INTERNATIONAL DEVICES & DIAGNOSTICS MONITOR

Vol. 2, No. 38
Sept. 26, 2016

IN THIS ISSUE

Harnessing Data at Heart Of CDRH Regulatory Priorities

The Center for Devices and Radiological Health released its top-10 list of regulatory priorities for fiscal year 2017.

The list adds some new topic areas, including clinical trial design and precision medicine, and it fleshes out existing areas, such as patient-reported outcome measures and reprocessing of devices.

The top 10 list is as follows:

1. Leverage "Big Data" for regulatory decision-making;
2. Modernize biocompatibility and biological risk evaluation of device materials;
3. Leverage real-world evidence and employ evidence synthesis across multiple domains in regulatory decision-making;
4. Advance tests and methods for predicting and monitoring medical device clinical performance;

(See **CDRH**, *Page 2)*

FDA Lacks Capacity to Regulate Laboratory-Developed Tests, Senators Say

The FDA does not have the capacity to regulate the tens of thousands of laboratory-developed tests currently being used across the country, senators said during a committee hearing on the future of regulation in the age of precision medicine.

"Is there anybody here that believes that the FDA architecture or the FDA talent exists today to be able to handle the processing of an [LDT] application or an approval three years from now?" asked Sen. Richard Burr (R-N.C.), during a Sept. 20 hearing before the Senate Health, Education, Labor and Pensions Committee.

Currently, most tests that are developed and used within a single facility are regulated by the Centers for Medicare & Medicaid Services, under the Clinical Laboratory Improvement Amendments (CLIA). They can include in vitro diagnostics, blood tests, and assays evaluating whether a patient will respond to a specific drug.

(See **Hearing**, *Page 4)*

CDRH, *from Page 1*

5. Develop methods and tools to improve and streamline clinical trial design;
6. Develop computational modeling technologies to support regulatory decision-making;
7. Enhance the performance of digital health and medical device cybersecurity;
8. Reduce healthcare-associated infections by better understanding the effectiveness of antimicrobials, sterilization and reprocessing of medical devices;
9. Collect and use patient input in regulatory decision-making;
10. Leverage precision medicine and biomarkers for predicting medical device performance, disease diagnosis and progression.

The center said priorities will be reassessed and updated as needed and will serve as a guide for making "strategic intramural research funding decisions." Projects funded through intramural sources are evaluated using a defined set of metrics to make sure the projects are meeting their goals.

CDRH Director Jeffrey Shuren said during the Medical Device Innovation Consortium on Sept. 21 that harnessing data is at the heart of the center's initiatives, so it's no surprise that leveraging big data for regulatory decisionmaking is at the top of his list.

To that end, Shuren laid out his vision for harnessing big data and bringing patient preferences into the equation.

CDRH's strategic priorities for 2014-15 focused on strengthening the clinical trial enterprise, and 2017 priorities build on these. Generating clinical trial data is the most expensive part of the regulatory requirements to get products to market, and there are serious limitations in conducting clinical trials with devices, Shuren said.

"You can't conduct a trial that will answer all the questions on a medical device," he said, because a clinical trial won't give you a true risk-benefit profile. That true risk-benefit profile can only be answered "in the wild," so the center is turning its focus on real-world use.

To get there requires the marriage of electronic health records and unique device identifiers to be able to track devices better. Terms will also need to be identified so that a national evaluation system for health technology (NEST) can solve those challenges in the postmarket setting.

The problem with clinical trials, he said, is that they are designed around the sponsor's needs rather than the patient's needs. Flexibility in the evidence-generating enterprise and digital health could enable the industry to "move away from the artificial constructs of premarket and postmarket cycles."

"Every time we make a decision on a device, we face uncertainty," Shuren said. "The question is how much do you accept?" The best way to answer that question is by using science to understand the uncertainty that patients are willing to accept under various circumstances, he suggested.

Value is increased by creating linkages between different data owners and pulling them together in an ecosystem to drive data standardization and create data use agreements.

A multi-stakeholder planning board for NEST is being run by the Duke Margolis Center for Health Policy, and a coordinating center run by the Medical Device Innovation Consortium will drive the activities of NEST, Shuren said (*IDDM*, April 11).

To expedite this, the FDA has committed $3 million to MDIC in fiscal year 2017 to get the enterprise off the ground. Under MDUFA IV the industry will give $6 million per year to the coordinating center that will translate into $33 million over the next six years for MDIC to bring this vision into a reality.

Read the CDRH report here: www.fdanews.com/09-22-16-FY17priorities.pdf; and read the NEST planning board report here: www.fdanews.com/09-22-16-NESTSeptreport.pdf.
— Tamra Sami

Big Data, National Device Evaluation System Take Center Stage at MDIC

Patients will play a bigger role in device assessments, and more data will come directly from patients in the future, FDA Commissioner Robert Califf told devicemakers.

"As a clinical investigator, I was always limited because of the amount of data you had to collect," he said. But now, patients are wearing devices that could provide continuous information. "The secretive clinical world needs to wake up," he said during the Medical Device Innovation Forum Sept. 21.

The FDA and the Centers for Medicare & Medicaid Services are interested in getting the best technology to patients earlier, he said, so there is a real need to create an ecosystem where quality systems and self-governance are built in.

The vision that the commissioner and CDRH Director Jeffrey Shuren painted is one in which a network enables the sharing of real-world evidence that comes from electronic health records, unique device identifiers, clinical data and postmarket information.

"We expect more evidence than the rest of the world," said Shuren, "which can create disincentives to bringing products to the U.S."

By sharing critical data, devicemakers can help reduce the time and cost of the total product lifecycle so that manufacturers find the U.S. market attractive without compromising safety and efficacy.

Postmarket Surveillance Coming

The agency has been talking about creating a national post market surveillance system for a number of years, but it is now ponying up the funds to make it a reality.

The FDA awarded MDIC $3 million in seed funding to establish the Coordinating Center for the Medical Device National Evaluation System for health Technology (NEST).

The initial phase will include demonstration projects piloting methods for tracking medical device data and patient-reported outcomes through the use of real-world evidence.

This use of real-world evidence to support product approvals has the potential to shift premarket data collection to the postmarket setting and to meet postmarket data collection commitments through a modern system that leverages electronic health information generated in the clinical and home setting.

Mark McClellan, director of the Duke-Margolis Center for Health Policy, outlined the next steps for the project, which will "become the national lynchpin" of the FDA's strategy for collecting real-world evidence (*IDDM*, April 11).

The former commissioner said the following issues will be critical in building an effective network:

- Broad-based support and public confidence on why data is being pulled together and how it's being used;
- Core financial support for governance and establishing standard practices and continuous learning for best practices;
- Leveraging the growing number of networks to pull data together for real-world use;
- Distributed capabilities and reliance on virtual networks to build a shared commitment using common data models and common shared methods; and
- Start in a realistic way with a feasible pilot program and build on capabilities.

The first projects will work on balancing premarket and postmarket data and increasing efficiency and the quality of safety surveillance.

Balancing postmarketing data could be accomplished by relying on existing registries and using the real-world evidence that already exists, he said. Increasing quality surveillance could also reduce the reporting burden on devicemakers by making that process automated.

The data that comes out of NEST could also be used to help build out the data needed for the MDIC Case for Quality metrics (*IDDM*, Aug. 15).
— Tamra Sami

Hearing, *from Page 1*

However, following advancements in genomic and molecular science, and their increasing use in guiding high-risk treatment decisions, the FDA proposed draft guidance in October 2014 for the agency to begin regulating LDTs using a risk-based framework. That guidance document has not been finalized.

Industry criticized the proposed regulation as having the potential to stifle innovation. The FDA already struggles to process premarket applications for in vitro diagnostics and would be further slowed if resources are stretched to include LDTs, stakeholders said in comments on the guidance (*IDDM*, Feb. 6, 2015).

"In today's ever-changing healthcare landscape, our mission is to help patients feel confident about the tests influencing their healthcare decisions — I'm not certain that the current FDA structure could provide that stability," said Sen. Orrin Hatch (R-Utah).

Costs Prohibitive

The senators heard testimony from the chairs of two major pathology departments, who said that their labs would not be able to shoulder the costs of seeking premarket approvals for each individual test, if such requirements were imposed.

"We would close the lab," said David Klimstra, the James Ewing Alumni Chair in Pathology at Memorial Sloan Kettering Cancer Center, whose department uses about 350 different LDTs. "There's no way that the institution could afford the costs associated with formal FDA review and approval of all of those tests. It's simply economically impossible."

Karen Kaul, chair of the department of pathology and laboratory medicine at NorthShore University Health System, agreed: "I think the regulatory expense burden would be such that we wouldn't continue personalized medicine. And I think it would have a big impact on the way that medical care is delivered today, for testing, in general. … [Patients] would not get the care they need."

In its draft guidance, the FDA said compliance with CMS standards under CLIA is not sufficient by itself to protect patient safety. High standards for clinical laboratory practices and methodologies can provide assurances in clinical use, but those standards "were not developed to provide assurances regarding the design, manufacture, and validation of the diagnostic device itself," the guidance said. The agency declared that premarket review and FDA regulations would ensure effectiveness.

"Most tests aren't regulated by the FDA, and most tests aren't reviewed by any external party to be sure that their results are accurate," said Sen. Elizabeth Warren (D-Mass.). "And I'm concerned that that means a lot of uncertainty for patients and doctors who are making important decisions based on these test results."

Potential Harm?

The committee's ranking Democratic, Sen. Patty Murray (Wash.), said she is worried about potential harm to patients, and described how the FDA recently alerted women and doctors that lab tests marketed as screening tools for ovarian cancer lacked evidence to support their effectiveness.

"This may have led to women deciding to delay or forego treatment," Murray said, and asked how the committee can help provide regulatory certainty for lab test developers.

Brad Spring, vice president of regulatory affairs and compliance at BD Life Sciences, said that FDA should be the regulatory body for LDTs, but not using the methods it has proposed.

"I don't think the current construct and framework will work in this situation. I think we need to see legislative reform," said Spring.

He listed several guidelines for future regulations, including equal application regardless of the type of entity, such as manufacturers, laboratories or research hospitals; test standards focused on analytical and clinical validity; clear jurisdiction between FDA, CMS, and state health departments and medical boards; and basing the level of oversight on each product's risk to patients.

(See **Hearing**, *Page 8)*

House Committee Grills Mylan CEO, FDA Official on EpiPen Price

If Mylan wants to improve access to its emergency allergy treatment EpiPen, then the company should lower the price of the drug, instead of marketing a generic version, members of the House Committee on Oversight and Government Reform said.

Committee members grilled Mylan CEO Heather Bresch and CDER Deputy Director Doug Throckmorton on the company's virtual monopoly of the epinephrine auto-injector market in a Sept. 21 hearing that lasted more than two hours.

In less than a decade, the price of Mylan's EpiPen rose to $608, up from about $100 in 2008. Bresch attributed this price to an increase in a cost of goods by about 100 percent. At $608, the company only makes $50 per EpiPen, Bresch said.

In August, Mylan announced its decision to introduce a generic EpiPen for half the cost of its name-brand product, but that move failed to assuage the committee's concerns.

Committee Chairman Jason Chaffetz (R-Utah) said the introduction of a generic EpiPen "begs the question" why the company provides the EpiPen for such a high price if it can market a generic version that is identical to the name-brand product.

He added that the price of the active ingredient is $1, giving the company ample opportunity to profit on the EpiPen, which became Mylan's first billion-dollar drug.

Rep. Elijah Cummings (D-Md.), the committee's Ranking Democrat, harked back to previous hearings with Valeant and Martin Shkreli, saying Mylan, like the other drugmakers, found a cheap drug and gouged consumers by raising the price.

Bresch evaded many of the questions, reciting the per-product revenue for each EpiPen.

FDA's Throckmorton likewise provided the committee with limited insight into how many ANDAs the agency has received for epinephrine auto-injector generics, citing confidentiality agreements.

The hearing left many unanswered questions, and Cummings requested that Bresch provide the figures the committee requested on the company's revenue for the product since its acquisition in 2007. — Josè Vasquez

FDA Issues Guidance on Joint Development of Antimicrobials, DX

The FDA is providing guidance for devicemakers that want to coordinate development of antimicrobial susceptibility tests with sponsors developing antimicrobial drugs.

Coordinated development of antimicrobial drugs and antimicrobial susceptibility tests (ASTs) should not be construed as companion diagnostics, the FDA said in draft guidance issued on Sept. 21.

Rather, the guidance describes interactions between devicemakers and drug sponsors for coordinating development, as well as explaining considerations for submitting separate applications to CDRH and CDER.

The guidance notes that review of the drug and device components would remain independent and that coordinated development would not affect MDUFA and PDUFA user dates.

The guidance points out that AST devices that test for in vitro susceptibility of bacterial pathogens are often developed after antimicrobial drugs are approved, and that coordinating development of new antimicrobial drugs with AST devices could shorten the time for clearing the device.

In addition, drug sponsors could benefit by having access to the AST device technology during clinical trials, and devicemakers could benefit by having access to clinical samples and isolates obtained during the drug development process to help validate their devices.

Currently, a 510(k) premarket notification is required for an AST device launched for the first time, or for changes to a cleared device. Similarly, a 510(k) would also be required when seeking to add a new approved antimicrobial drug to an existing AST panel.

(See **Antimicrobial***, Page 8)*

FDA Classifies Magnetic Surgical Instrument Systems as Class II

The FDA issued a final order on Sept. 21 that classified magnetic surgical instrument systems as Class II devices with special controls.

Firms that intend to market this type of device must submit a premarket notification and comply with the special controls listed in the final order.

A magnetic surgical instrument system is used in laparoscopic surgical procedures and consists of several components, including surgical instruments and a magnetic controller.

Companies marketing a magnetic surgical instrument system must adhere to the following special controls:

- In vivo performance data must demonstrate that the device has the ability to grasp, hold, retract, mobilize, or manipulate soft tissue and organs;
- Non-clinical performance data must demonstrate that the system performs as intended. Performance characteristics must be tested for magnetic field strength testing characterization; ability of the internal surgical instrument to be coupled, de-coupled and re-coupled with the external magnet;
- The patient-contacting components must be biocompatible and sterile;
- Methods and instructions for reprocessing reusable components must be validated;
- Performance data must support shelf life by demonstrating continued sterility;
- Training must be developed and validated by human factors testing; and
- Labeling must include: magnetic field safe zones; instructions for proper device use; a screening checklist to ensure that all patients and operating staff are screened from bringing ferromagnetic implants, devices, or objects near the external magnet; and reprocessing instructions for reusable components.

EU Considers Joint Health Technology Assessments

The EU is considering adopting an EU-wide health technology assessment model for drugs and devices.

Although the European Commission signs off on what products can be placed on the market, the pathway to market access is dictated by individual member states via health technology assessments to determine the clinical and economic value of a given product.

A network of national authorities was established in 2013, and while participation is voluntary, member states have willingly participated and indicated strong interest in moving toward an EU-wide HTA system.

Substantial work has already been completed through Joint Actions (EUnetHTA), and a third Joint Action has been established that will run through 2020. At present there are more than 70 members and observers participating.

The Joint Actions' main focus is on developing common HTA methodologies and pilot projects to develop and maintain IT tools and to build capacity.

In a recent report, the commission identified the lack of "binding mechanisms for mutual recognition of joint assessments" as one of the major shortcomings of the current HTA system.

The report notes that each national HTA costs around € 30,000 to national bodies and € 100,000 to the industry. "Assuming that 10 Member States carry out HTAs for one (and the same) technology and that these could be replaced by one joint report, 70 percent savings could be realized," the report said.

The medical device industry raised concerns that EU cooperation is focused on the "pharma model" for market access, and stakeholders requested that any initiative at the EU level be sector-specific.

Stakeholders also questioned whether market access and pricing decisions should be made at the EU level.

Read the European Commission report here: www.fdanews.com/09-22-16-ECReport.pdf.
— Tamra Sami

Upcoming Rules in Australia to Allow Earlier Access to Medical Devices

The Australian government announced it will allow earlier access to investigational devices under new regulations that the Therapeutic Goods Administration plans to roll out in the next few years.

The Ministry of Health said the government will adopt most of the recommendations from an independent review of the country's drug and device regulations in 2014.

The reforms include improving access to medical devices by expediting approval, particularly for products already approved in comparable countries such as the U.S. and the European Union.

The independent review found that Australian patients get access to innovative products up to 15 months later than patients in the U.S. and EU.

The new regulations will allow three pathways for medical devices, one of which is an expedited pathway for medical devices under certain conditions.

The other two pathways involve conformity assessments in Australia and using marketing approval from another comparative country as the basis for approval in Australia.

Along those lines, the TGA will develop transparent criteria to designate "suitably qualified bodies" within Australia to undertake conformity assessments. The criteria will include capacity to set specific requirements for different classes of devices, and the criteria will be developed in consultation with industry stakeholders.

Australia's regulations for medical devices will align most closely with those under the European Union framework, the report said.

(See **Rules**, *Page 10)*

Australia Recalls Rehab Assist's Carry Bars for C-Series Ceiling Hoists

Australia's Therapeutic Goods Administration is recalling Rehab Assist's carry bars used with its C-Series ceiling hoists due to the potential for a plastic attachment swivel to break.

Ceiling hoists are used to help lift and move patients with limited mobility. They involve a track attached to the ceiling from which a carry bar is suspended, and the patient is moved via a sling hung from the carry bar.

Some C-Series carry bars are attached to the track using a plastic swivel, which could separate from the carry bar, resulting in a patient fall. There have been nine incidents worldwide in which the plastic swivel mechanism has been reported as damaged.

Read the notice here: www.fdanews.com/09-22-16-Ausrecall.pdf.

Antimicrobial, *from Page 5*

The FDA recommends that devicemakers and drug sponsors discuss coordinated development early on in the drug development process so that data to help develop AST devices could be generated during clinical trials.

Interactions don't need to be restricted to a single devicemaker, the FDA says, stressing that the availability of a drug to multiple devicemakers for use during AST device development "may increase clinical laboratories' access to AST devices at the time of drug approval or shortly thereafter."

The guidance recommends that both the drug sponsor and devicemaker submit their coordinated development plans to CDER and CDRH for review.

An investigational device exemption may be needed if the AST device under development is to be used for clinical trial enrollment, and this should be discussed with CDRH through the pre-submission process, the guidance suggests.

Read the draft guidance here: www.fdanews.com/09-21-16-Draftguidance.pdf. — Tamra Sami

Hearing, *from Page 4*

Regarding the more than 60,000 tests being used today, "we have to have some sort of grandfathering involved," said Spring. "You can't just automatically take them off the market."

Jeff Allen, CEO of Friends of Cancer Research, said he supported FDA regulation, and recommended prioritizing the LDTs that address the highest risks to patients, such as large-scale genomic screening, or prostate-specific antigen tests. Also, professionals using the tests and interpreting the results may not know whether the test has been confirmed to work, he said.

"I think there's an expectation that when you go into your doctor's office, you're going to be told the best information that a medical professional can provide to you — based on a whole host of tests and analyses, and their medical interpretation of the symptoms that you're describing to them," said Allen. "And frankly, patients shouldn't have to worry about this." — Conor Hale

Guidance Addresses Computational Modeling in Device Submissions

The FDA issued final guidance on standardizing the way companies report computational modeling and simulation studies, paving the way for more computer modeling in medical device trials.

Currently, the FDA handles computational modeling data on a case-by-case basis, which has led to a lack of clarity for industry. The guidance provides recommendations on formatting, organization, and content of reports of computational modeling studies used to support device submissions.

The guidance sets out uniform ways of reporting computational modeling data in five subject matter areas: fluid dynamics and mass transport; solid mechanics; electromagnetics and optics; ultrasound; and heat transfer. It does not address proper verification or validation procedures or how to design a computational modeling study. The final guidance is almost identical to draft guidance issued in January 2014.

Sponsors are given a 13-part outline, which the FDA says should be used in preparing computational modeling reports for any device submission. The executive summary should provide "a concise overview of the computational modeling or simulation study" and include the type of analysis, conclusions, and up to five key words related to the study.

The agency also recommends a system configuration section to discuss the components of the device to be evaluated and any "assumptions and simplifications used to generate the system configuration, as compared to the actual device and environment."

The rationale behind these changes, which might include size or mathematical convenience, should also be described, the guidance says. Other important information includes details on the equations or constitutive laws governing the system, and biological, chemical and physical properties of all systems used in the computational modeling analysis.

Results of the computational modeling study should be presented "with sufficient level of details" and properly labeled. These may be presented in more than one format, the FDA says. In a separate section, submitters should address any known limitations of the data, such as how assumptions used in the model might have affected the output, the guidance explains.

Finally, sponsors should provide information regarding the methods used to validate the computational model.

Read the final guidance here: www.fdanews.com/09-21-16-Finalguidance.pdf. — Tamra Sami

Infections Associated with Reprocessed Bronchoscopes

The FDA issued a warning on infections associated with reprocessed flexible bronchoscopes.

Based on its preliminary investigation, the FDA said the risk of infection presented by reprocessed bronchoscopes appears to be lower than the risk of infection presented by reprocessed duodenoscopes.

Last year, reprocessed endoscopes caught the FDA's attention due to numerous antibiotic-resistant infections reported. As a result, the agency issued final guidance in March 2015 strengthening controls on reprocessing (*IDDM*, March 16, 2015).

Noting recurrent issues, the agency said the same procedures for reprocessing should be applied to bronchoscopes:

- Strictly adhere to manufacturer's reprocessing instructions;
- Immediately remove from service for assessment and repair or replace any bronchoscopes that fail a leak test;
- Follow the manufacturer's recommendations for preventive maintenance and repair of the device;
- Implement a comprehensive reprocessing quality control system; and
- After reprocessing, store bronchoscopes in a manner that will minimize the likelihood of contamination.

Read the safety notice here: www.fdanews.com/09-22-16-safetyalert.pdf. — Tamra Sami

Rules, *from Page 7*

The Commonwealth government deferred establishing a registry for high-risk implantable devices, noting that further consultations with stakeholders were needed to assess the risks and benefits of establishing such a registry.

Minister of Health Susan Ley said the reforms "strike the right balance" between consumer protection and reducing red tape for companies importing or manufacturing medical devices.

The Medical Technology Association of Australia (MTAA) praised the government's response, and said it was "encouraged" by the government's recommendation for greater use of overseas assessments to expedite access to life-saving products.

The association also said it welcomed the government's decision to defer establishing registries for high-risk implantable devices.

"Well-designed registries are extremely costly and careful consideration needs to be given to defining areas of high risk for selection and implementation of a registry," MTAA said.

The regulations will also relax vetting requirements for advertising medical products, but stiffer penalties will be imposed when it comes to noncompliance, the report indicated.

Small- to mid-sized companies will be offered additional guidance, such as targeted regulatory material, information sessions and assistance via dedicated help lines and advice.

Read the government report here: www.fdanews.com/09-20-16-Australiaregs.pdf. — Tamra Sami

BRIEFS

FDA Clears GI View's Colonoscope

GI View has received FDA 510(k) clearance for a colonoscope device that is disposable, self-propelled, and joystick-controlled. The device now allows for therapeutic access to take biopsies or perform polypectomies.

The Aer-O-Scope uses a soft multi-lumen tube to reduce pressure on the colon wall. The tube is also hydrophilic, which reduces friction between the bowel and scope by more than 90 percent.

CE Mark Granted for Lotus Edge

Boston Scientific has received a CE Mark for its aortic valve system, the Lotus Edge valve system for aortic valve replacement in patients with severe aortic stenosis who are at high risk for surgical valve replacement.

This next generation of development for the system includes the Adaptive Sea technology, which minimizes leaking.

ViewRay Obtains CE Mark for MRI System

ViewRay has received a CE Mark for its advanced linear, accelerator-based, MRI-guided radiation therapy system. The MRI device builds on the first generation MRIdian system, but uses cobalt with linear accelerator technology.

The company has also submitted its 510(k) application for the MRIdian Linac technology in the United States.

FDA Clears Lithoplasty System

The FDA granted clearance to Shockwave Medical's Lithoplasty System for treatment of calcified plaque in patients with peripheral artery disease (PAD).

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- Effective Management of Front and Back Inspection Rooms – Secrets You've Never Heard and Answers to Questions You've Always Wanted to Ask
- A Day in the Life of an FDA Field Investigator – How Inspectors Prepare and Approach Assigned Inspections

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MARC-HENRI WINTER, Staff Fellow, Division of International Compliance Operations, OC, CDRH, FDA (invited)

ARMANDO ZAMORA, Deputy Director, Office of Enforcement and Import Operations, Office of Global Regulatory Operations and Policy, ORA, FDA (invited)

DAVID CHESNEY, Principal and General Manager, DL Chesney Consulting, LLC

BRYAN J. COLEMAN, Senior Director Pharmaceutical & device Consulting Services, EAS Consulting Group

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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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