INTERNATIONAL DEVICES & DIAGNOSTICS MONITOR

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IN THIS ISSUE

Judge Dismisses All Claims In Medtronic Securities Suit

A federal judge in Minnesota has thrown out remaining charges against Medtronic in a securities case involving allegedly false statements about the bone graft treatment Infuse and a second-generation product, Amplify.

Citing statute of limitations issues, U.S. District Judge John Tunheim told the institutional investor plaintiffs that he would grant Medtronic's motion for summary judgment on their remaining claims, dismissing them with prejudice.

The West Virginia Pipe Trades Health & Welfare Fund, Employees' Retirement System of the State of Hawaii and Union Asset Management Holding, AG, brought their lawsuit in 2013 in the U.S. District Court for the District of Minnesota, alleging that Medtronic's false statements about Infuse and promises about Amplify artificially inflated the company's stock prices.

(See **Medtronic**, *Page 2)*

Steris, Synergy Shareholders to Vote On Merger in Wake of FTC Defeat

Shareholders of Steris and UK-based Synergy Health voted in favor of their proposed merger last Friday following a court's refusal to stop the deal over the objections of the Federal Trade Commission.

The votes followed a decision issued Sept. 24, in which Judge Dan Polster of the U.S. District Court for the Northern District of Ohio refused to issue a temporary restraining order and preliminary injunction halting Mentor, Ohio-based Steris' proposed acquisition of Synergy, indicating that he thought X-ray sterilization, the process at the heart of the FTC's case, isn't ready for the U.S. market.

In a short statement issued Oct. 1, the FTC said it has decided not to appeal the district court's decision.

Last October, Steris — which offers gamma irradiation, ethylene oxide sterilization and laboratory services for devicemakers

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Their complaint also named several company executives, but claims had been dropped against all except ex-CEO Bill Hawkins. The remaining claim against him stemmed from a third quarter 2011 earnings call, when he was asked whether the FDA was going to delay its approval of Amplify and if that would negatively affect Infuse sales.

According to the plaintiffs, Hawkins responses falsely suggested that he didn't know the approvability status of Amplify, even though the FDA had sent a letter before Jan. 28, 2011, saying the product wouldn't be approved. In a March 9, 2011, 10-Q filing, Medtronic disclosed that the FDA had sent it a non-approval letter for Amplify.

The plaintiffs also accused Medtronic of manipulating early clinical studies of Infuse and obfuscating adverse events associated with the product. In June 2011, the company had faced tough questions from members of the U.S. Senate following reports that doctors investigating Infuse did not report dangerous adverse events in patients who received the device. A report on the investigation found that Medtronic had ghostwritten and edited journal articles by physician consultants on Infuse. These consultants received royalties and consulting fees from the company.

Further, an analysis in *The Spine Journal* found 13 Medtronic-sponsored studies reported no adverse events with Infuse. The journal calculated the adverse event rate as being between 10 percent and 50 percent.

According to court documents, Medtronic submitted filings to the U.S. Securities and Exchange Commission admitting that the journal's analysis could have an impact on future sales. The company's stock experienced a one-day decline of about 3 percent and dropped even more the next week.

Statute of Limitations

As Tunheim notes in court documents, there is a two-year statute of limitations on securities claims cases, and the clock starts ticking when plaintiffs discover evidence constituting a violation.

He barred the claim against Hawkins, stating the plaintiffs didn't file by March 9, 2013 — exactly two years after the SEC filing disclosed that the FDA would not approve Amplify.

Although the plaintiffs maintained that Medtronic had not raised this defense with this specific charge, Tunheim disagreed. He also ruled they had plenty of time to file against Medtronic for hiding clinical trial results, but they had missed that cut-off point as well. — Elizabeth Hollis

FDA Issues Safety Advisory Following Brain Injury Reports

The FDA is advising healthcare professionals to strictly follow the instructions for using for cranial perforators with automatic clutch mechanisms following reports of more than 200 injuries related to their use.

A cranial perforator is designed to stop drilling automatically after penetrating the skull to prevent the tip from plunging into the patient's brain. However, failure to follow the manufacturer's instructions can result in the clutch mechanism not engaging, leading to an adverse patient event.

Between January 2005 and August 2015, more than 300 medical device reports associated with use of the perforators were filed. Injuries include perforation of the brain's protective covering just beneath the skull, bleeding, brain contusion, cerebral tissue damage and decreased function of the brain.

Patients have experienced seizures, damage to the portion of the brain responsible for language, delayed or prolonged hospital stays and the need for additional procedures.

The communication doesn't single out a specific manufacturer or brand of device; rather, it emphasizes the need to strictly follow the instructions for use to ensure proper use.

The safety communication is available here: www.fdanews.com/10-05-15-cranial-communication.pdf. — Elizabeth Hollis

U.S. Government Averts Shutdown As Budget Negotiations Loom

President Barack Obama signed a measure last week to fund the federal government at fiscal year 2015 levels through Dec. 11, averting a government shutdown.

The measure easily passed the Senate by a 78 to 20 vote and the House by a vote of 277 to 151. The funding provision was part of H.R. 719, a transportation bill.

The president and lawmakers have nine weeks to avoid a shutdown and work out a longer-term budget deal through the fiscal year ending Sept. 30, 2016.

In event of a shutdown, an FDA contingency plan provided for limited activities related to user fee-funded programs.

The agency also would have maintained certain critical activities, such as emergency consumer protection, enacting high-risk recalls, civil and criminal investigations and import entry review. — Kellen Owings

NICE: Evidence Does Not Back Routine Use of Blood Tests

The UK's healthcare costs regulator has decided not to back three new blood tests that are intended to speed the identification of bloodstream bacteria and fungi for routine use in the National Health System.

In draft documents published last week, the National Institute for Health and Care Excellence says too much uncertainty exists over whether Roche Diagnostics' LightCycler SeptiFast Test Mgrade, Molzym Molecular Diagnostics' SepsiTest and Abbott Diagnostics' Iridica BAC BSI assay could offer additional clinical benefits.

The tests are intended to identify pathogens that could lead to sepsis. Patients suspected of having sepsis are given high-potency antibiotics; however, widespread — and potentially unnecessary — use of these products has led to increased fears of antimicrobial resistance.

Carole Longson, director of NICE's Center for Health Technology Evaluation, acknowledges that having tests to identify pathogens in hours rather than days could prove beneficial for patients in heading off sepsis. She adds that these tests could offer clinical advantages, but the committee couldn't assess the size of the benefits, and further study may be required.

One sticking point for NICE was the applicability of the clinical outcome studies to the UK; for the most part, these assessments were conducted in Europe, and the U.S. Clinical specialists told the body that even though sepsis treatment is based on international guidelines, outcomes, including duration of a patient's stay in the intensive care unit, usually can't be extrapolated to the UK due to variances in antibiotic prescribing practices around the world.

In terms of obtaining results, NICE officials were told that the shorter turnaround times seen in studies may not be replicated in real-world experience, unless a molecular service is available 24 hours a day.

Comments on the draft guidance will be accepted through Oct. 21. Specifically, the committee wants input on the following questions:

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence? and
- Are the provisional recommendations sound, and a suitable basis for guidance to the NHS?

A second NICE advisory committee will meet Nov. 4 to discuss comments received and further examine the initial findings.

The consultation document is available here: www.fdanews.com/100515-NICE-Consult.pdf. – Elizabeth Hollis

Steris, *from Page 1*

and other industries — announced its intention to buy UK-based Synergy for $1.9 billion in cash and stock, citing it as a way to accelerate international growth.

As the deal moved forward, Synergy said it was abandoning plans to bring X-ray sterilization to the U.S. Currently, the only two sterilization processes are gamma and e-beam.

Synergy's X-ray method could have proven highly disruptive to the U.S. market, which has two major players — Steris and larger rival Sterigenics. Combined, those two companies account for about 85 percent of all U.S. contract sterilization services.

The addition of Synergy could have given Steris and unfair advantage, the FTC has maintained, adding that the two abandoned the X-ray plans only after the commission began investigating the tie-up. While Steris and Synergy have maintained that using X-ray was not a sound financial strategy, the FTC has disagreed.

Polster determined that the two companies were right to worry.

"The evidence … shows that, despite Synergy's best efforts to advance the X-ray project, news on the economic front worsened," according to court documents.

For example, in January 2015, IBA, a company providing equipment for the X-ray sterilization process, priced its equipment at about $6 million — more than 25 percent of the capital cost for one facility. The price was more than Synergy had anticipated. "The evidence shows that, despite Synergy's best efforts, it was unable to harness the capital costs to build x-ray facilities in the United States. Synergy has only $25 [million] to $40 million per year to spend on capital projects. The cost of building two x-ray facilities was estimated to be well over that budget," Polster says.

In addition, customers the FTC had cited as interested in X-ray may not have been as keen about the business model as the commission believed.— Elizabeth Hollis

Wanted: Applicants for French Health Advisory Committees

France's Agence nationale de sécurité du medicament et des produits de santé is looking for external experts to help assess the benefits and risks of health products, including medical devices.

Committee members will be tasked with updating existing risk management plans, reassessing risks and benefits of products, monitoring medical devices, initiating market halts and implementing preventive measures to help minimize the risks associated with using health products.

The committee will have 18 members, to include:

- Four medical device professionals with therapeutic competence;
- Seven professionals with expertise in pharmacovigilance, medical devices, pharmacoepidemiology, toxicology, clinical biology, hospital engineering or social science;
- Three experts in general medicine;
- One dispensing pharmacist;
- One hospital pharmacist; and
- Two representatives from healthcare system user associations.

Those interested may send an application package detailing their expertise, a letter with their public health background, resume and list of publications by email to candidatures.experts@ansm.sante.fr until Oct. 31.

To minimize the risk of conflict of interest, candidates must waive or give up any personal compensation from companies, institutions or organizations whose activities fall within the committee's scope. Further they, must disclose any potential conflicts of interest from the last five years at each meeting. They also may not serve as a principal investigator in preclinical or clinical trials involving a product that could fall under the committee's purview.

Read an overview in French of the committees and their responsibilities here: www.fdanews.com/10-05-15-ANSM-form.pdf. — Elizabeth Hollis

Industry, Regulators Examine Shared View of Risk Strategies

What are the barriers holding stakeholders back from having a shared view of risk? That question was at the heart of discussions held during a summit co-convened last week by the Association for the Advancement of Medical Instrumentation and the FDA.

One issue is the sheer number of interconnected medical devices in hospitals. As Alan Lipschultz, president of HealthCare Technology Consulting, warned, many stakeholders continue to evaluate products in isolation.

"One must be cognizant of the ecosystem your product is being used in," he said, emphasizing that companies should remember that other devices will be added to the system, thus adding risks.

Also while employees should be trained to be risk managers for all devices, many institutions have established barriers. Employees may get training on certain technology, but the institutions will not allow them to use that equipment.

In addition to training, stakeholders identified the need to coalesce around a common terminology for risk. As standards, the FDA, clinicians and medical device professionals have different definitions for common terms.

Indeed, "severe injury," "where appropriate" and "state-of-the-art" have been defined differently by various stakeholders. Causing confusion is the different definitions of risk in pre- versus postmarket settings.

The lack of a common terminology can lead to delayed decision-making, an unnecessary focus on definitions and an excuse for people to not do the tough work of risk management.

Risk management also is important when making changes to a device. The following changes can have a particular impact on public safety:

(See **Summit**, *Page 6)*

Summit, *from Page 5*

- Intended design changes;
- Manufacturing process changes;
- Manufacturing material changes;
- Transportation route changes;
- Supplier changes;
- Change in intended use;
- Change in intended users;
- Software bugs fixes;
- Field services actions; and
- Removal of a product from the field.

When asked who should have the responsibility for tackling the challenges facing risk management, attendees named top executives within the organization.

These executives should ensure that risk management is incorporated throughout the product lifecycle.

The meeting, held just outside Washington, D.C., attracted roughly 200 attendees from government, academia, the medical device industry and healthcare delivery organizations.

It marked the seventh time AAMI and the agency have joined forces on a summit focusing on a problem confronting HDOs and the medical device industry.

A report detailing the summit's findings is slated to be released later this year. — Elizabeth Hollis

Bard to Take Over Full Ownership of Medicon JV

Murray Hill, N.J.-based C. R. Bard has agreed to take over full ownership of a Japanese joint venture that it has operated with Kobayashi Pharmaceutical since 1972.

As a result of the agreement, the Osaka-based Medicon JV will become a wholly owned Bard subsidiary. Medicon sells Bard urology products and vascular stents, among other items, in Japan. Kobayashi sells pharmaceutical products in Japan and markets consumer products, such as heat therapy patches, in the U.S.

The deal is expected to close next month, with Kobayashi receiving about $25.1 million. It will receive additional payments over the next decade, for a total of $93.6 million.

Bard Chairman and CEO Timothy M. Ring says the transaction will allow his company to enhance its presence in Japan, the third largest healthcare market in the world, particularly as growth opportunities there evolve. — Elizabeth Hollis

FDA Issues Call for Consumer Representatives

Consumer groups wanting to select members for FDA advisory panels are being asked to indicate their interest.

According to a *Federal Register* announcement published Oct. 1, the FDA wants members for the following panels of the Medical Devices Advisory Committee:

- Anesthesiology and Respiratory Therapy Devices Panel;
- Circulatory System Devices Panel;
- Dental Products Devices Panel;
- General and Plastic Surgery Devices Panel;
- General Hospital and Personal Use Devices Panel;
- Hematology and Pathology Devices Panel;
- Molecular and Clinical Genetics Panel;
- Neurological Devices Panel;
- Obstetrics and Gynecology Devices Panel; and
- Ophthalmic Devices Panel.

The agency will accept nominations through Dec. 31. Parties may submit their statements of interest in the selection process by email to kimberly.hamilton@fda.hhs.gov.

Consumer representative nominations may be submitted through a portal at www.accessdata.fda.gov/scripts/FACTRSPortal/FACTRS/index.cfm.

The *Federal Register* announcement is available here: www.fdanews.com/100515-nominees-advisory.pdf. — Elizabeth Hollis

Agency Puts Communications, Device Inspections at Center Stage

When communicating with FDA staff, it is vital that sponsors respond to agency questions during the timeframe requested, or they risk getting a hold letter with additional requests.

Sergio de del Castillo, acting *de novo* policy analyst within the Center for Devices and Radiological Health's Office of Device Evaluation, offered that advice during the two-day FDA Small Business Regulatory Education for Industry meeting, which took place last week in Silver Spring, Md. "If you are not willing to work with them in that regard, we will be forced to take other options," he cautioned attendees.

Del Castillo told the audience that company representatives discussing their products with agency staff should be ready to tell their stories, clearly explaining to reviewers why the device is safe and effective.

He also touched on Q-submissions, which are used for pre-submissions, informational meetings, study risk determinations, formal early collaboration meetings, submission issue meetings and PMA day 100 meetings. He emphasized that it is important for devicemakers to demonstrate that they have listened to agency review staff and considered their suggestions.

"It can be frustrating to the reviewer to take the time to have the dialog, and [he or she gets] the premarket application, and it looks [as if] you have not incorporated the feedback that we have given," he emphasized. He tells devicemakers who include those suggestions to be sure to flag those sections in the submission. Those who have not should be prepared to explain why.

Del Castillo said he has fielded many questions on how often members of industry should contact agency staff. He instructed that while they may be anxious about their submissions, FDA staff members also have competing priorities.

He added that companies may face pages and pages of questions from agency staff during the interactive review process. That process is intended to allow for increased informal interaction between the FDA and applicants, with an eye toward preventing unnecessary delays in the application's review. The FDA is not trying to intimidate companies with all of these questions, he said, but is aiming for transparency in a bid to obtain information in an orderly manner.

Inspections

Marc Neubauer, a medical device specialist at the FDA's Baltimore District Office, provided an overview of what medical device companies should expect during inspections.

He said companies have false assumptions when an inspector comes to their door. For example, some contract manufacturers believe the agency doesn't have the authority to inspect them, and that is not the case.

"No two FDA inspectors are alike," Neubauer said, so a company can get zero observations during one inspection and 10 the next. It very much depends on the experience of the investigator.

To minimize any potential investigation surprises, Neubauer advised companies to do the following in the five days ahead of an inspection:

- Make sure you're registered;
- Locate your listings;
- Coordinate document retrieval — if it is off-site, this will give you a chance to gather what you need;
- Obtain resources for the inspection, flying in support staff, if necessary;
- Review procedures, documents, open CAPAs and file MDRs; and
- Perform a complete makeover of your quality systems.

When asked what a firm may do if it disagrees with observations made during an inspection, Neubauer said companies may challenge the findings. If the observation remains on the Form 483, the firm may challenge it. Neubauer advised them to separate that observation from the rest of the findings. If the firm is judged to be correct, the FDA will send it an annotated 483. — Elizabeth Hollis

Tornier-Wright Merger Takes Major Step Forward

The Federal Trade Commission has agreed to the sale of Tornier's U.S. rights and assets related to its total ankle and total silastic toe joint replacements to Integra Lifesciences. The move came ahead of a vote by Wright Medical Group and Tornier to combine.

The pair announced last month that they would sell rights to these orthopedic devices to Integra, as the FTC had maintained that the proposed $3.3 billion merger would reduce competition for these products.

Under a proposed order, which will be open for public comment until Oct. 30, Wright and Amsterdam-based Tornier will supply Integra with the ankle replacements for up to three years and the toe joint replacements for one. Integra also will receive the intellectual property, manufacturing technology and existing inventory under the FTC proposal.

Following the closure of the comment period, the FTC will make its final decision on the deal. The companies expect to close the merger by the end of the year.

According to an FTC analysis, Wright and Tornier dominate the total silastic big toe joint replacement market, holding 60 percent and 38 percent, respectively.

There is more competition in the total ankle replacement market, with Wright, Tornier, and Stryker accounting for 44 percent, 19 percent and 31 percent of 2014 sales, respectively.

At least one analyst sees the combined company, which will be known as Wright Medical Group N.V., as an attractive target in the long term. "[W]e believe the new Wright will prove quite compelling from a takeout perspective to one of the larger orthopedic players and eventually find a suitor," writes Ben Andrew with William Blair & Company Equity Research.
— Elizabeth Hollis

Peru Unveils Update to Device Registration Requirements

Peruvian health officials have amended regulations related to medical devices in a move that could prove beneficial for foreign and domestic manufacturers.

The Dirección General de Medicamentos, Insumos y Drogas, Peru's medical device regulator, officially released a notice last month detailing the rules, including how manufacturers should make changes to their sanitary registration.

"Changes in medical devices with sanitary registration are classified in minor and major changes, according to the level of risk to the people's health or their impact on the quality, safety and efficacy of the medical devices," explains Maritza Reátegui-Valdiviezo, senior partner at Muñiz, Ramírez, Pérez-Taiman & Olaya.

For minor changes to the registration, companies need to send a notice to the country's Autoridad Nacional de Productos Farmacéuticos, Dispositivos Médicos y Productos Sanitarios and implement the change within six months. If a major change is made, the company needs to send an application justifying the adjustment, as well as documentation backing up its request.

Reátegui-Valdiviezo,adds that minor changes would include a new company name, address of the sanitary registration holder, a different technical director or an updated taxpayer number.

Other minor complementary changes and major changes will be specified in a corresponding guideline pending with the Autoridad Nacional de Productos Farmacéuticos, Dispositivos Médicos y Productos Sanitarios

Reátegui-Valdiviezo, tells *IDDM* that the changes will prove beneficial to industry. "It facilitates the commercialization of the products, bearing in mind that products or devices with characteristics other than those authorized by DIGEMID may not be put in circulation." She adds that sanctions for marketing a device with a different label than the one approved have been lowered from $12,000 to $3,600. — Elizabeth Hollis

BRIEFS

Boston Scientific Launches Captivator

Boston Scientific has begun marketing its Captivator endoscopic mucosal resection device, a minimally invasive alternative to esophagectomy. The device enables the staging and removal of precancerous tissue and early esophageal cancer in the upper gastrointestinal tract in an outpatient setting. The Marlborough, Mass., devicemaker also has enrolled the first patient in a multicenter postmarket registry aimed at studying the Captivator's use in removing abnormal tissue growth in Barrett's Esophagus, a common precursor to cancer.

Medtronic Snaps Up Lazarus Effect

Device giant Medtronic has acquired Lazarus Effect, a producer of acute ischemic stroke products used to capture and remove clots, in an all-cash transaction valued at $100 million.

Lazarus Effect manufactures a technology that complements Medtronic's Solitaire stent retriever platform. The device, dubbed the Lazarus Cover, received CE mark approval in November 2014. Regulatory approval in the U.S. is pending.

FDA Greenlights Hearing Aid

The FDA has given its blessing to a new hearing aid that uses a laser diode and direct vibration of the eardrum to amplify sound. Developed by Menlo Park, Calif.-based EarLens, the contact hearing device is intended for adults with mild to severe sensorineural hearing impairment. It differs from traditional hearing aids in that the tympanic membrane transducer component is custom-molded to the patient's eardrum and contains a driver mechanism that directly stimulates the membrane.

FDA Approves Bayer's Betaconnect

The FDA has signed off on Bayer HealthCare's Betaconnect, an electronic autoinjector for the treatment of relapsing-remitting multiple sclerosis. The device offers customizable injection speed and depth settings. Betaconnect will be available in early 2016 for patients taking Betaseron, a drug used to reduce relapses in people with relapsing forms of the disease.

Merck, Pfizer to Collaborate With Dako

Pharmaceutical giants Merck and Pfizer will work with Agilent Technologies' Dako unit, with an eye on developing a companion diagnostic test. The agreement enables the companies to develop the test to assess programmed death-ligand 1 protein expression levels in tumor tissue, along with its microenvironment. The test is part of the protocols in ongoing clinical trials of avelumab, an investigational immune checkpoint inhibitor.

Neuravi Unveils Stroke Device

Galway, Ireland-based Neuravi has launched the EmboTrap revascularization device for the treatment of acute ischemic stroke. The device will be marketed through the sales and distribution network in Belgium, Denmark, Finland, France, Germany, Ireland, Italy, the Netherlands, Norway, Spain, Sweden and Switzerland. The device is designed to retrieve and retain clots while restoring blood flow to the brain. It is not approved in the U.S.

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An interactive workshop presented by
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"Companies must provide truthful and accurate information in their marketing applications…The American public expects and deserves no less."
— Janet Woodcock, M.D., Director, CDER

FDA Data Integrity

From Data Creation to Long-Term Archive

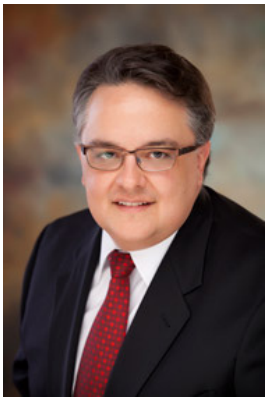
Dec. 8-9, 2015

Embassy Suites Raleigh-Durham Airport/Brier Creek • Raleigh, NC

FDA data integrity requirements are among the most strenuous that regulated industries have to comply with. Your electronic records must be trustworthy and reliable across their entire data lifecycle — from initial data creation through long-term archival.

In the FDA Data Integrity workshop you will learn the following:

- The types of data integrity violations identified during recent FDA inspections
- FDA expectations for review of electronic laboratory data
- What actions to take if data integrity concerns are identified within your company or at a contractor
- What is really required by the FDA, EMA, Health Canada and other regulating agencies
- How to quickly parse warning letters for data integrity expectations
- FDA investigator tactics and questions to expect about your data integrity
- The eight practical elements of data integrity
- What to look for when conducting quality audits of data integrity
- How to map your data flow
- How to incorporating data integrity compliance into the day-to-day operations
- How to qualify record and archival storage vendors
- How to develop a media migration strategy



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"John takes on complicated regulation and breaks it down into easily managed steps and projects applicable to any company."
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"John is not only a subject matter expert, he is also a great speaker. He understands how to keep the audience engaged by encouraging their participation. Thumbs up to John."
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FDA Data

From Data Creation t

Dec. 8-9, 2015 • Embassy Suites Raleigh-

WORKSHOP AGENDA

DAY ONE
TUESDAY, DEC. 8, 2015

8:30 a.m. – 9:00 a.m.
REGISTRATION & CONTINENTAL BREAKFAST

9:00 a.m. – 9:15 a.m.
INTRODUCTION AND WELCOME

9:15 a.m. – 10:45 a.m.

I. **Data Integrity: What's Really Required?**
   - a. Core regulatory requirements — FDA, EMA, Health Canada and more
   - b. Overlooked guidances — what you don't know will hurt you
   - c. How to quickly parse warning letters for data integrity expectations
   - d. FDA investigator tactics and questions about your data integrity
   - **e. Interactive Hands-On Exercise:** Attendees act as FDA investigators in different company types to find the data integrity controls FDA expects during an inspection

10:45 a.m. – 11:00 a.m. REFRESHMENT BREAK

11:00 a.m. – 12:00 p.m.

II. **Suppliers and Data Integrity: Who's Actually Accountable?**
   - a. FDA's view — accountability versus responsibility
   - b. Dealing with your regulated data at critical suppliers
   - c. Contractual components to address data integrity risks
   - d. Handling SaaS providers, hosted IT systems and cloud computing
   - e. Managing data integrity with CROs and outsourced clinical sites
   - f. Overseeing data integrity at your CMO and contracted services
   - g. Addressing data from suppliers of raw materials
   - **h. Interactive Hands-On Exercise:** Attendees act as FDA investigators to review the data integrity controls from several case study companies have in place over their suppliers — should the sponsor/purchaser get a warning letter?

12:00 p.m. – 1:00 p.m. LUNCH

1:00 p.m. – 2:15 p.m.

III. **Practical Realities: The Business Costs of Poor Data Integrity**
   - a. Real world business costs of poor data integrity
   - b. Legal pitfalls for senior management from poor data integrity
   - c. Practical quality costs of poor data integrity
   - **d. Interactive Hands-On Exercise:** Attendees review several case studies to determine costs and dangers of poor data integrity

2:15 p.m. – 2:30 p.m. REFRESHMENT BREAK

2:30 p.m. – 4:30 p.m.

IV. **Critical Data Integrity Elements to Prove Compliance**
   - a. Eight practical elements of data integrity (ALCOA+ in practice)
   - b. Narrowing the scope
   - c. Risk-based data integrity controls — a simplified approach
   - d. Verifying data integrity controls at suppliers
   - e. Qualifying personnel — from CV to training
   - f. Defining roles and responsibilities
   - g. Conducting quality audits of data integrity — what to look for and why
   - h. Monitoring, metrics and communication
   - i. Policies and SOPs to consider
   - j. Scanning, true copies and source data
   - **k. Interactive Hands-On Exercise:** Using case studies, attendees identify likely risks and select the most appropriate controls for each situation

4:30 p.m. – 5:00 p.m.

V. Day One Wrap Up and Review
   - **a. Interactive Hands-On Exercise:** Attendees identify 3 compelling reasons for their own company to adopt data integrity controls now

DAY TWO
WEDNESDAY, DEC. 9, 2015

9:00 a.m. – 9:15 a.m.
WELCOME AND QUICK LEARNING RECAP

9:15 a.m. – 10:30 a.m.

VI. **Modern Validation Protocol**
   - a. Validation by risk level — it's all about the data
   - b. Sampling and test cases — FDA's view
   - c. FDA's view of supplier-provided validations
   - d. Taking advantage of the traditional DQ\IQ\OQ\PQ format
   - e. Example FDA-"approved" test cases for data integrity-based validation
   - **f. Interactive Hands-On Exercise:** Attendees review case study validation tests to see if data integrity is actually being verified

10:30 a.m. – 10:45 a.m. REFRESHMENT BREAK

10:45 a.m. – 12:00 a.m.

VII. **Mapping Your Data Chain-of-Custody**
   - a. Data mapping defined
   - b. Steps to map your data flow across the data lifecycle
   - c. Benefits to mapping your chain-of-custody — business and the FDA
   - **d. Interactive Hands-On Exercise:** Work in teams to data map a sample data flow from several case studies (one cGCP and one cGMP)

12:00 p.m. – 1:00 p.m. LUNCH

1:00 p.m. – 2:15 p.m.

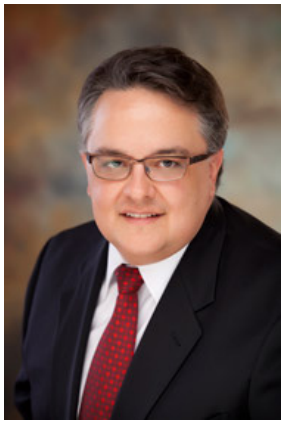
VIII. **Advanced Tactics to Cut Costs and Reduce Your Workload**
   - a. Change management — from preapproved to emergency
   - b. Containing costs with cross-functionality
   - c. Incorporating data integrity compliance into the day-to-day operations of departments and supervisors
   - d. Creating a site master data integrity compliance plan
   - e. Data integrity governance
   - **f. Interactive Hands-On Exercise:** Draft a communication to be sent out by

Integrity

o Long-Term Archive

Durham Airport/Brier Creek • Raleigh, NC

MEET YOUR INSTUCTOR



John Avellanet is an award-winning FDA compliance expert known for his business-savvy, pragmatic advice and engaging speaking style.

Mr. Avellanet was the lead author of several certification courses on Good Manufacturing Practices (GMP) and Quality System Regulation (QSR) supplier management for the US Regulatory Affairs Professional Society.

Last year he co-authored the book *Pharmaceutical Regulatory Inspections* with several current and former regulatory agency officers, and his industry classic, *Get to Market Now! Turn FDA Compliance into a Competitive Edge in the Era of Personalized Medicine*, was featured highlight of BIO 2011.

Prior to founding his lean compliance consulting firm, Cerulean Associates LLC, Mr. Avellanet was a former Fortune 50 combination device C-level executive who created, developed, and ran his company's compliance programs to achieve ISO, DEA, BIS and FDA compliance. During his career, he had to defend decisions to investigators, auditors, and litigators alike. He now brings his hard-won, real-world expertise and practical advice to his corporate clients worldwide. A former FDA and US Department of Justice prosecutor has said of Mr. Avellanet, "He is the best in the business. Period."

your senior team to all company employees about good data integrity that will actually lower your workload and encourage self-compliance

2:15 p.m. – 2:30 p.m. REFRESHMENT BREAK

2:30 p.m. – 3:30 p.m.

IX. **Data Integrity, Recordkeeping and Archival Controls**
   a. Records to retain to prove good data integrity controls
   b. Basics of bit rot and other risks to archived data
   c. Developing a media migration strategy
   d. Qualifying record/archival storage vendors
   e. Interactive Hands-On Exercise: Attendees work in teams to outline a sample set of data integrity controls and auditing plans for several case study companies

3:30 p.m. – 4:00 p.m.

X. **Building Your Business Case for Defensible Data Integrity**
   a. Quick tips for talking to senior management about data integrity
   b. A sample data integrity action plan — nine brainstorming questions
   c. Interactive Hands-On Exercise: Attendees work with the expert instructor to draft their own personal, business case and prioritized plan for implementing a data integrity control framework at their company

4:00 p.m. – 4:30 p.m.

XI. Wrap Up and Final Questions

4:30 p.m.

XII. Adjournment

YOUR COURSE MATERIALS

Each participant will receive a folder and flash drive packed with tools and reference materials in a combination of both electronic and hard copy format you can put to use right away, including:

- Presentation slides
- A set of detailed handouts including examples and hands-on exercises
- Two sample policies – ready for you to implement now
- One sample SOP and form – ready for immediate implementation
- Eight sample checklists – ready for you to use right away
- Two quick guides and templates – ready for you to use immediately
- And more….

WHO WILL BENEFIT

- Executive management
- Regulatory affairs
- Quality assurance/quality control
- Legal and compliance officers
- Clinical research directors
- Consultants/service providers
- CAPA specialists
- Compliance information managers
- GMP compliance officers
- GMP training managers
- Heads of internal audits
- QA documentation managers
- QA/QC managers and directors
- Quality systems managers
- Systems analysts
- Training personnel

FDA Data Integrity

From Data Creation to Long-Term Archive

Dec. 8-9, 2015 • Embassy Suites Raleigh-Durham Airport/Brier Creek • Raleigh, NC

HOTEL RESERVATIONS

To reserve your room, call the hotel at the number below. Be sure to tell the hotel you're with the FDAnews Workshop to qualify for the reduced rate. Only reservations made by the reservation cutoff date are offered the special rates, and space is limited. Hotels may run out of discounted rates before the reservation cutoff date. The discounted rate is also available two nights before and after the event based on availability. Hotel may require first night's room deposit with tax. Room cancellations within 72 hours of the date of arrival or "no-shows" will be charged for the first night's room with tax.

DATES/LOCATION:

Dec. 8-9, 2015
Embassy Suites Raleigh-Durham Airport/Brier Creek
8001 Arco Corporate Drive
Raleigh, NC 27617
Toll Free: (800) EMBASSY
+1 (919) 572-2200
www.RaleighDurhamAirportBrierCreek.EmbassySuites.com
Room rate: $179.00 plus 12.75% tax
Reservation cut-off date: Nov. 20, 2015

TUITION

Tuition includes all workshop sessions, workshop written materials, two breakfasts, two luncheons and daily refreshments.

CANCELLATIONS/SUBSTITUTIONS

Written cancellations received at least 21 calendar days prior to the start date of the event will receive a refund -- less a $200 administration fee. No cancellations will be accepted -- nor refunds issued -- within 21 calendar days from the start date of the event. A credit for the amount paid may be transferred to any future FDAnews event. Substitutions may be made at any time. No-shows will be charged the full amount. In the event that FDAnews cancels the event, FDAnews is not responsible for any airfare, hotel, other costs or losses incurred by registrants. Some topics and speakers may be subject to change without notice.

TEAM DISCOUNTS

Significant tuition discounts are available for teams of three or more from the same company. You must register at the same time and provide a single payment to take advantage of the discount. Call +1 (703) 538-7600 for details.

FOUR EASY WAYS TO REGISTER

Online: www.fdanews.com/FDADataIntegrity
Fax: +1 (703) 538-7676
Phone: Toll free (888) 838-5578 (inside the U.S.)
or +1 (703) 538-7600
Mail: **FDAnews,** 300 N. Washington St., Suite 200
Falls Church, VA 22046-3431 USA

☐ **YES!** I want to attend **FDA Data Integrity: *From Data Creation to Long-Term Archive*** I understand the fee of $1,797 includes all workshop sessions, workshop materials, two breakfasts, two luncheons and daily refreshments.

FDANEWS
300 N. Washington St., Suite 200
Falls Church, VA 22046-3431

(Please see "Team Discounts" above for tuition discounts when you send a team of three or more.)

Attendee 1: Name _____ Title _____ Email _____

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