INTERNATIONAL DEVICES & DIAGNOSTICS MONITOR

Vol. 3, No. 43
Oct. 30, 2017

IN THIS ISSUE

FDA Issues Guidance for New Breakthrough Devices Program

The FDA released draft guidance on a new program aimed at expediting access to breakthrough medical devices.

The program will replace the agency's Expedited Access Pathway and Priority Review Program, adding elements of the agency's Innovation Pathway. The new program was established by the 21st Century Cures Act to help speed development and review of certain medical devices to ensure timely patient access.

The draft guidance describes the process for seeking a breakthrough device designation and includes a template device firms can use to submit a request. It also includes the criteria agency staff will use to evaluate applications, and discusses how the agency will go about reviewing devices granted breakthrough designations.

FDA Commissioner Scott Gottlieb said the program introduces "a more agile pre-submission process."

(See **Program**, *Page 2)*

FDA Clarifies When New 510(k)s Are Required for Device Updates

The FDA issued final guidance on when to submit a new 510(k) for a planned change to an existing device.

The agency issued separate guidances for non-software changes — updated from 1997 — and for software changes, closely following draft versions issued in August 2016.

The took a least burdensome approach, seeking to "lower barriers to innovation and improve patient care by reducing unnecessary submissions to the FDA for changes that could not significantly affect device safety or effectiveness, so patients can benefit from upgraded products more quickly," according to FDA Commissioner Scott Gottlieb.

The same general principles are recommended in both guidances, including determining whether the intent of the change is to

(See **510(k)**, *Page 2)*

510(k), *from Page 1*

significantly affect the safety or effectiveness of the existing device, and analyzing all new risks and changes to existing risks that could result from the change, using an initial risk-based assessment.

However, the guidance on software changes, which includes firmware, provides additional questions and factors to consider. For example, a new 510(k) is not likely required for a change only made to strengthen cybersecurity without any other impact on the software or device. But a change that could significantly affect clinical functionality or performance specifications of the product is likely to require a new submission.

Additional factors to consider for software changes relate to the most common types of changes, such as to the infrastructure, architecture and core algorithm. The guidance provides an extensive example list of the different situations in which a new 510(k) is likely or not likely required.

Read the guidance on non-software changes here: www.fdanews.com/10-25-17-Nonsoftwarechange.pdf.

Read the guidance on software changes here: www.fdanews.com/10-25-17-Softwarechange.pdf.

FDAnews will present a Nov. 12 webinar on the final guidances. See here for details: www.fdanews.com/510kchangeanalysis.

Program, *from Page 1*

Sponsors may reap a number of benefits under the program. The FDA "may accept a greater degree of uncertainty of the benefit-risk profile for these devices if the uncertainty is sufficiently balanced by other factors," such as the probable benefits to patients of having earlier access and adequate postmarket controls, the draft guidance states.

Breakthrough devices will receive a priority review status and may also qualify for an expedited review of manufacturing and quality systems.

According to the draft guidance, a breakthrough designation may be granted to devices that provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating human disease or conditions, and represent breakthrough technologies:

- For which no approved or cleared alternatives exist;
- That offer significant advantages over existing approved or cleared alternatives… to reduce or eliminate the need for hospitalization, improve patient quality of life, facilitate patient's ability to manage their own care, or establish long-term clinical efficiencies; or
- The availability of which is in the best interest of patients.

Device-led combination products may also qualify for a breakthrough designation. However, such products may take longer to review than others as they may raise novel scientific and regulatory challenges.

Read the draft guidance here: www.fdanews.com/10-25-17-BreakthroughDevicesProgram.pdf.

Upcoming FDAnews Webinars and Conferences

Sharpen your understanding of regulatory compliance at these upcoming FDAnews events. Click on the links below for details.

WEBINAR

Medical Device Reimbursement Integration A Better Approach for Commercial Success
Nov. 7, 2017, 1:30 p.m. - 3:00 p.m. ET
www.fdanews.com/mdreimbursement

CONFERENCE

12th Annual FDA Inspections Summit
Nov. 1-3, 2017, Bethesda, MD
www.fdanews.com/fdainspectionssummit

Gottlieb: Puerto Rico Device Firms Still Operating Below Capacity

Helping to restore medical manufacturing in Puerto Rico has been the "highest priority" at the FDA since hurricanes Maria and Irma struck, Commissioner Scott Gottlieb told a congressional committee on Oct. 24.

None of the facilities in Puerto Rico have reached 70 percent of their pre-storm capacity, Gottlieb said at a House Energy and Commerce subcommittee hearing on the recent hurricanes. The agency has planned more than 200 site visits to plants on the island, he said.

A focus of the FDA's efforts is maintaining electrical power for the factories because most are running on generators. Many generators are old, however, so they cannot be counted on for sustained operation, and they all need fuel to operate, he said.

In an Oct. 20 statement, Gottlieb said the agency is monitoring about 50 types of medical devices manufactured in Puerto Rico to mitigate the potential of a countrywide shortage. Blood-related devices, such as diabetic insulin pumps, are at the top of the agency's priority list.

Puerto Rico has more than 50 medical device facilities manufacturing upwards of 1,000 devices, according to Gottlieb, and some are the only facilities that manufacture a certain type of device. The agency has teamed up with about 10 manufactures on the island to restore production as quickly as possible, he said.

In rare cases, Gottlieb said, the FDA looks to imports to cover shortages. For example, Baxter, a manufacturer of IV solution bags, has drawn on its plants abroad to make up for production losses at its Puerto Rico facility. But for most products, imports cannot fill U.S. needs, he said.
— Gregory Roberts, Ana Mulero

FDA Clears First Medical Device Development Tool

A clinical outcome assessment questionnaire for measuring health outcomes reported by patients with congestive heart failure or weakened heart muscle became the first FDA-qualified medical device development tool.

Patients' answers to the Kansas City Cardiomyopathy Questionnaire can be used in a benefit-risk assessment to support new device submissions and post-approval studies, CDRH Director Jeffrey Shuren said in a blog post with Hilda Scharen, CDRH's director of medical device development tools.

The questionnaire includes 23 inquiries for patients' about their perceived health status, including the impact of heart failure symptoms on quality of life, as well as physical and social limitations.

The FDA's voluntary Medical Device Development Tools program is intended to facilitate finding measuring tools proven to be accurate, efficient and reliable to help streamline regulatory review processes. It also provides a collaboration mechanism for developers and manufacturers in the development and adoption of these tools, the FDA said.

There is no application fee and anyone can propose a tool for qualification under program, which consists of four phases. Two of those, the incubator phase and pre-qualification phase, are optional. It also includes three different development tool categories — clinical outcome assessment, biomarker test or nonclinical assessment model.

The FDA considers five factors when determining whether to qualify a development tool proposed under the program: the tool's description; the context of use; the public health impact; the strength of evidence; and the advantages and disadvantages.

FDA Commissioner Scott Gottlieb said the agency is undertaking a "comprehensive policy effort to facilitate the development and validation of these kinds of medical device development tools."

Gottlieb said the agency expects to qualify more tools in the near future. Wearable technologies, for example, have the potential to provide fundamentally better ways of measuring clinical outcomes, he said.

DHS Warns of Cybersecurity Risks In Boston Scientific Cardiac Systems

The Department of Homeland Security issued a warning about two security vulnerabilities in Boston Scientific's portable cardiac rhythm management systems.

All versions of the Zoom Latitude device are affected, and the vulnerabilities may allow hackers to obtain patients' health information, the DHS said.

Physical access is required for successful exploitation but even cyber attackers with a low skill level would be able to exploit the products' vulnerabilities.

The products communicate with patients' implanted pacemakers and defibrillators. They use a cryptographic key to encrypt patients' health information prior to having it transferred to removable media, but not while they are inactive.

BSC directed customers to maintain the devices in a secure location when they are not being used.

Sanofi Files Patent Infringement Suit Against Mylan Over Lantus Generic

Sanofi sued Mylan in the U.S. District Court for the District of New Jersey alleging the generic manufacturer infringed on 18 of its patents covering an insulin pen.

According to the complaint, Mylan notified the company last month of its NDA for an insulin glargine pre-filled pen and vial-drug that runs afoul of Sanofi's patents covering the branded insulin glargine products Lantus and Lantus SoloSTAR.

Sanofi said it received an offer of confidential access from Mylan for the NDA, but its efforts since then to obtain a copy of the NDA were fruitless.

Sanofi requested a discovery order for the NDA and an injunction to block Mylan using the 18 patents.

Read the full complaint here: www.fdanews.com/10-25-17-Sanofi.pdf.

12th Annual FDA Inspections Summit

An FDANEWS Conference

Nov. 1-3, 2017 • Bethesda, MD (Washington, DC)

The FDA has a new Commissioner, Scott Gottlieb, and everyone in the drug and medical device industry has heard all the talk about fewer regulations and efforts by the agency to use more "carrot" and less "stick." The approach typically changes whenever a new administration, and new Commissioner, take the reins.

But the FDA always — **always** — does inspections, and is forever looking for a way to do them differently and better. You can't afford to be caught off guard. Warning letters, 483 citations, and hits to your reputation can cost you time, energy and money!

Come to Washington, DC, Nov. 1-3, for the 12th Annual **FDA Inspections Summit**, the must-attend conference of the regulatory year from FDAnews. Here's where you:

Meet the FDAers whose actions spell fortune — or failure ... lawyers and consultants who fight for you ... industry hot-shots who've sussed out how to navigate a hyper-regulated milieu — *and still prosper.*

Discover how the reorganization of the ORA affects your specific products ... the metrics revolution that is pointing quality regulation in a new direction ... the new rules affecting postmarket adverse event reporting and cGMP ... how to deal with difficult inspections ... and *so much more*!

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Or call toll free: (888) 838-5578 (inside the U.S.) or +1 (703) 538-7600

PTAB Grants First Review Extension

In a first-of-its-kind ruling, the Patent Trial and Appeal Board extended the deadline to reach a final decision on an inter partes review of a medical device patent owned by Hologic.

Chief Judge David Ruschke's order to extend the deadline by up to six months came in light of the recent ruling in Aqua Products v. Matal.

The Aqua Products decision stated that the burden of convincing the PTO that any claim is unpatentable must fall on the challenging firm rather than the patent owner. This set a precedent that affects the burden of proof that the patent board applies and could affect the parties' argument, according to Ruschke.

Ruschke explained in the Oct. 5 court order that because of the potential impact of Aqua Products and limited amount of time for the board and parties to analyze the guidance provided in Aqua Products and apply it to this proceeding, the chief judge determined that good cause exists to extend the one-year period for issuing a final written decision.

In April 2016, Minerva Surgical requested a PTAB review of Hologic's patent 6,872,183, claiming "reasonable likelihood" that it is "unpatentable over the cited prior art." Hologic's patented devices provide ablation treatment of tissues in the interior linings of the uterus using a procedure in which fluid is introduced to inflate the uterus and perforations that could result in fluid leakage are detected using a pressure sensor.

Minerva Surgical used several patents issued prior to Hologic's to present the argument that "uterine ablation devices equipped with pressure sensors and having leak/perforation detection functionality were already well known and described in the prior art before the '183 patent." — Ana Mulero

Magellan Distributed Unapproved Testing Systems, FDA Says

The FDA sent an Oct. 23 warning letter to Magellan Diagnostics as part of an ongoing investigation based on data showing its blood lead testing systems provided false results.

An investigation at Magellan's manufacturing facility in North Billerica, Massachusetts was launched in May after the FDA issued a warning to the healthcare community not to use any of the firm's blood lead testing systems — LeadCare; LeadCare II; LeadCare Plus; and LeadCare Ultra — as they have provided results that are lower than the actual level of lead in the blood samples.

Magellan, a subsidiary of Meridian Bioscience, received a Form 483 after the FDA's May 10 through June 29 site inspection revealed several significant violations, including commercial distribution of two versions of its LeadCare systems with significant labeling modifications that had not received the FDA's approval or clearance, as well as failing to submit medical device reports to the agency within 30 days after becoming aware of the inaccurate test results.

The agency "is deeply concerned by this situation and is warning laboratories and health care professionals that they should not use any Magellan Diagnostics' lead tests," CDRH director Jeffrey Shuren, said in the May notice, adding that the agency is "aggressively investigating this complicated issue to determine the cause of the inaccurate results."

Magellan began notifying customers in 2014 of new incubation times for blood samples in an attempt to prevent the systems from underestimating lead values. The modifications were made after a study concluded that there is a "reproducible trend of increased [lead] signal with increased Sample/Treatment Reagent incubation time," which in turn raised an issue with the original intended use of the systems.

Although the labeling was cleared when it called for immediate analysis of the blood treatment

(See **Systems**, *Page 6)*

FDA Warns Pelvic Therapies To Cease Unapproved Activities

The FDA warned Pelvic Therapies in Carlsbad, California to "immediately cease activities" that resulted in the medical devices manufactured at its facility being adulterated and misbranded.

The agency issued a warning letter after agency officials concluded, in a review of marketing claims and materials available online, that its Essential TheraWand, Premium TheraWand, PelviWand-LA and PelviWand-V were introduced for commercial distribution without receiving the required approvals or clearances from the FDA.

The firm promoted several intended uses for the devices, such as for endometriosis and Crohn's diseases, that have not been evaluated by the FDA.

In addition, Pelvic Therapies did not fulfill the FDA's annual registration and listing requirements for fiscal year 2017. This has resulted in all of its devices being misbranded.

Pelvic Therapies was initially responsive to the CDRH's request for information but it refused entry when the Los Angeles District Office attempted a "for-cause" inspection, according to the warning letter.

Read the warning letter here: www.fdanews.com/10-24-17-PelvicTherapies.pdf.

Systems, *from Page 5*

reagent mixture, the company failed to submit to the FDA for evaluation of safety and effectiveness the added incubation times of 4 hours for its LeadCare II System and 24 hours for its LeadCare Ultra System.

The changes "could significantly affect the safety or effectiveness of the device and requires submission of a new 510(k)," the warning letter states.

Magellan was also cited for several other GMP violations, including inadequate risk analysis and complaint handling, and leaving multiple corrective actions open for "extensive periods without activity."

Read the warning letter here: www.fdanews.com/10-24-17-MagellanDiagnostics.pdf.

Patient Information Sharing May Enhance Engagement, FDA Says

Sharing information collected by medical devices with patients "may assist them in becoming more engaged with their healthcare providers in making sound medical decisions," the FDA said in guidance for device manufacturers.

The guidance, which follows on a 2016 draft, addresses cases in which patients request the information, such as pulse oximetry data, heart electrical activity and rhythms monitored by a pacemaker.

Although not required to do so by law, manufacturers generally may share such information without obtaining FDA clearance in advice, the agency said, and the information won't be subject to labeling regulations.

Read the guidance here: www.fdanews.com/10-27-17-MedicalDevices.pdf. — Gregory Roberts

PEOPLE ON THE MOVE

Endologix named **John Onopchenko** as chief operating officer. Onopchenko brings almost three decades of executive leadership experience in medical devices. Most recently, he served as executive vice president for Acutus Medical. Prior to that role, he was executive vice president and COO at Volcano Corporation. He previously spent 10 years at Johnson & Johnson, where he led medical device investments and was responsible for worldwide operations for advanced sterilization products.

Mauna Kea Technologies appointed **Olivier Regnard** as deputy chief executive officer and chief financial officer. Regnard brings nearly 20 years of finance, accounting and operational experience. Prior to joining Mauna, he served as deputy CEO and CFO at Latécoère. Previously, he spent nearly 15 years at Deloitte.

Synaptive Medical appointed **Peter Wehrly** as CEO. Wehrly brings more than 20 years of experience as a global executive. Synaptive Medical is a Toronto-based medical device and technology company.

IMDRF Clarifies When Authorities Can Share Confidential Information

The International Medical Device Regulators Forum released final guidance that lays out procedures for sharing confidential postmarket surveillance for medical devices among regulators.

The guidance covers criteria to be used for deciding when to exchange information, procedures to follow, requirements for IMDRF members participating in the National Competent Authority Reporting (NCAR) exchange program, and what forms to use for exchanging information.

The forum's National Competent Authority Report Working Group released the final guidance following the IMDRF meeting in September in Ottawa, Canada (*IDDM*, Oct. 2).

The guidance covers sharing information when there is a serious health threat associated with a medical device, defined as any event that results in imminent risk of death, serious injury or serious illness that requires prompt medical action. It further defines a serious injury as:

- A life-threatening illness or injury;
- A permanent impairment of a body function or permanent damage to body structure; or
- A condition necessitating medical or surgical intervention to prevent permanent impairment of body function.

The NCAR program will be used to exchange information relating to significant concerns or potential trends that individual authorities have observed in their jurisdictions but have not yet resulted in recalls or Field Safety Corrective Actions (FSCAs).

A trend noticed by an NCA is circulated when the frequency of the event associated with the device is significantly higher than the frequency recorded in the devicemaker's file or is significantly higher than the frequency observed with similar devices.

Examples of trends include the review of data from a national registry that indicates a potential concern regarding high revision rates such as hip prostheses for metal-on-metal implants. Other such trends could come from reviews of adverse event data and literature for a specific medical device.

An NCA may request or share information about a specific device or class of devices concerning:

- An event or events;
- An increased seriousness or frequency to what was previously reported;
- Major weaknesses and/or major deviations regarding a manufacturer's quality management system; and
- Regulatory status changes of a device.

Participation in the NCAR program will be limited to IMDRF Management Committee regulators from Australia, Brazil, Canada, China, Europe, Japan, Russia and the U.S.

Regulators who want to participate in the program must have confidentiality arrangements in place with other participating NCAs and the NCAR Secretariat.

The guidance notes that "none of the information in the NCAR may be released without the explicit authorization of the authoring NCA."

Read the NCAR guidance here: www.fdanews.com/10-24-17-IMDRFpostmarketguidance.pdf.

APPROVALS

FDA Issues Emergency Use Authorizations for Zika Testing Devices

The FDA issued two Emergency Use Authorizations for Zika virus in vitro diagnostic tests.

The EUAs follow a Health and Human Services determination last February that there is significant potential for a public health emergency involving the virus. The authorization applies to the TaqPath Zika Virus Kit, distributed by Thermo Fisher, and Columbia University's CII-ArboViroPlex assay.

Abbott Wins FDA Marketing Nod for Smartphone-Compatible Cardiac Monitor

The FDA cleared Abbott's launch of the Confirm Rx, first smartphone-compatible insertable cardiac monitor.

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

Approvals, *from Page 7*

Patients can connect the implant to their smartphone using Abbott's myMerlin mobile app to enable continuous monitoring of their heart rhythms. The device transmits data to a physician via the mobile app on a set schedule.

OptiScan Biomedical's OptiScanner 5000 Receives 510(k) Clearance

OptiScan Biomedical won 510(k) clearance for the OptiScanner 5000 glucose monitoring system.

The device monitors plasma glucose levels and determines dysglycemia in surgical intensive care unit patients. The bedside system enables physicians to manage patient glucose levels in the ICU.

The OptiScanner 5000 previously received CE Mark certification for use in the EU.

Viveve Wins Approval For Viveve System in Mexico

Viveve Medical received approval from the Mexican regulatory authority, COFEPRIS, to market its Viveve System. The device is used for treatment of vaginal introital laxity after childbirth.

The device has been cleared in more than 50 countries. The company plans to submit an investigational device exemption to the FDA to conduct a pivotal trial.

Medizone International Receives CE Mark For AsepticSure Disinfection System

Medizone International received CE mark approval for its AsepticSure disinfection system.

The system combines oxidative compounds (O3 and H202) to produce a mixture of free radicals (trioxidane) with much higher oxidative potential than ozone or hydrogen peroxide alone.

Medizone has released the system for use in Canada, and several other global markets.

Australia Approves Anika's Monovisc For Treatment of Osteoarthritis Pain

Anika Therapeutics was granted regulatory approval in Australia for Monovisc, its single injection viscosupplement for the treatment of pain associated with osteoarthritis of all synovial joints, including the hip and knee.

The device is already available in more than twenty countries, including the United States, Canada, and various European countries. It was recently approved in India and Taiwan.

Creavo Medical Secures 510(k) Clearance for Vitalscan

Creavo Medical Technologies received FDA 510(k) clearance for Vitalscan, a device used to scan for chest pain in patients.

The battery-powered, portable device uses magnetocardiography to scan at a patient's bedside to help physicians rule-out ischemic heart disease. Vitalscan displays and stores electromagnetic fluctuations caused by heart activity.

DarioHealth Gains CE Mark for iPhone-Compatible Smart Glucose Meter

DarioHealth received a CE Mark for its Dario blood glucose monitoring system.

The device is compatible with the iPhone 7 and iPhone 8.

The company is seeking approval for the device in the U.S., Canada, and Australia.

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JULIE LARSEN
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

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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 Counsel 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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