INTERNATIONAL DEVICES & DIAGNOSTICS MONITOR

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IN THIS ISSUE

Canada Proposes Significant Hike in User Fees for Devices

Health Canada has proposed fee hikes for reviewing medical devices, as well as licensing and postmarket surveillance and enforcement activities.

Fees, last revised in 2011, fall short of the agency's new goal of covering 90 percent to 100 percent of costs, Health Canada said.

The department "faced with an increased volume of work as well as added complexity from globalization, technological advancement and more sophisticated data and systems," it said.

Some of the proposed new fees are dramatically higher than current fees. For example, a license application for a Class III medical device would increase from $5,691 (US$4,528) to $13,861 (US$11,029).

A Class III device application for a near-patient in vitro diagnostic device — defined as an IVD that is intended for use outside a laboratory, for testing at home or at the point of care, such as

(See **Fees**, *Page 2)*

FDA Posts Updated Inspection Manual Chapter

The FDA recently updated its Investigations Operations Manual chapter on inspections of domestic and international sites.

The fifth chapter of the manual lays out the authority of agency investigators to enter and inspect facilities, the scope and approach of their inquiries, as well as their procedures for preparing Form 483s and post-inspection notification letters.

The 127-page chapter covers medical devices, drugs, and biologics, as well as food and tobacco product inspections conducted by the Office of Regulatory Affairs.

While hard copies of the manual as a whole are typically published annually in the spring, individual chapters can be updated online throughout the year.

(See **Manual**, *Page 2)*

Manual, *from Page 1*

Issuing written observations is mandated by law and ORA policy, and the observations listed in 483s should be significant, the manual says.

Observations of questionable importance should not be listed on the 483, but instead discussed with the firm's management, to explain how uncorrected problems can become violations. In addition, deviations from agency guidance should not be cited on a 483.

"Investigators and analysts should make every reasonable effort to discuss all observations with the management of the establishment as they are observed, or on a daily basis, to minimize surprises, errors, and misunderstandings when the FDA 483 is issued," the manual says.

The manual goes on to list examples of reportable observations, including undesirable conditions or practices, and instances of faulty manufacturing.

The document also directs investigators to determine the firm's policies for receiving supplier guarantees for raw materials and issuing guarantees on their products, as well as what departments are responsible for promotion and advertising — though promotional materials should not be collected on a routine basis.

The manual's updated Chapter 5 on establishment inspections is available here: www.fdanews.com/10-18-17-FDAInspectionManual.pdf.

Fees, *from Page 1*

a pharmacy, a health care professional's office or the bedside — would increase from $9,687 (US$7,708) to $32,267 (US$25,675).

Fees to review changes in manufacturing processes, facility, equipment of quality control procedures would increase from $1,433 (US$1,140) to $9,956 (US$7,922). A Class III significant change would jump from $5,330 (US@4,241) to $11,127 (US$8,854), under the proposal.

A few fees would be lower. For example, applications for new licenses and renewal of licenses would drop from the current $8,109 (US$6,452) to $4,500 (US$3,581).

The agency would also eliminate Class IV medical device applications for near-patient IVDs or for devices that contain human or animal tissue fee categories. Instead, it would consolidate all license applications for Class IV medical devices into a single fee category that would reduce the administrative burden. The standard 75-day service standard would remain the same.

Currently, private label applications for devices are exempt from paying fees. The new proposal would charge a fee to recover the cost for processing label license applications and amended license applications for Class II, III and IV medical devices.

Health Canada will likely require full payment of fees before reviewing or processing begins. Currently, the fee payments for device applications can either be made in full upfront if the fee is less than $5,000 (US$3,979), or it can be staggered with 75 percent payable once it is accepted for review, with the remaining 25 percent payable when the review is completed.

Read the full proposal here: www.fdanews.com/10-17-17-Canadafees.pdf.

First U.S. Surgery With 3D-Printed Implant

A custom 3D-printed composite sternum and ribcage implant was used in a surgical operation in the United States for the first time and only the second time in the world, the Australian device manufacturer Anatomics announced on Oct. 18.

The implant and the PoreStar technology it uses have not been cleared for commercial distribution in the U.S. The surgical team at NewYork-Presbyterian/Weill Cornell Medical Center obtained permission to use the implant in August through the FDA's expanded access program. The program allows the use of investigational devices for special patient needs.

In 2015, CDRH received a total of 215 compassionate use submissions for investigational device exemption supplements — down from 228 in 2014 — and 170 compassionate use requests for devices without IDEs — up from 112 in 2014.

Anatomics engineers used high-resolution CT scans of the patient's chest to design the custom implant and sent a biomodel of the patient's sternum and ribcage to Australia's Commonwealth Scientific & Industrial Research Organization's 3D-printing laboratory. The surgery was later performed on a patient who had been diagnosed with chondrosarcoma — a rare cancer, resistant to chemotherapy and radiotherapy, which affects individuals' bones and joints. — Ana Mulero

AdvaMed Petitions for Relief From India's Device Price Caps

AdvaMed filed a petition with the U.S. Trade Representative seeking relief from India's new price controls on certain medical devices.

Earlier this year, health authorities in India set price caps on coronary stents and knee replacement implants (*IDDM*, Aug. 21).

Under the new regulations, prices were slashed by up to 85 percent for coronary stents and 70 percent for knee implants on average, according to AdvaMed.

India is also reportedly considering price caps for other medical devices, such as orthopedic implants and catheters.

"If price controls extend to all US exports of medical devices, except capital equipment and in vitro diagnostics (because neither category has ever been mention as candidates for price controls), over $700 million of US exports could be adversely affected," AdvaMed wrote in the petition.

AdvaMed President and CEO Scott Whitaker said India has neglected to correct inefficiencies in the health care system. Whitaker also expressed concerns that the new price caps could hinder innovation and limit patient access to high-quality, life-saving medical devices.

Indian authorities should use "market-based alternatives that would allow for price differentiation for individual products, based on technological differences, and unimpeded patient access," he said.

The petition urges the USTR to suspend or withdraw, partly or entirely, India's benefits under the Generalized System of Preferences, a preferential tariff program. — Ana Mulero

FDA Warns Kelyniam Global For GMPs, Unapproved Products

Devicemaker Kelyniam Global drew a warning letter from the FDA after failing to adequately address numerous GMP issues observed in a May inspection of its Canton, Connecticut facility, including the manufacturing of unapproved implants.

In its response to a Form 483 report issued after the inspection, the firm failed to provide documentation to support its promises to correct the problems, and just said it would create a CAPA for each nonconformance and perform relevant evaluations.

Problems identified in the inspection included a failure to validate several device design changes and to initiate complaint investigations.

(See **Warning**, *Page 4)*

CDRH Extends Experiential Learning Program for 2018

CDRH is extending its Experiential Learning Program for agency staff into 2018 and is calling for submissions from potential participants.

The agency launched the collaborative staff training program this year to help close the knowledge gap between emerging technology and pre-market reviews of medical devices.

Participants in the program gain a better understanding of the products they review, how they are developed, challenges related to quality systems development and management in the product life cycles, and how medical devices fit into the larger healthcare system, the agency said.

Read the agency's Oct. 18 notice here: www.fdanews.com/10-20-17-Notice.pdf.

Warning, *from Page 3*

Other deficiencies were related to device master records, process validation, and procedures for accepting new materials.

The facility lacked testing documentation for cranial implants and maxillofacial implants, had been using test reports for implant cleaning validation that haven't been approved, and it lacked requirements to ensure that new material meets specifications.

Management had not reviewed the firm's quality system since Jan. 11, 2016, the FDA investigator found. The inspection also revealed that the firm lacked CAPA procedures. One ineffective corrective action involved failing to verify that employees were being trained on the most current device revisions.

In addition, the firm's Customized Cranial/Craniofacial Implants had not received a PMA approval or an investigational device exemption, so they were adulterated and misbranded, according to the warning letter.

The firm also failed to get 510(k) clearance prior to manufacturing a new version of its Custom Skull Implant. "CSI option #2 Temporal Suture System is an operating principle change which leads to the submission of a 510(k)," the agency said.

Read the warning letter here: www.fdanews.com/10-18-17-KelyniamGlobal.pdf. — Ana Mulero

483 Roundup: FDA Targets Five Devicemakers for Noncompliance

The FDA flagged device firms in the U.S., Germany, the United Kingdom, the Czech republic, and India for a range of issues, including MDR reports, CAPA failures and other GMP issues.

BEKA Hospitec: The FDA cited a German medical device manufacturer for noncompliance issues related to MDR reports, complaint handling, as well as device master records and history records.

The agency's Form 483 report issued after inspecting the facility from Jan. 30 to Feb. 2 observed that MDR and complaint reports were not completed after several events that called for them, including the firm's Carlo lift lowering onto a patient's face leaving a bruise, a lift bar "breaking at the swivel connection point just after the patient was transferred to a bed," and a lift shaft bolt "shearing while a patient was in the lift, causing the patient to fall and the carry bar to fall on the patient's chest."

The investigator also observed that BEKA Hospitec had not established design validation protocols and acceptance criteria before performing validation activities on its Sina Comfort Shower Trolley.

Research Instruments: UK-based Research Instruments drew a Form 483 from the FDA over documentation, device history maintenance and procedural issues.

The manufacturer failed to identify products' acceptance status and did not conduct effectiveness reviews of the facility's quality system, the agency found in an inspection in April.

Certain management reviews were not conducted in 2015, 2016 and 2017, and senior management officials were not present during at least one management review, the agency said.

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

Effective 483 Responses

A response to a Form 483 is not a routine or informal communication and should be given the same attention and care you would give to defending your company from a federal indictment—because that's what a 483 actually is.

The response "needs to be treated with the same level of sincerity, effectiveness, clarity as any situation would be if you were involved in any other kind of law enforcement setting," says Gordon Richman, vice president and regulatory compliance counsel to Danaher Diagnostics Platform.

The purpose of the response is to make your case to the FDA: convince the agency that you take its warnings seriously, are committed to improvement and have a solid, detailed plan for fixing your deficiencies. Unfortunately, the FDA provides no guidance on what it expects to see in a response. Even worse, it gives you only 15 days to deliver it.

It also becomes part of the agency's official administrative record, and it's really the first opportunity for the company to get its side of the story in that record. FDA investigators are generally very good at what they do, Richman says, but there can be misunderstandings and miscommunications.

"They don't always get it right, and there's usually some additional information the [company] thinks of or obtains after the inspection is over that provides further clarity to the story," he says. "So it's important for the company to put its foundation in place in that record."

And it's not just what gets put on paper that's important. "The actions that the company takes, the meeting of its commitments, the thoroughness of its review and assessment to other activities that may be related are really important," Richman says.

The most important step in developing a response is analyzing the observations in the 483.

What is the investigator saying? What was the underlying concern? What did interactions with the investigator during the inspection add to understanding the observation?

Excerpted from the *FDAnews* book: *Effective 483 Responses: Focus on CAPA Violations*.

483s, *from Page 5*

Embrace Health Care: Embrace Health Care lacked adequate complaint handling, product acceptance, CAPA or written MDR procedures when the FDA inspected its New Hampshire facility in July, according to a Form 483 report.

The firm had no procedures for analyzing sources of quality data, investigating the cause of nonconformities, identifying needed actions to prevent recurrences of nonconformities, among other CAPA deficiencies.

The FDA investigator also noted the facility lacked an adequate quality system and procedures, such as those for internal audits.

Healthy Spirit: An FDA inspection of Healthy Spirit's manufacturing facility in Maryland revealed 14 nonconformities related to required procedures, documentation, complaint handling, management reviews, and employee training.

The investigator inspected the facility from May into July and found that the firm had not established procedures for finalizing acceptance, designing or maintaining device history records of its EasyRest Adjustable Sleep System. The facility also lacked instructions for installation and inspection and test procedures for the system, according to the Form 483.

The firm also lacked procedures for device labeling and Unique Device Identification, and an explanation for why certain customer complaints were not required to be documented.

Documentation of damaged mattresses received since 2013 and CAPA actions initiated to address supplier nonconformities was not provided. The firm was also unable to produce supplier selection and evaluation records.

Healthy Spirit had not documented internal audit reports since 2012 or management reviews of its quality management system since 2013, the agency said.

Olympus Medical Products Czech: The FDA found inadequate production monitoring, CAPAs and equipment inspection procedures in an April inspection of the Olympus Medical Products Czech facility in the Czech Republic.

A Form 483 issued following the inspection noted the firm had only performed visual inspections on its equipment, with no assurance that visual inspection was adequate to ensure the product is made to the correct specifications.

Read the BEKA Hospitec Form 483 here: www.fdanews.com/10-18-17-bekahospitecgmbh483.pdf.

Read the Research Instruments Form 483 here: www.fdanews.com/10-18-17-researchinstrumentsltd483.pdf.

Read the Embrace Health Care Form 483 here: www.fdanews.com/10-18-17-embracehealthcarellc483.pdf.

Read the Healthy Spirit Form 483 here: www.fdanews.com/10-19-17-healthyspiritllc483.pdf.

Read the Olympus Medical Products Form 483 here: www.fdanews.com/10-19-17-olympusmedicalproductsczech483.pdf.

PEOPLE ON THE MOVE

SafeHeal named **Karl Blohm** as CEO. Blohm is a senior executive with more than 25 years of experience managing international business operations, combining capital equipment and medical devices. He was most recently vice president - international at GI Dynamics, and previously served in various roles at Accuray, EndoGastric Solutions, and Siemens.

Mazor Robotics appointed **Ron Tavlin** as vice president of business development. Tavlin has more than 25 years of experience with public and private companies. Prior to joining Mazor, he was a consultant for the Medtronic ventures and corporate development teams. Previously, he was chief operating officer of BlueWind Medical, and a co-founder and managing partner of Omega Capital.

In vitro diagnostics company **Atlas Genetics** named **Jeffrey R. Luber** as CEO. Luber brings broad experience in the life sciences industry. Most recently, he led the sale of Good Start Genetics to Invitae and entered into strategic partnerships with Roche Diagnostics and Amazon.

EMA Details Brexit Continuity Plan and Staff Retention Efforts

The European Medicines Agency will try to maintain "business as usual" for as long as possible throughout the U.K.'s planned exit from the European Union, according to a newly released continuity plan.

When and if Brexit goes ahead, the EMA may face additional challenges in implementing the EU's new medical device and IVD regulations.

To account for what it describes as a possibly "unprecedented loss of expertise and experience over a rather short timeframe" — following the move of its headquarters from London to a yet-to-be-determined EU city — the EMA plans to implement a dedicated Brexit recruitment strategy for new hires.

The official selection of one of 19 potential host cities for the EMA is expected to be announced Nov. 20. A survey of agency staff last month showed the choice of location could result in a significant percentage of employees deciding not to make the move.

The EMA also plans to bolster its entitlements for staff and families, and to provide other services to encourage employee retention. Once a new city has been selected, the agency will develop a second continuity plan for the physical move.

Earlier this year, the EMA laid out how it would prioritize activities into three categories in the event staffing levels begin to drop, and began reducing resources for the lowest-ranked tasks to free up resources for the transition.

The new business continuity plan provides more detail: the highest-priority core scientific activities include maintaining quality defect reporting to the EMA and the European regulatory network, issuing urgent safety restrictions and variations, and suspending or withdrawing approvals for centrally authorized products, including those due to quality defects. Testing and inspections, as well as supporting IT work, will also be prioritized.

Medium-priority activities include preparation for new and revised legislation, institutional cooperation with member states, and the work of the EMA's Small- and Medium-sized Enterprise Office, as well as work in health technology assessments.

Slightly lower medium-priority undertakings incude the development of guidelinest, scientific advice and certification, scientific advisory groups and product registries.

The full EMA Brexit continuity plan is available here: www.fdanews.com/10-16-17-EMABrexitContinuityPlan.pdf. — Conor Hale

APPROVALS

CelioFlex Miniprobes Earn CE Mark For Use in Robotic-Assisted Surgery

Mauna Kea Technologies received a CE Mark for its CelioFlex UHD Confocal Miniprobes for use with Cellvizio in robotic-assisted surgery procedures.

The miniprobes provide visualization of body cavities, organs, and canals during endoscopic and laparoscopic surgical procedures, including robotic-assisted procedures.

The company has received clearance to sell a wide range of Cellvizio applications in more than 40 countries, including the United States, Europe, Japan, China, Canada, Brazil and Mexico.

FDA Clears Siemens Healthineers' Terra 7T MRI Scanner

The FDA has signed off on Siemens Healthineer's Magnetom Terra magnetic resonance imaging (MRI) scanner for diagnostic imaging.

The scanner is the first 7T MRI system cleared for clinical use in the country. It produces cross-sectional images of the head and knee using Siemens' software platform as well as image reconstruction technology, allowing speeds up to 20 times more than previous scanners.

Philips Receives 510(k) Clearance For Ultrasound Device

Royal Philips received 510(k) marketing clearance for the eL18-4 transducer for ultrasound exams to detect abnormalities in the small organs close to the skin.

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

Approvals, *from Page 7*

The transducer can be used to assess diseases and disorders of small organs such as breasts, testicles and thyroid, as well as musculoskeletal injuries like sprains.

Neuronetics' MDD Therapy System Snags Shonin Approval

Neuronetics received Japan's Shonin approval for a transcranial magnetic stimulation non-drug treatment option for major depressive disorder treatment.

The NeuroStar Advanced Therapy system uses MRI magnetic field pulses to non-invasively stimulate underactive areas of the brain delivering electroconvulsive therapy. It also provides real-time feedback to physicians.

The system is approved for commercial distribution in the U.S. and is CE marked.

Stryker Receives FDA Clearance For Cementless Knee Implant

Stryker's Joint Replacement division received FDA 510(k) market clearance for its cementless Mako Total Knee with Triathlon Tritanium.

The implant combines the motion features of Stryker's Triathlon knee implant with a highly porous biologic fixation technology. The device's tibial baseplate and metal-backed patella components are made using proprietary manufacturing technology.

FDA Expands Use for NuVasive's Magnetic Limb Device

NuVasive received expanded 510(k) clearance for its magnetic limb lengthening technology.

The PRECICE system was previously approved for femur and tibia limb lengthening. The new indications for use include fracture fixation, pseudoarthrosis and bone transport, which allows for bony tissue to be regenerated.

The implantable platform uses an external remote controller for non-invasive, customizable treatments on long bones using an internal gear system that can be controlled remotely with permanent magnets.

TransEnterix Scores FDA Approval For Robotically-Assisted Surgical Device

The FDA granted 510(k) marketing clearance to TransEnterix Surgical for its robotically-assisted surgical device for facilitating minimally invasive surgery.

The Senhance system enables surgeons to accurately control laparoscopic instruments with three separate robotic arms. Surgeons can also use the system for 3-D visualization of the surgical field.

The system provides force feedback for assessing the stiffness of tissue and eye-tracking for accurately controlling the robotic arms.

Instrumentation Laboratory Receives FDA Clearance for HemosIL Assay

Instrumentation Laboratory received 510(k) clearance for its HemosIL AcuStar assay for detection of antibodies associated with heparin-induced thrombocytopenia (HIT) and HemosIL AcuStar HIT Controls.

The assay is a fully automated, chemiluminescent reagent on a hemostasis testing system for the qualitative detection of platelet factor 4 (PF4)-heparin complex IgG antibodies associated with HIT. The chemiluminescent technology enables high analytical sensitivity and precision.

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FDA INSPECTIONS SUMMIT

#1 EVENT FOR QUALITY, COMPLIANCE AND INSPECTIONAL READINESS PROFESSIONALS

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Lead Quality Systems and Compliance Consultant, King and Spalding, former FDA Deputy Associate Commissioner for Regulatory Operations

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

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Senior Partner, Director Inspection Readiness Services, BioTeknica

FDA SPEAKERS:

ELLEN MORRISON
Associate Commissioner, OMPTO, ORA, FDA

CAPT SEAN BOYD
Acting Director, Office of Compliance, CDRH, FDA

CAROL BENNETT, J.D.
Deputy Director, Office of Regulatory Policy, CDER, FDA (Invited)

NIRAJ MEHTA, Ph.D.
Associate Director for Global Regulatory Policy, Office of Global Regulatory Operations and Policy, OC, FDA

DOUGLAS STEARNS
Director, Office of Enforcement and Import Operations, ORA (Invited)

NOVEMBER 1-3, 2017 | DOUBLETREE BETHESDA BETHESDA, MD (WASHINGTON, DC)

2017 SUMMIT HIGHLIGHTS

NEW FOR 2017!

FDA's ORA Reorg and What it Means for Inspections

Preparing for the MDSAP Audit Process: A Case Study from the Manufacturer's Perspective

Building Your Best Internal Audit Team for Quality Results

Plus twin tracks for drug/biologics and device manufacturers and two pre-conference workshops,focusing on FDA Inspection Management and QSIT Secrets.

Expert panels featuring current and former FDA officials and industry professionals:

- FDA Field Investigators: What They Look For, What Problems are Emerging and AMA (Ask Me Anything)
- The US/EU Mutual Recognition of Drug GMP Inspections: Practical Consequences for Manufacturers
- European Medical Device Regulations — Preparing for the Storm

FEATURED EXPERT SPEAKERS:

JOHN AVELLANET, Managing Director and Principal, Cerulean Associates LLC

KATLIN BACKFIELD, Attorney at Law, Consultant, Backfield PLLC

PETER LEININGER, Counsel, King & Spalding; former Associate Chief Counsel for Enforcement in FDA's Office of Chief Counsel

CONNIE HOY, Executive Vice President of RA/QA, Cynosure

IBIM TARIAH, Ph.D., Technical Director, BSI Americas Inc.

DAN O'LEARY, President, Ombu Enterprises LLC

SUSAN SCHNIEPP, Fellow, Regulatory Compliance Associates, Inc.

CYNTHIA SCHNEDAR, Executive Vice President, Regulatory Compliance, Greenleaf; former Director of the Office of Compliance, CDER, FDA

VICKY STOAKES, President, IntegRx, Inc.; former FDA Chemist, ACNA and Investigator, Atlanta District Office Drug Cadre

KARL VAHEY, Vice President Manufacturing Quality, Patient Monitoring and Recovery, MITG, Medtronic

Pre-conference Workshops Agenda

WED., NOV. 1 (1–5 p.m.)

DRUGS & BIOLOGICS TRACK

Flawless FDA Inspection Handling and Response

Rated #1 Pre-Conference Workshop in Inspection Summit History — Updated for FDA's New Inspection Techniques!

John Avellanet of Cerulean Associates — one of the industry's top inspectional readiness experts — is back to teach proven techniques to manage FDA investigators on-site, how to defend yourself where it's appropriate and craft 483 responses that fend off warning letters.

Plus, in a special portion of this must-attend pre-conference, he'll explain how the FDA's New Inspection Protocol Project inspection technique could trip up companies that have always had good compliance records. He'll profile a company that had years of clean inspections, only to be blindsided with a bad inspection based on NIPP. You can't afford to miss this session!

Compliance pros know that getting an FDA investigator in and out as quickly as possible is the best strategy. The longer an FDA investigator is on site, the more likely you'll be handed a multi-page 483.

And if you think racking up those observations are bad, even worse is crafting a response, plowing it through your internal departments and getting it back to the FDA in just 15 days. Oh, did we mention the response must be detailed, provide a well-documented root cause analysis and spell-out solutions to assure the problem never happens again?

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 manage a 483 observation and not get a warning letter.

Attendees will learn:

- The results of a case study of how a firm that passed 9 previous inspections suddenly failed under FDA's new NIPP inspection technique
- Critical inspection preparation techniques every member of your team must commit to memory — especially useful for those surprise FDA visits
- Hidden tactics FDA investigators use to test your controls and are taught to probe your answers for weakness
- How to speed the inspection to minimize the risk of 483 observations, while always remaining respectful
- What really needs to be in your regulatory inspection handling SOPs — tips for cutting corporate-speak and unnecessary verbiage that doesn't help
- How to write an inspection response designed to reduce the likelihood of a warning letter — and tips and tricks to get sign-offs quickly from even the toughest groups (like legal)
- What FDA staff look for in your replies and the top red flags they notice

BONUS: Attendees will receive:

- A sample regulatory inspection handling 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

To QSIT or Not To QSIT – That is not the Question!

Customized, Interactive and Full Of Valuable Take-Aways, This Pre-Conference Workshop is a Must Attend

Some industry experts and ex-FDAers are saying that QSIT is outdated, incomplete and FDA investigators are not always following the Guide to Inspections of Quality Systems, QSIT during inspections. It's true FDA inspections can vary and many times investigator's may not follow QSIT to the letter. So, what then is a device manufacturer to do to prepare?

Device manufacturers can spend time focusing on why it's not fair, or they can focus on being ready for anything. This interactive pre-conference workshop will do just that.

FDAnews is proud to have Medical Device Inspection expert Julie Larsen, Principal/Director, Inspection Readiness Services at BioTeknica, provide her insights for preparing for inspections, including risk based approaches and using the QSIT's details to assure your next inspection is squeaky clean.

Julie knows Inspections, the inspection guidances, the QSIT guidance, and how to prepare device companies of all sizes and all product classes. In just four hours, you'll learn the current issues in application of this important inspection technique and numerous take-away ideas you can put to immediate use.

This interactive workshop will dive deep into these key issues:

- Applying risk principals to inspection preparation
- Pros and cons of using the QSIT's specifics to assure your internal audits have covered and confirmed compliance with FDA's expectations
- Examples of companies that have used the QSIT in both positive and negative ways — many of these will surprise you!
- Tips and tricks for being uber-prepared — especially being prompt with answers to investigators' questions and being able to produce documents in a timely manner
- Experiential learning for SMES through simulated inspections

Unlike other preconferences you've attended in the past, Julie will break attendees into working groups to flush out inspectional problems attendees are having. She'll then offer her insights on the best-in-class tools available and best practices to solve your problems.

BONUS: In addition to Julie's expert tips, attendees will receive these MUST-HAVE reference documents worth the registration fee alone, including:

- A detailed Inspection preparation checklist that attendees can immediately apply to their current inspection prep SOP
- 10 key questions to use in assessing your company's state of readiness for an FDA QSIT inspection

Julie Larsen, Principal/Director, Inspection Readiness Services, BioTeknica

Braulio Ortiz , Principal/Project Manager/Senior Quality Engineer, BioTeknica

Day 1 Agenda

THURS., NOV. 2

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

8:30 a.m. – 8:45 a.m.

Opening Comments by Chairperson Steve Niedelman, Lead Quality Systems and Compliance Consultant, King and Spalding, former FDA Deputy Associate Commissioner for Regulatory Operations

8:45 a.m. – 9:30 a.m.

FDA's ORA Reorg and What it Means for Inspections

The FDA reorganized its Office of Regulatory Affairs inspectorate to more closely align inspection efforts with the myriad types of products it regulates — essentially organizing staff by area of expertise instead of geographic region. Will inspections happen more frequently? Does this make inspection outcomes more predictable or less? Will inspections be conducted faster if they are done by experts, or will they take longer to go through more detail? Associate Commissioner Ellen Morrison will discuss the latest developments and talk about what to expect from the changes.

Ellen Morrison, Associate Commissioner, OMPTO, ORA, FDA

9:30 a.m. – 10:15 a.m.

The World of FDA Quality Metrics: Yesterday, Today and Tomorrow

CDER and CBER have the Quality Metrics Submission guidance. CDRH has the Case for Quality initiative. All centers are driving towards a culture of quality within the life sciences industry. Marla Phillips has a unique perspective that comes from working on both sides of the line. With the FDA, she co-led the CDRH metrics initiative, and with PricewaterhouseCoopers, she co-led the pharmaceutical metrics initiative. Her presentation will examine the difference between the two initiatives, their progress, the differences and the similarities in their metrics. From her industry experience, she will examine the potential impacts, the unintended outcomes and how to protect everyone's time from doing busy work that does not achieve the end goal. She will also share her thoughts of where these initiatives are headed.

Marla A. Phillips, Ph.D., Director, Xavier Health, Xavier University; former Head of Quality at Merck's North Carolina facility

10:15 a.m. – 11:00 a.m.

Postmarket Adverse Event Reporting and cGMP: What You Absolutely Need to Know

The FDA issued two final rules that set forth the postmarket safety reporting and current good manufacturing practices (cGMP) requirements for combination product and constituent part sponsors. This session summarizes key concepts and provides insightful case studies about how the rules work in the real world.

(cont.)

Katlin Backfield, Attorney at Law, Consultant, Backfield PLLC; former Associate Chief Council for Drugs, OCC, FDA

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

David Chesney, Principal and General Manager, DL Chesney Consulting, LLC; former FDA District Director for the San Francisco office

11:30 a.m. – 12:15 p.m.

FDA Regulatory Policy Roadmap: FDA Shares its Priorities for 2018

The FDA is constantly looking at new and more efficient ways to regulate drugs and medical devices. Under a new commissioner, the Office of Regulatory Policy (ORP) has identified a specific set of priorities that you need to know about. Some issues are very familiar, such as responding to an opioid epidemic that Commissioner Scott Gottlieb has called his "highest immediate priority." Other initiatives are less publicized but just as important. How will the agency modernize its assessment of manufacturing facilities? How does it manage innovations in drug development? Now that Gottlieb has made getting more generic drugs approved a priority, what are the implications for regulatory development? Will initiatives to harmonize efforts with international regulatory organizations mean changes domestically? Carol Bennett, Deputy Director Office of Regulatory Policy at CDER will review the recent actions within CDER and the outline priorities looking into 2018.

Carol Bennett, JD, Deputy Director, Office of Regulatory Policy, CDER, FDA (Invited)

12:15 p.m. – 1:00 p.m.

Cautionary Tales: Words to the Wise on Compliance

Those who fail to learn from the mistakes of others are destined to repeat them. Using real situations encountered by pharmaceutical and biologics firms, discover strategies for staying up-to-date with FDA cGMP regulations. Examples of non-compliance are presented with suggestions for applying these lessons and improving your regulatory compliance strategies.

Vicky Stoakes, President, IntegRx, Inc.; former FDA Chemist, ACNA and Investigator, Atlanta District Office Drug Cadre

1:00 p.m. – 2:00 p.m. | **LUNCH**

2:00 p.m. – 3:30 p.m.

The US/EU Mutual Recognition of Drug GMP Inspections: Practical Consequences for Manufacturers

In March, the US and European Union signed a mutual recognition agreement (MRA) to recognize each other's drug GMP inspections. This is good news for the industry that should see fewer inspections. However, it doesn't come without some concerns. First, each inspection now has greater consequences as any problem will now be a red flag for multiple agencies. Also, if regulatory agencies share information, what does that mean for information confidentiality? Plus, the EMA retained authority to conduct inspections in "extraordinary circumstances," but what does that mean, exactly? The FDA has until November to assess regulatory authorities in eight EU countries to trigger the start of the implementation of the agreement. How close are they? The agreement doesn't mean European GMP regulations are less important — in fact, they are as important as ever. Come hear experts describe the practical implications of this agreement for drug GMP inspections so you're not caught off guard.

Moderator: David Chesney, Principal and General Manager, DL Chesney Consulting, LLC; former FDA District Director for the San Francisco office

Niraj Mehta, Ph.D., Associate Director for Global Regulatory Policy, Office of Global Regulatory Operations and Policy, OC, FDA

Cynthia Schnedar, Executive Vice President, Regulatory Compliance, Greenleaf; former Director of the Office of Compliance, CDER, FDA

Katlin Backfield, Attorney at Law, Consultant, Backfield PLLC

Peter Leininger, Counsel, King & Spalding; former Associate Chief Counsel for Enforcement in FDA's Office of Chief Counsel

3:30 p.m. – 3:50 p.m. | **BREAK**

MEDICAL DEVICES TRACK

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

Julie Larsen, Principal/Director, Inspection Readiness Services, BioTeknica

11:30 a.m. – 12:15 p.m.

CDRH's New Inspection Strategy for 2018: How it Will Impact Your Company

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

- The new inspection approach/strategy for medical devices in 2017-2018 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

CAPT Sean Boyd, Acting Director, Office of Compliance, CDRH, FDA

12:15 p.m. – 1:00 p.m.

Preparing for the MDSAP Audit Process: A Case Study from the Manufacturer's Perspective

Manufacturers entering the Medical Device Single Audit Program undergo an assessment performed by a single third-party inspector that proves compliance in the US, Canada, Australia, Brazil, the EU and Japan. The audit process is not what you're used to compared to an FDA or ISO audit. Cynosure has successfully certified two manufacturing sites in the last year. The Cynosure facility in MA (1,000 people) was audited as part of the MDSAP in October 2016 and their facility in NY (40 people) was audited to the MDSAP in March 2017. Both facilities passed the audit with only minor findings.

Executive Vice President of RA/QA Connie Hoy will take you through the preparation process from the manufacturing perspective. You will also hear what lessons they learned along the way, what they would have done differently and how it compares to a corporate audit versus a small manufacturing plant audit.

This presentation will cover:

- What they did to prepare for the audit
- The audit flow and how it differs from QSIT and ISO audits

(cont.)

- The differences and similarities between preparing the two plants
- What they would do differently to prepare now that they have undergone the process

Connie Hoy, Executive Vice President of RA/QA, Cynosure

1:00 p.m. – 2:00 p.m. | **LUNCH**

2:00 p.m. – 3:30 p.m.

Panel Discussion: European Medical Device Regulations — Preparing for the Storm

Like a line of thunderstorms developed on a weather front, various regulatory agencies will move through your company to check up on the Quality Management System. Each visit will be different because they will look at different aspects. The FDA will check your adherence to US regulations. The MDSAP will help prepare you for Canada, Australia, Brazil and other jurisdictions in the program. The unknown factor is the status of the MDR Notified Bodies (NB). There aren't any yet, as the regulation moves through its transition process. We do know that qualifying NBs will conduct audits that are more rigorous than under the directives. The MDR Annex VII, Section 4.5. Conformity Assessment Activities, lists specific requirements for the NB to cover during an audit.

This expert panel will take you through the changes and what you need to know to be prepared to continue to market or bring your product to market in Europe.

Moderator: Lenita Y. Sims Spears, Senior Quality Consultant/Senior Regulatory and Compliance Counsel, BioTeknica

Dan O'Leary, President, Ombu Enterprises LLC

Ibim Tariah, Technical Director, BSI Americas Inc.

Karl Vahey, Vice President Manufacturing Quality, Patient Monitoring and Recovery, Medtronic

3:30 p.m. – 3:50 p.m. | **BREAK**

Plenary Session Panel Discussion

3:50 p.m. – 5:15 p.m.

FDA Field Investigators Panel: What They Look For, What Problems are Emerging and AMA (Ask Me Anything)

Ever wonder what an investigator is thinking when they receive their next inspection assignment? What framework they follow, and what affects their thinking during an inspection? This presentation will give you a glimpse into the inner workings of an investigator's mind before, during and after an inspection.

Attendees will learn:

- What information does an investigator have before he or she shows up at your door?
- Do investigators prepare differently for different companies, plants or products?
- What is the first thing they notice when they enter a plant?
- How do investigators 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

PLUS, this panel will take your questions (anonymously if you wish). So, here is your chance to ask questions and get answers straight from investigators in the field every day! Don't miss this opportunity to get your answers!

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

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

8:30 a.m. – 8:45 a.m.

Opening Comments by Chairperson Steve Niedelman, Lead Quality Systems and Compliance Consultant, King and Spalding, former FDA Deputy Associate Commissioner for Regulatory Operations

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 2018, and changes to how the office approaches the process. This session will ensure attendees have the latest information on how they can more proactively prepare for FDA investigators.

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

Douglas Stearns, Director, Office of Enforcement and Import Operations, ORA (Invited)

9:30 a.m. – 10:15 a.m.

Building Your Best Internal Audit Team for Quality Results

An internal audit of your quality management system should be a collaboration, not a confrontation, with auditor and auditee working together to spot issues that weaken your system. You need to move your audit team beyond the "blame and shame" mindset that can keep them from openly and honestly sharing the information you need to work out solutions and make your QMS stronger.

Your internal audits can be a positive and productive experience for all if you apply the lessons in this session:

- How to train your employees to handle audits in the most productive way;
- How to select the best auditor to work with your team;
- How to follow the internal audit with corrective action;
- How to report audit findings to management and get them to buy in to suggested solutions; and
- How to evaluate your internal auditing system's effectiveness.

Susan Schniepp, Distinguished Fellow, Regulatory Compliance Associates, Inc.

10:15 a.m. – 10:30 a.m. | **BREAK**

10:30 a.m. – 12:00 p.m.

How to Deal with Difficult Inspections

Co-Chair Steve Niedelman and long-time industry expert, David Chesney, 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.

Steve Niedelman, Lead Quality Systems and Compliance Consultant, King and Spalding LLP; former FDA Deputy Associate Commissioner for Regulatory Operations

David Chesney, Principal and General Manager, DL Chesney Consulting, LLC; former FDA District Director for the San Francisco office

12:00 p.m. | **SUMMIT 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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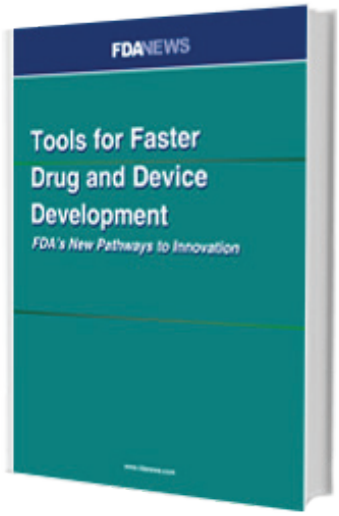

Tools for Faster Drug and Device Development: *FDA's New Pathways to Innovation*

Speed and efficiency of the drug and device development processes has long been a concern of the FDA.

Manufacturers that are using new and unique development tools, such as biomarkers, can apply to the agency's development tool qualification program to have them approved for use in other development efforts.

According to CDER Director Janet Woodcock a national repository of tools approved by the FDA will accelerate the development of new products because researchers will not have to prove a tool's reliability every time they use it.

In **Tools for Faster Drug and Device Development: *FDA's New Pathways to Innovation*** noted FDA law expert Jim O'Reilly lays out the current landscape of drug and device development tool research. He explains how the 21st Century Cures Act has established an updated, multi-stage process for development tool qualification and explores how the FDA will implement it. You'll learn:

- What the FDA means by "qualified" data
- How to show that new tools can identify safety risks as well as prove efficacy
- Standards the agency may set for approval of such tools as biomarkers and clinical outcomes assessment
- And more…

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