INTERNATIONAL DEVICES & DIAGNOSTICS MONITOR

Vol. 3, No. 33
Aug. 21, 2017

IN THIS ISSUE

Conservative Groups Ask Congress To Block Return of Medical Device Tax

Congress should permanently wipe out the suspended Affordable Care Act tax on medical devices scheduled to resume Jan. 1, a coalition of conservative groups said in a letter to House and Senate leaders.

The letter, signed by the representatives of 36 groups, led by anti-tax crusader Grover Norquist of Americans for Tax Reform, said the tax impairs the industry's ability to "innovate, invest, and create jobs."

Under the 2010 health law, the 2.3 percent excise tax on medical devices went into effect on Jan. 1, 2013. But in December 2015, Congress imposed a two-year moratorium on the tax, for 2016-17, as part of a consolidated spending measure (*IDDM*, April 14).

The tax applies to medical devices such as X-ray equipment, MRI machines, surgical instruments and pacemakers, but not to products such as eyeglasses, hearing aids and wheelchairs typically retailed to individual consumers. Its repeal enjoys bipartisan support.

Read the full letter here: www.fdanews.com/08-16-17-Devicetax.pdf. — Gregory Roberts

China's High Court Pushes for Severe Penalties for Falsifying Device Clinical Trials

China's high court called for severe criminal punishments for deliberately falsifying medical device clinical trial reports and other related documents, issuing a judicial interpretation that takes effect Sept. 1.

The Supreme People's Court of China specified the interpretation would apply to non-clinical research institutions, clinical trial institutions, contract research organizations and their staff, and that submitting false documents to the Chinese Food and Drug Administration would constitute material fraud.

In addition, the use of fraudulent drug approval documents in the production and sale of fake drugs — as well as deliberate use of

(See **China**, *Page 2)*

Good News, Bad News for BD: OK On Lead Tests, But Other Problems

The FDA said it could find no evidence that tubes made by Becton Dickinson for Magellan Diagnostics' blood lead-level testing devices contributed to inaccurate readings from the devices, which Magellan had suggested as a cause.

But the agency cited several other problems discovered in an inspection of BD's plant in Franklin Lakes, New Jersey earlier this year.

"We have not determined that the BD tubes or any other brand of tube is linked to the cause of the inaccurate lead test results," Alberto Gutierrez, director of CDRH's office of IVDs and radiological health. "We are continuing to aggressively investigate the matter."

The FDA said the inspection is not a final determination that the tubes are not responsible for the inaccurate results.

The FDA issued a warning on May 17 that Magellan's LeadCare test systems may have yielded results indicating lower levels of lead than the actual levels in the blood. Magellan had earlier advised its customers that the errors may have been due to design changes in BD blood collection tubes.

The FDA investigation of BD's New Jersey plant cited the company for inadequate validation and documentation procedures related to device design and for shortcomings in reporting and investigating complaints and malfunctions.

Among those shortcomings were failures related to BD's response to the issues that prompted the May warning, the FDA said, in is Form 483 report.

"Information received by your firm in May 2015, identifying potential complaint information for K2EDTA tubes possibly contributing to the suppressing of lead values in blood, was not investigated, evaluated and documented formally in your complaint handling database," the report said. "To date, the information has not been translated into your complaint system."

In a finding that BD workers lacked training to do their jobs, the report said, "Specifically, troubleshooting/complaint information related to technical issues with your firm's K2EDTA tubes in the detection of lead poisoning was relayed from another manufacturer to your firm via email in 2015. This information was not forwarded for review and evaluation by your designated complaint handling unit, nor was it documented with your formal complaint handling software."

Read the BD inspection report here: www.fdanews.com/08-18-17-BD483.pdf. — Gregory Roberts

China, *from Page 1*

the drug in non-clinical and clinical studies — would also carry strict punishments, the court said, naming five years' imprisonment, fines and provisions for heavier penalties.

In a statement, the CFDA said the measure will be a powerful deterrent to application materials fraud. The interpretation also included pharmaceutical studies, data and registrations.

The high court's judicial interpretation, in Chinese, is available here: www.court.gov.cn/zixun-xiangqing-55952.html. — Conor Hale

Minnesota Judge Throws Out Devicemakers' IP Dispute

A federal judge threw out an intellectual property dispute between two medical device manufacturers and ruled that all still-live claims must be tried in India.

In its complaint, India-based Phoenix Cardiac Devices accused Minnesota-based Mardil of running afoul of the two devicemakers' August 2012 IP license agreement, under which both companies were to develop their own independent cardiac device based on Mardil's intellectual property.

Phoenix argued the other devicemaker filed a reissue application in January 2014 for a patent involving Mardil's VenTouch device and involving uses Mardil agreed were off-limits during the non-compete period, which was effective through August 2015.

In an Aug. 14 ruling, Judge Michael J. Davis of the United States District Court for the District of Minnesota noted the U.S. Patent and Trademark Office did not actually grant a reissue of the patent, and no patent meeting the definition of "intellectual property" under the contract covers the device.

Davis concluded all remaining issues should be resolved by arbitration in India, where the unit Phoenix is suing is based.

Read the full judgment here: www.fdanews.com/08-15-17-minnesota.pdf. — Zack Budryk

Five Deaths from Obesity-Treatment Balloons Prompt New Labels

Two manufacturers of liquid-filled balloons for obesity treatment have revised their labeling to include warnings of the risks.

The FDA approved the two systems in 2015. They are designed to aid weight loss by taking up space in the patient's stomach. The Obera devices are filled with a saline solution, and the ReShape devices are filled with saline and dye.

The agency said it could not yet identify the root cause or positively attribute the deaths to the devices or their insertion procedures, and said it will continue working with the two companies to resolve the issue.

In an Aug. 10 safety alert, the FDA repeated recommendation for providers to closely monitor obesity patients who have received internal medical placements of liquid-filled balloons implicated in the deaths of five people since 2016.

The FDA reported that four of the deaths involved the Obera Intragastric Balloon System, manufactured by Apollo Endo Surgery, and the fifth involved the ReShape Integrated Dual Balloon System, made by ReShape Medical.

Three of the deaths occurred in one to three days after placement, and the FDA said it has not definitely established if those deaths occurred because of the balloon devices or from complications from the insertion procedures. The agency said two other deaths were attributed to complications — a gastric perforation in an Obera patient, and an esophageal perforation in a ReShape patient.

In February, the FDA wrote providers to alert them to reports of two types of adverse events associated with the balloons. In some patients, the balloons overinflated with air or more liquid in their stomachs; in others, patients developed acute pancreatitis.

Read the FDA alert here: www.fdanews.com/08-14-17-Obesityballoons.pdf. — Gregory Roberts

India Sets Price Controls For Knee Implants

Health authorities in India have imposed price caps on orthopedic knee implants.

The price for cobalt chromium implants, used in four-fifths of knee-replacement surgeries in India, will go down 65 percent on average under the new regulations, Indian media reported.

In announcing the caps, the National Pharmaceutical Pricing Agency referred to "unjustified, unreasonable and irrational" markups on the implants, leading to "exorbitant" prices.

The NPPA earlier this summer imposed price caps on cardiac stents.

Sweden Issues Guidance On Notified Bodies

Sweden's Medical Products Agency issued guidance on the new EU procedures for appointing a notified body that will go into effect on Nov. 26. The agency promised to issue further updates when there's "more clarity around notified bodies in the EU."

The agency flagged three documents released by the EU's Notified Body Operations Group (NBOG), including a draft list of documents to be submitted in an application for designation as a notified body, and a list of codes and types of devices to specify the scope of a notified body designation for medical devices and for IVDs.

The NBOG recently posted separate application forms on its website for submissions by conformity assessment bodies applying for designation as a notified body under the medical devices Regulation (MDR) or under the in vitro diagnostic devices regulation (IVDR).

The draft list of documents includes general and organizational requirements, quality management requirements, resource requirements, and process requirements for the proposed notified body.

The draft list of codes and types of devices for notified body designation for medical devices includes:

- Active implantable devices;
- Active non-implantable devices for imaging, monitoring and/or diagnosis;
- Active non-implantable therapeutic devices and general active non-implantable devices;
- Non-active implants and long-term surgically invasive devices;
- Non-active non-implantable devices; and
- Technologies for medical devices.

The draft list of codes and types of devices for in vitro diagnostic devices includes IVDs intended to be used for:

- Blood groups;
- Tissue typing;
- Cancer markers;
- Human genetic testing;
- Determining markers of infectious diseases and immune status;
- Screening or confirming a specific disease;
- Defining or monitoring physiological status and therapeutic measures;
- Quantitative or qualitative assigned values; and
- Sterile laboratory and clinical uses and IVDR manufacturing technologies.

As part of the EU regulatory overhaul, all notified bodies will be re-designated and required to have documented procedures regarding unannounced on-site audits of manufacturers and, when applicable, subcontractors and suppliers.

Notified bodies will also notify competent authorities when they grant certificates for high-risk devices, and the authorities may request additional information from notified bodies (*IDDM*, May 12).

Read the Medical Products Agency notice here: www.fdanews.com/08-15-17-Swedennotifiedbodies.pdf.

PEOPLE ON THE MOVE

Ra Medical Systems appointed cardiologist **Maurice Buchbinder** and veteran electronics industry executive and venture capitalist **Martin Colombatto** to its board of directors. The company manufactures cardiovascular and dermatology catheters and excimer lasers.

Voxello, a developer of communication solutions for hospitalized patients, named **Clareece West** and **Chuck Peters** as directors. West has served for more than 28 years in leadership roles in clinical operations, regulatory, data management, safety, sales, marketing, mergers and acquisitions, and restructuring. She is currently general manager and vice president of the regulatory science business unit within the specialty solutions division at Cardinal Health. Peters is currently chairman of Folience, an Iowa-based holding company.

483 Roundup: FDA Flags Six Device Firms for GMP, Other Deficiencies

The FDA found a wide range of GMP and other violations during inspections of six devicemakers.

Medtronic: Medtronic failed to inspect incoming deliveries of parts before including them in the production of insulin infusion pumps at the company's plant in Northridge, California, the FDA said.

The company received shipments of molded polycarbonate sleeves, used to provide spacing between the casing of insulin pumps and their drive motors, since November 2014 and automatically released them uninspected for use in production under the company's "dock to stock" system, the agency said, in a Form 483 issued following a March inspection.

In addition, a company inspector certified the parts had been inspected on one form and, on another, noted none were, the FDA said.

Similar dock-to-stock treatment was accorded to other lots of items repackaged and relabeled by Medtronic for infusion-pump production. The facility also received 100 spools of spring wire and sampled just one for inspection, 12 short of the required number, the agency said.

The company also could not find one lot of infusion pump belt clips that its tracking system said was awaiting inspection. Initially, the company said the clips had been moved to production. Later, it said they were included in an engineering evaluation, but there were no supporting records.

Medtronic also failed to establish adequate procedures for storing materials and equipment, mingling parts headed to the scrap heap with others approved for use, the agency said.

Nytone Medical Products: A Utah manufacturer of bedwetting alarms failed to spell out requirements its suppliers must meet and to establish a design-change procedure, the FDA said in an inspection report.

The company, Nytone Medical Products, also had not documented the corrective actions it had taken in response to complaints, and had not verified the effectiveness of those actions, the FDA said.

The findings concerning supplier requirements and design-change procedures are repetitions of inspection results from 2009 and 2014, the FDA said.

Burke: A Kansas manufacturer of bariatric hospital beds, air mattresses, wheelchairs and scooters was cited by the FDA for documentation and procedural lapses.

The company, Burke Inc., mishandled customer complaints and suggestions, the agency said. The reports of complaints and suggestions were not dated consistently, and were not evaluated to determine if an investigation was needed, the agency said.

The company also failed to establish assembly procedures for several of its products. In addition, the facility's supplier records were incomplete, the agency said.

Integrity Systems: The FDA dinged Integrity Systems for incomplete records, inadequate process validation and software problems.

The agency issued a Form 483 report after a May/June inspection of the devicemaker's Olive Branch, Miss., facility. Device history records did not demonstrate the devices were made in accordance with device master records in at least three cases.

Investigators also found the firm's procedures did not address documentation and monitoring of processing times for all processes or document the processing times.

In addition, the facility failed to validate the software it used for management of inventory and documentation of quality system records.

Casco Manufacturing Solutions: Casco Manufacturing Solutions landed a Form 483

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

483s, *from Page 5*

from the FDA for problems with device master records, document control procedures and equipment maintenance.

The FDA issued the form following a May/June inspection of Casco's Cincinnati facility. According to investigators, the company did not have established DRMs for its birthing bed device, it had no established procedure for changes to quality documents such as procedures and forms, and updates to such documents included no description of the changes.

The documentation also did not follow the company's own quality records procedure, with multiple corrections made using white-out.

Lastly, the company did not establish a maintenance schedule for one of its devices. The facility's director of operations told investigators that blades in the machine were switched out weekly but that process was not defined or documented.

Turbo Wheelchair: The FDA cited Turbo Wheelchair for failure to maintain device master records, complaint files or MDR procedures.

The agency issued a Form 483 following an April/May inspection of the firm's Louisville, Ky., facility. The company had no device master records for three of the five devices it manufactured, and the records it did maintain failed to reflect current specifications.

The company also did not maintain adequate device history records. The manufacturing records the company president provided consisted of only a checklist to aid in assembling the devices, with no specifics for labeling or DMR compliance.

The firm also had no quality systems and procedures or overall quality plan, and lacked procedures for accepting incoming materials or evaluating suppliers. According to the company president, no contracts or agreements existed with service providers or suppliers. Moreover, the firm had no written CAPA procedures or procedures for handling service operations.

Lastly, according to the FDA, the firm had no procedures for medical device reporting, nonconforming products or for rework.

Read the Medtronic Form 483 here: www.fdanews.com/08-11-17-medtronicinc483.pdf.

Read the Nytone Form 483 here: www.fdanews.com/08-11-17-nytonemedicalproductsinc483.pdf.

Read the Burke Form 483 here: www.fdanews.com/08-11-17-burkeinc483.pdf.

Read the Integrity Systems Form 483 here: www.fdanews.com/08-16-17-integritysystemsllc483.pdf.

Read the Casco Form 483 here: www.fdanews.com/08-16-17-cascomanufacturingsolutionsinc483.pdf.

Read the Turbo Wheelchair Form 483 here: www.fdanews.com/08-16-17-turbowheelchairincinc483.pdf. — Gregory Roberts and Zack Budryk

Australia's TGA Issues Guidance On Pre-Submission Meetings

Australia's Therapeutic Goods Administration is urging devicemakers to meet with the agency before submitting conformity assessment applications.

The agency said it highly recommends pre-submission meetings for novel devices and devices used for urogynecological procedures. The meetings are most beneficial for new or emerging technologies, novel medical devices, combination products and medicines with a companion diagnostic.

Pre-submission meetings can provide a common understanding of what supporting documentation is needed to evaluate an application as well as resolve any issues before the application is submitted, the TGA noted, in the update to its 2013 guidance.

The updated guidance introduces numerous changes covering applications for conformity assessments for medical devices.

The agency clarified that it can offer advice on concerns companies have relating to existing studies of a proposed data package, but it does not address issues that require evaluation of data and it does not give advice on developing a data package or on the number of studies required to support an application.

Devicemakers wishing to request a pre-submission meeting should submit a meeting request form and say whether they want a teleconference, videoconference or a meeting in person. Companies should tell the agency who will be attending, including consultants and their titles. Requests for meetings should allow at least four weeks advance notice but not more than two months, the agency said.

Companies should submit a briefing package two weeks before the meeting to allow the agency time to analyze data, including:

- An agenda;
- A summary of relevant information for the device;
- Any supplementary information relevant to the objectives of the meeting, such as questions for the TGA;
- Summaries describing results of relevant studies, development plans that deviate from current guidelines or practices;
- Any issues with the study design or evidence required; and
- Meeting presentation with a full set of slides scheduled to be presented at the meeting.

No new material should be presented during the meeting that is not included in the full briefing package, the guidance says. If important new information becomes available within the preceding two-week period, companies should send an updated presentation to the TGA at least 48 hours before the scheduled meeting.

After the meeting, the agency will provide a summary of the agreed outcomes and any action items. Devicemakers should include a copy of the final meeting record in the application dossiers for TGA conformity assessment certificate submissions.

Read the TGA guidance here: www.fdanews.com/08-15-17-TGAmeetings.pdf.

APPROVALS

FDA Approves New Zika Assay

The FDA issued an emergency use authorization for a PCR assay for detection and differentiation of RNA from Zika virus, dengue virus, chikungunya virus, and West Nile virus in serum, and for the detection of Zika virus RNA in urine.

The CII-ArboViroPlex rRT-PCR assay was developed by Columbia University's Center for Infection and Immunity.

The assay is intended for use with specimens collected from individuals with clinical signs and symptoms associated with Zika virus infection or a history of residence in or travel to a region with active Zika transmission at the time of travel, or other epidemiological criteria.

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

Approvals, *from Page 7*

Camber Spine Technologies Wins FDA Clearance for Spinal Implant

Camber Spine Technologies received 510(k) clearance from the FDA to market its SPIRA Open Matrix ALIF spinal implant devices.

The implants are indicated for use in skeletally mature patients with degenerative disc disease. The 3D-printed devices increase fusion rates and spinal stabilization.

The series, including five SPIRA spinal interbody cages for cervical, lateral, and posterior lumbar spine, will be released in the U.S. in the coming months.

Glytec Receives 510(k) Approval for Diabetes Management Software

Glytec announced its fourth FDA 510(k) clearance, adding additional capabilities to its Glucommander diabetes management system.

The latest approval encompasses a titration module for inpatients undergoing enteral nutrition, an insulin-to-carb ratio titration option for outpatients, more flexible messaging for dose adjustments, and improved workflow capabilities.

The company claims the platform delivers safety improvements and annual savings as high as $20,000 per licensed acute care bed.

Apple Wins Patent For Electronic Health Data Monitor

Apple secured a patent for an electronic health data device, indicating the company's continued interest in medical devices.

The device computes health data using sensors and electronic interfacing with the user's body parts. It uses a camera, a proximity sensor, an ambient light sensor and a processing unit to track measures ranging from blood pressure index and pulse rate to oxygen saturation.

The patent award follows reports that the company has plans for a noninvasive blood sugar monitor. It is collaborating with glucose monitoring company Dexcom to integrate glucose sensors with Apple watches.

FDA Clears Renovis' Fifth Titanium Structure Implant System

Renovis Surgical has secured FDA 510(k) clearance for its 3D-printed titanium interbody fusion systems.

The system includes direct posterior or transforaminal implants of multiple widths, heights and lengths. Renovis previously received FDA clearance for four other porous titanium structure product groups.

The technology allows bones to attach to implant surfaces and have the potential for biologic fixation deep into the pore structure.

iCubate Blood Infection Assay Gets FDA Clearance

The FDA cleared iCubate's iC-System and blood infection assay for marketing.

The iC-System is the firm's first approved assay, based on technology developed by the company to detect several pathogens at once and identify potentially pathogenic bacteria or resistance markers.

The system and assay provide test results as much as 48 hours earlier than conventional tests, the company said.

FDANEWS

Customer Service
(888) 838-5578 • +1 (703) 538-7600
customerservice@fdanews.com

Editorial: Declan Conroy
+1 (703) 538-7644
dconroy@fdanews.com

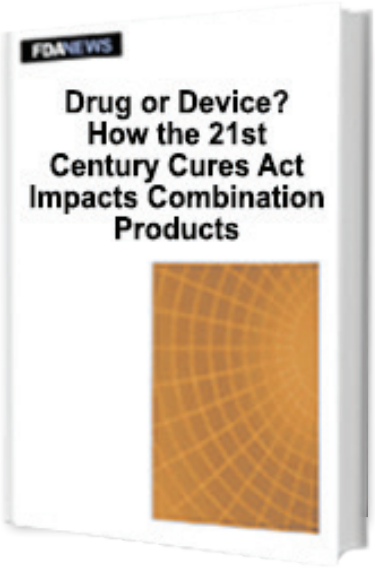
Ad Sales: Jim Desborough
+1 (703) 538-7647
jdesborough@fdanews.com

Multi-User Sales: Jeff Grizzel
+1 (703) 538-7669
jgrizzel@fdanews.com

300 N. Washington St., Suite 200 • Falls Church, VA 22046-3431 • Phone: (888) 838-5578 • +1 (703) 538-7600 • www.fdanews.com

Reporters: Conor Hale, Zack Budryk, Gregory Roberts

President: Cynthia Carter



Drug or Device? How the 21st Century Cures Act Impacts Combination Products

Combination products remain one of the most difficult regulatory challenges for life sciences innovators.

Which FDA Center has the lead?

Will I need one marketing application or two?

Will I need a drug to be cross-labeled and approved for use with my device?

These and many more questions can make combination product sponsors feel like they are entering an unforgiving regulatory labyrinth.

The 21st Century Cures Act requires the FDA — over the next several years — to issue guidance that will create a structured process and best practices for managing the development and reviews of drug/device/biologic combinations. The law provides for a streamlined approach to GMP for combination products similar to what the agency has recently announced through rule and guidance.

Drug or Device? How the 21st Century Cures Act Impacts Combination Products takes a close look at the FDA's new authority governing combination products, as well as several new provisions under the 21st Century Cures Act that could usher in a new era of interdisciplinary product reviews at the FDA. You will learn:

- How the 21st Century Cures Act defines primary mode of action
- How to use pre-RFD (Request for Designation) meetings with the FDA to hammer out a customized review process that meets the sponsor's needs
- And more...

Order your copy of **Drug or Device? How the 21st Century Cures Act Impacts Combination Products** for practical advice on the newest changes in the law on combination products and a look around the corner at how sponsors of combination products should seek to position their products to ensure a least burdensome and optimal regulatory pathway.

FOUR EASY WAYS TO ORDER

1. **PHONE:** Toll free (888) 838-5578 or +1 (703) 538-7600
2. **WEB:** www.fdanews.com/54330
3. **FAX:** +1 (703) 538-7676
4. **MAIL:** FDAnews
   300 N. Washington St., Suite 200
   Falls Church, VA 22046-3431

☑**Yes!** Please send me ____ copy(ies) of ***Drug or Device? How the 21st Century Cures Act Impacts Combination Products*** at the price of $397 for each PDF.

Name _____

Title _____

Company _____

Address _____

City_____ State _____ Zip code _____

Country _____

Telephone _____

Fax _____

Email _____

METHOD OF PAYMENT

❑ Check enclosed (payable to FDAnews)

❑ Bill me/my company. Our P.O.# _____

❑ Charge my credit card:
❑ Visa ❑ MasterCard ❑ American Express

Credit card no. _____

Expiration date _____

Signature _____
(Signature required on credit card and bill-me orders)

Virginia customers add 6% sales tax.

17FLYR-N