INTERNATIONAL DEVICES & DIAGNOSTICS MONITOR

Vol. 3, No. 35
Sept. 4, 2017

IN THIS ISSUE

FDA Unveils Spike in MDUFA Fees Effective Oct. 1

The FDA released user fee rates for fiscal 2018 including some significant increases and a new fee for de novo applications.

The standard fee for a premarket application is increasing from $234.495 to $310,764.

The newly established de novo classification fee will be $93,229 for standard applications and $23,307 for small businesses.

Registration fees, which must be paid in full prior to submitting any review requests, are increasing from $3,382 to $4,624. All domestic and foreign medical device establishments, including small businesses, must pay the registration fee.

Small businesses, defined as having gross sales not exceeding $100 million during the most recent tax year, qualify for reduced application

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

Cyber Risk Prompts Abbott Recall of 465K Pacemakers

In the first ever recall for a cybersecurity risk, Abbott recalled 465,000 implantable pacemakers for a firmware update to reduce the risk of unauthorized access. The update requires an in-person visit with a healthcare provider.

The company emphasized that there were no known reports of successful hacks and said hacking would involve "a highly complex set of circumstances."

The impacted radio frequency-enabled pacemakers (Accent, Anthem, Accent MRI, Accent ST, Assurity and Allure) were manufactured by St. Jude Medical, and St. Jude had been involved in a legal battle for about a year before its acquisition by Abbott in early January.

St. Jude was hit with a lawsuit from cybersecurity firm MedSec and investment firm Muddy Waters that issued reports in 2016 on the vulnerabilities to cybersecurity threats in the company's pacemakers and other cardiovascular devices. The vulnerabilities were later confirmed by the FDA and St. Jude later released patches to fix the problem.

Phase-in of New Device Regulations Extends Beyond Brexit

UK regulators have outlined the schedule for phasing in new European Union regulations on medical devices – although the UK will no longer be in the EU by the time the regulations take full effect.

The UK triggered the two-year Brexit process on March 29, setting the UK's departure from the EU for March 29, 2019. Negotiations are ongoing between the UK and EU about the post-Brexit regulatory structure.

The new EU Regulations for medical devices (MDR) and in vitro diagnostic medical devices (IVDR) regulations debuted on May 25, meaning that as of that date, devices can enter the market provided they comply with the new regulations, the UK's Medicines and Healthcare products Regulatory Agency said.

But companies can proceed to market under the previous regulations until May 26, 2020 for general medical devices and until May 26, 2022 for in vitro medical devices. After those dates, the new regulations will apply to all market entries in the respective device categories.

The new regulations for medical devices include new risk classification criteria, increased requirements for clinical evidence and changes to reporting schedules.

MDUFA, *from Page 1*

fees. The small business fee for a premarket application is increasing from $58,624 to $77,691. Requests for "small business" status must be submitted before Sept. 30, 2017. The agency released separate user fee guidance for small businesses.

All types of 510(k) applications, including traditional, abbreviated, and special, are subject to fees, but there is no user fee for 510(k)s submitted on behalf of an FDA-accredited third-party reviewer.

A standard panel-track supplement fee is increasing from $175, 871 to $233, 073, and a 180-day supplement fee will increase from $35, 174 to $46,615. For small businesses, the panel-track supplement fee is increasing from $43,968 to $58,268, and the 180-day supplement fee will be $11,654, up from $8,794.

Read the FDA's MDUFA IV user fee notice here: www.fdanews.com/08-31-17-UserFeeNotice.pdf.

Read the FDA device guidance for small businesses here: www.fdanews.com/08-31-17-deviceguidance.pdf. — Ana Mulero

MDUFA User Fees (Standard)

Application Type	FY 2018	FY 2017
510(k)	$10,566	$4,690
513(g)	$4,195	$3,166
De novo classification	$93,229	NA
PMA, PDP, PMR, BLA	$310,764	$234,495
Panel-track supplement	$233,073	$175,871
180-day supplement	$46,615	$35,174
Real-time supplement	$21,753	$16,415
BLA efficacy supplement	$310,764	$234,495
PMA annual report	$10,877	$8,207
30-day notice	$4,972	$3,752

MDUFA User Fees (Small Business)

Application Type	FY 2018	FY 2017
510(k)	$2,642	$2,345
513(g)	$2,098	$1,583
De novo classification	$23,307	NA
PMA, PDP, PMR, BLA	$77,691	$58,624
Panel-track supplement	$58,268	$43,968
180-day supplement	$11,654	$8,794
Real-time supplement	$5,438	$4,104
BLA efficacy supplement	$77,691	$58,624
PMA annual report	$2,719	$2,052
30-day notice	$2,486	$1,867

FDA Issues Guidance On Real-World Evidence

The FDA finalized guidance on the use of real-world evidence to support the agency's regulatory decisions on medical devices.

The agency will use the new criteria outlined in the guidance to determine whether real-world data meet its quality standards for decision-making, safety surveillance, and supplementing information gathered during clinical trials. More specifically, the agency may use real-world data for evaluating biomarkers, new indications, and de novo classification requests, among other potential uses.

Sponsors planning to collect real-world data from a device that is not being used in the normal course of medical practice may be required to obtain an investigational device exemption, the agency said.

An electronic health record is one example of a potential real-world data source. Because such sources are widely varied in terms of relevance and reliability, the sources should have certain characteristics before the data can be used as real-world evidence.

Quality assessments on real-world data will depend on the specific regulatory question. Among the many factors the FDA will consider when evaluating RWD are:

- Adherence to a common definitional framework for collecting key data points;
- Timeliness of data entry, transmission, and availability;
- The sources and technical methods used for data element capture; and
- Whether a common data capture form was used.

The agency has scheduled a webinar on Oct. 10 at 1:00 p.m. EST to review the guidance.

Read the guidance here: www.fdanews.com/08-31-17-NewFDAGuidance.pdf. — Ana Mulero

FDA to Accept IEC Standards in 510(k) Submissions for Diathermy Devices

The FDA issued draft guidance on compliance policies for 510(k) submissions for ultrasonic diathermy devices.

When the guidance is finalized, manufacturers conforming with the International Electrotechnical Commission (IEC) standards — IEC 60601-2-5 and IEC 61689 — will not have to comply with the radiation safety performance standards in 21 CRF parts 1010 and 1050.10, the agency said.

The change will help manufacturers avoid duplicate efforts. The agency acknowledged the advantages of a universal set of device-specific criteria and requirements and said conformance with certain IEC standards would provide at least the same level of protection of the public health and safety from electronic product radiation as the FDA performance standards for ultrasonic therapy products.

Class II ultrasonic diathermy devices are used to apply deep heat within a patient's body to treat conditions like muscle spasms and joint contractures. Not all medical devices that use ultrasound are included in the scope of the guidance. It applies only to devices employing ultrasonic 73 energy at a frequency beyond 20 kilohertz using a single plane circular transducer per treatment 74 head producing non-convergent beams perpendicular to the face of the treatment head.

Under the new guidance, the FDA will not have confirm a manufacturer's compliance with 21 CRF 1050.2 if it conforms to the identified IEC standards and include the following statement in device labeling:

"Complies with 21 CFR Subchapter J, except for conformance with IEC 60601-2-5 and 120 IEC 61689 instead of the performance standards in 21 CFR 1050.10. See for more 121 information FDA's guidance 'Policy Clarification and Premarket Notification [510(k)] 122 Submissions for Ultrasonic Diathermy Devices,' dated August 31, 2017."

Manufacturers choosing to comply with the IEC standards should include the information listed in the guidance in their 510(k) submissions.

Read the draft guidance here: www.fdanews.com/08-31-17-DiathermyGuidance.pdf.

Australia Issues Update On Medical Device Reform

Australia's Therapeutic Goods Administration released a status report on regulatory reforms for medical devices, including upcoming changes.

The first phase of the reforms — largely focused on assessment pathways — was passed by the Australian parliament in June. The overall goal of the reforms is to provide earlier access to new medical devices by increasing flexibility in the pre-market assessment processes, including a new expedited approval mechanism.

The reforms will also enhance post-market surveillance and "improve the integration of pre- and post-market activities," the TGA said.

Upcoming reforms for devices include:

- A single complaint handling function within TGA for advertising compliance;
- Enhanced sanctions and penalties related to advertising offenses;
- An expedited pathway for novel medical devices and designation of conformity assessment bodies in Australia to undertake medical device conformity assessment certification;
- Use of approvals from comparable overseas regulators to support listing on the Australian Register of Therapeutic Goods (ARTG); and
- Harmonization of medical device regulations to align with the EU medical device regulatory framework, which includes up-classification of surgical mesh from Class IIb to Class III and patient implant identification cards.

One of the biggest changes for devicemakers operating in Australia is the proposed conformity assessment pathway. Three new pathways are being proposed that would allow:

- Conformity assessments to be completed by a TGA-designated commercial body in Australia whereby the TGA would develop a model similar to that in the EU. These bodies would need to be located in Australia and would assess devices against Australian requirements;
- Using an overseas marketing approval for a device that has been assessed by a comparable overseas regulator or approved by a comparable overseas regulator (this is the way most devices are approved in Australia currently); and
- Expedited approval for novel medical devices in certain circumstances.

The agency anticipates releasing new guidance this month that would cover enhanced post-marketing compliance monitoring, additional evidence sources for de novo evaluation, use of international evaluation reports and assessment timeframes and fees.

Read the TGA report here: www.tga.gov.au/mmdr.

German Notified Body Extends Timeline For MEDDEV Rev. 4 Implementation

European notified body TÜV SÜD said the EU medical device regulation finalized May 5 includes specific clinical requirements that are not consistent with the MEDDEV 2.7/1 Rev. 4 guidance on clinical evaluations for device manufacturers and notified bodies.

In the 3-year transition to the new EU regulation, the Munich, Germany-headquartered group decided to extend the implementation timeline for the MEDDEV 2.7/1 Rev. 4 state-of-the art methods of clinical evaluation to May 25, 2020.

TUV SUD said the extension is only possible if the requirements on clinical evaluation and active post-market surveillance of the applicable directive MDD and/or Active Implantable Medical Devices Directive are fulfilled.

Three-year Transition

In the implementation timeline for MEDDEV 2.7/1 Rev. 4, from July 31, 2017 to May 25, 2020:

- Every submission can still follow the currently used methodology in the MEDDEV 2.7/1 Rev. 3 or another comparable method;
- Every submission shall include a plan for how to reflect the current state-of-the-art method for clinical evaluation (MEDDEV 2.7/1 Rev. 4 or another comparable method);
- Technical documentation shall either include a plan to implement state-of-the-art methodology — for example, in MEDDEV 2.7/1 Rev. 4 — or be part of a general plan by the manufacturer; and
- Every clinical evaluation report signed after May 26, 2020 shall reflect the current state-of-the-art method of clinical evaluation by either following the Rev. 4 of MEDDEV or another comparable method.

Although not legally binding, the EU MEDDEV guideline promotes a common approach for EU notified bodies to undertake conformity assessments for CE marking.

Medical device manufacturers are already facing significant hurdles in the EU because of tougher clinical data requirements and the steep drop in the number of notified bodies available to approve medical devices for sale in the EU.

Higher standards under the EU's MDR have cut the number of notified bodies significantly, and more are expected to drop out this year. Waiting lists for product approvals are now longer, and some CE marks have been suspended without warning or have not been renewed in time, according to Gert Bos, executive director and partner at Qserve Group in the Netherlands.

The remaining notified bodies are becoming more strict in granting CE marks, he said. This is in part because MEDDEV 2.7.1guidelines published last year were meant to align with provisions in the MDR and provide general principles for clinical evaluations and have introduced more thorough pre- and post-market data collection requirements.

High-risk products under the new MDR must be supported by the manufacturer's own pre-market data for the device under review. The data also must be gathered from real-world use instead of focus groups. According to Bos, more than 90 percent of devices currently marketed in the EU might not currently meet these requirements.

The MDR requires post-market clinical data for currently marketed devices, as well as a plan to generate such data for any new product being launched. This requires manufacturers to implement new procedures for lifecycle management and traceability.

"The window of opportunity is closing" as the MDR is being implemented, and notified bodies are getting more and more selective in terms of which manufacturers they choose to work with," Bos said.

Another important change is that these notified bodies are now focusing on full compliance to the legal requirements instead of looking for sufficient evidence on conformity, he said.

"In the transfer to the EU MDR and IVDR, there will not be any harmonized standard in the

(See **Deadline***, Page 6)*

Judge Rules Case Against St. Jude Defibrillators Can Go Ahead

A federal judge ruled St. Jude may not dismiss a patient's allegations over manufacturing-defects and negligence related to the company's implantable cardiac defibrillator (ICD) in a case filed with the U.S. District Court for the Northern District of California.

In an Aug. 23 court order, Judge Edward J. Davila concluded there was sufficient evidence for a "plausible connection" between the identified manufacturing defects related to the Riata Leads and the patient's injuries.

The patient alleged he underwent cardiovascular surgery to have St. Jude's Riata Leads implanted in 2003, 2007 and 2015, and in November 2016, he "was shocked an estimated sixteen to twenty times, causing irreparable harm to his heart, body, and mind" when the leads malfunctioned as he slept.

An internal audit St. Jude conducted in 2005 on malfunctioning Riata Leads concluded that the defibrillators had "potentially serious insulation problems." The FDA issued a Form 483 several years later flagging the company for potential violations.

However, it wasn't until 2010 that St. Jude identified the problems with its ICDs in a "Dear Doctor" letter, which was reclassified by the FDA a year later as a product recall. Failures associated with lead insulation abrasion on the St. Jude Riata and Riata ST Silicone Endocardial Defibrillation Leads may cause the conductors to become externalized, the agency said. "If this occurs, the product may cause serious adverse health consequences, including death."

Read the court order here: www.fdanews.com/08-31-17-StJudeCourtOrder.pdf. — Ana Mulero

Deadline, *from Page 5*

early days, so the conformity assessment cannot use the presumption of conformity via use of standards as is widely practiced," he said.

Notified bodies will find it harder to disagree with the various agencies' recommendations. "The essence of the notified body work will not change, but the reality might well find more black and white strict interpretations" (*IDDM*, July 10).

Read the TÜV SÜD notice here: www.fdanews.com/08-29-17-TUVSUD.pdf.

483 Roundup: FDA Cites Three Device Firms for CAPAs, Complaints

The FDA issued Form 483 reports to three devicemakers over inadequate CAPAs, complaint handling and other deficiencies.

Michael D. Williams: A Florida device specification developer lacked adequate CAPA procedures, complaint files and sampling plans, according to the FDA.

The FDA issued a Form 483 to Michael D. Williams' Davie, Florida, facility following a June inspection. According to investigators, the office's CAPA procedures lacked requirements for ensuring information on quality problems was properly transmitted to those responsible for ensuring quality.

The office also left key information out of complaint files, including device names, dates complaints were received, and complainant addresses and phone numbers. More than 600 complaints of 1,089 logged between November 2014 and June 2017 did not specify the nature and details of the complaint.

The agency also hit the company on its design control procedures, noting the procedures failed to ensure that ensure the design addresses the intended device use.

The company had no procedures for quality audits or purchasing control, and did not keep records of its evaluation of label printers or package suppliers. The firm's sampling plans for its device mouthpiece fit testing was not based on a statistical rationale, and the facility lacked written procedures to control labeling activities.

The company also had no written procedures for re-packaging or document approval.

Biolife: Florida-based Biolife drew a Form 483 with four observations following a June 2017 FDA inspection. The investigator flagged the Sarasota facility's inadequate design change documentation and medical device reporting procedures.

The firm had failed to report information from customer complaints to the FDA that appeared to meet the definition of adverse events, the agency said.

The facility also lacked procedures for corrective and preventive actions, and the firm failed to take appropriate action to prevent the recurrence of quality problems. One CAPA initiated for out -of -specification results during calibration of equipment, said the equipment had been out of tolerance for a fourth consecutive year.

Healthline Medical Products: The FDA flagged Healthline Medical Products for six deficiencies identified in a June 2017 inspection of the firms' facility in Winter Garden, Florida, including CAPA problems, complaint investigations, product specifications, supplier evaluations, and device history records.

The FDA inspector found inadequate CAPA documentation of CAPA procedures. For example, the firm failed to validate corrective actions taken in response to a complaint involving a shower chair device that was determined to have been damaged during shipment. The corrective actions included training employees to use the proper amount of packaging material and developing a new package insert to caution users to inspect devices for damage upon receipt.

In addition, the firm's records of complaint evaluations did not consistently include all the relevant details of the4 complaint and the investigation.

The facility also failed to ensure that all purchased products and services conformed to specifications and the evaluation of potential suppliers was not documented.

Finally, the facility's device history record did include all device labeling. For example, the records did not refer to the package insert on cleaning instructions or to the insert covering inspection of the device for damage.

Read the Biolife Form 483 here: www.fdanews.com/08-31-17-biolifellc.pdf.

Read the Healthline Medical Products Form 483 here: www.fdanews.com/08-31-17-healthlinemedicalproductsinc.pdf.

Read the Michael D. Williams Form 483 here: www.fdanews.com/08-31-17-michaeldwilliamsddspa.pdf. — Zack Budryk and Ana Mulero

APPROVALS

Malin Corporation Wins Marketing Clearance for Peripheral Embolization Plug

Malin Corporation secured 510(k) clearance for its Hourglass Peripheral Embolization Plug.

The device enables accurate, stent-like delivery, allowing physicians to securely deliver the plug for immediate occlusion of the blood vessel. It is already approved in Europe.

FDA Approves Abbott's HeartMate 3 Implantable Pump

Abbott received 510(k) clearance for the HeartMate 3 implantable pump for heart failure patients awaiting a transplant.

The approval is the latest for the HeartMate line of left ventricular assist devices first developed by Thoratec. Thoratec was brought to Abbott in a $25 million merger earlier this year after they were acquired by St. Jude Medical.

The device features magnetic levitation in the pump's impeller, resulting in less trauma to blood cells as they pass through. The device won CE Mark approval in the European Union in October 2015.

Regentis Biomaterials Gets Expanded CE Mark for GelrinC

Regentis Biomaterials received an expanded CE Mark in the European Union for its GelrinC hydrogel-based resorbable treatment for focal cartilage defects in the knee, covering GelrinC products manufactured using denatured human fibrinogen.

The approval expands on previous approvals clearing versions of the device manufactured using denatured bovine-sourced fibrinogen. The GelrinC implant is designed to naturally degrade within 6 to 12 months as it's replaced by cartilage.

FDA Approves Tandem's Insulin Pump

Tandem Diabetes Care received FDA approval of its t:slim X2 Insulin Pump with Dexcom G5 Mobile continuous glucose monitoring integration.

The device is the first sensor-augmented insulin pump approved to let users make treatment decisions without pricking their finger.

The pump's software will also be available to current t:slim X2 Pump users at no cost.

C.R. Bard Lands Additional Indication For Drug-Coated Balloon Catheter

C.R. Bard received premarket approval from the FDA for its drug-coated balloon CTA catheter for a new indication for end-stage renal disease.

The device is the first and only drug-coated balloon approved for ESRD patients with stenotic lesions. The device was previously approved for treatment of superficial femoral artery and popliteal artery disease.

Medtronic Gets CE Mark For Left Heart Lead

Medtronic has received a CE Mark for its Attain Stability Quad MRI SureScan Left Heart lead in Europe. The device works with the company's quadripolar cardiac resynchronization therapy-defibrillators (CRT-D) and CRT-pacemakers (CRT-P).

The unit features a helix that works like an anchor to secure the lead, adapting to the anatomy of each individual patient. The device is currently undergoing a clinical trial in the U.S.

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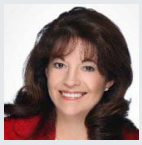
JULIE LARSEN
Senior Partner, Director Inspection Readiness Services, BioTeknica

FDA SPEAKERS:

ELLEN MORRISON
Associate Commissioner, OMPTO, ORA, FDA



ROBIN NEWMAN
Director, Office of Compliance CDHR, FDA (Invited)

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

DANA CORRIGAN, J.D.
Associate Commissioner, Office of Global Regulatory Operations and Policy, OC, FDA (Invited)

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

MARK BROWN, Partner, King & Spalding

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

No More 483s - QSIT Secrets to Assure Clean Inspections

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

Recently, a top FDA investigator — in a candid moment — said "I'm still amazed I can go to a firm and they haven't read the QSIT guide."

After 18 years, too many devicemakers ignore the Quality System Inspection Techniques (QSIT) Guidance to their peril.

FDAnews is proud to have QSIT expert Julie Larsen, Principal/Director, Inspection Readiness Services at BioTeknica, provide her secrets for using the QSIT's details to assure your next inspection is squeaky clean.

Julie knows the QSIT guidance, and how to apply it, to device companies of all sizes and all product classes. In just four hours, you'll learn the hidden traps inside this important inspection technique and several take-away ideas you can put to immediate use.

This interactive workshop will dive deep into these key issues:

- How to use 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
- Best industry tools for internal audits

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 QSIT 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

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

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

Dara Corrigan, J.D., Associate Commissioner, Office of Global Regulatory Operations and Policy, OC, FDA (Invited)

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

Mark Brown, Partner, King & Spalding

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

Robin Newman, Director, Office of Compliance, CDRH, FDA (Invited)

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.)

Day 1 Agenda (cont.)

THURS., NOV. 2

- 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: Julie Larsen, Principal/Director, Inspection Readiness Services, 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

Day 2 Agenda

FRI., 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 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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