corporate behavior

9:30 a.m. – 10:15 a.m.

The Regulatory Intelligence Platform

Being prepared for inspections means that you understand both the internal and external data that affect your products. Now more than ever there is an expectation that companies are analyzing and acting on this data

In this session, you'll learn:

- What is regulatory intelligence and how does it affect your business
- How to leverage regulatory intelligence as integral part of inspection readiness
- What data is available through open systems and what you should be looking at
- What should be included in your regulatory intelligence platform

10:15 a.m. – 10:30 a.m. | BREAK

10:30 a.m. – 12:00 p.m.

After the Election: A Look Ahead To What a New Administration Could Bring and the Impact on the FDA

In this election year, if almost anyone tells you that they know who the next president is going to be or exactly what's going to happen at FDA in 2017 and beyond is probably just whistling in the wind. But these panelists bring incredible inside knowledge and decades of experience in the nitty-gritty of Washington politics to provide an educated analysis of FDA operations. Here's what you'll hear discussed at this lively, interactive session about the future of FDA:

- Will there be increased efforts at global regulatory harmonization or more country-by-country compliance
- Will there be increased agency enforcement or more reliance on voluntary industry compliance
- Will there be increased legislation or rollbacks in regulation

12:00 p.m. | CONFERENCE ADJOURNS

"Great and interesting sessions. Great panel discussions and attendee participation."

— Johanna Stamates, Executive Director - Research Compliance and Quality Assurance, University of Miami

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PRE-CONFERENCE WORKSHOP ONLY

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LIVESTREAMING

We know that not everyone can travel to the 11th Annual FDA Inspections Summit, so we have decided to stream it live! It's a great way to see sessions as they happen. Registration is quick and accessing the live sessions is as simple as clicking your mouse. BONUS: Includes six month access to archived session recordings after the conference.

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The FDA Inspections Summit — now in its 11th year — has fast become the "go-to" event for regulatory, compliance and quality assurance professionals and the one place to discover the tools and techniques to improve your inspectional readiness.

Join us for this rare opportunity to interact with top officials from CDER, CDRH, the Office of Regulatory Affairs and other outstanding industry leaders to discuss debate and uncover the latest priorities, expectations and best practices.

NO OTHER conference brings together so many of the industry's inspectional professionals. This is your one chance to come to the nation's capital and interact with the top minds in the FDA arena. As you network with these senior-level professionals, you'll discuss the latest developments from the FDA and Congress and how you need to position your firm to assure successful inspections.

WHO SHOULD ATTEND?

- Executive Management
- Regulatory Affairs
- Quality Assurance/Quality Control
- Legal and Compliance Officers
- Consultants/Service Providers