INTERNATIONAL DEVICES & DIAGNOSTICS MONITOR

Vol. 2, No. 15
April 11, 2016

IN THIS ISSUE

Citizen Petition Seeks Ban of Boston Scientific Surgical Mesh

Boston Scientific is rejecting allegations that it used counterfeit materials in its urogynecologic surgical mesh implants, fighting back against a law firm's claims that the company's devices are made of defective material from China.

Houston-based Mostyn Law filed a citizen petition with the FDA on March 31, asking the agency to issue a Class 1 recall of the products. The petition was filed on behalf of Teresa Stevens, a West Virginia woman who suffered health problems after receiving a Boston Scientific pelvic mesh implant.

The law firm alleges Boston Scientific ran out of FDA-approved supplies and "started using counterfeit resin from China with no history as to when it was made, how it was made, who made it, no title, and was smuggled out" in a series of transactions.

(See **Mesh**, *Page 4)*

Industry Hits Back at FDA's Safety Communication Proposal

Industry and other stakeholders are taking the FDA to task over draft guidance for communicating new information on safety issues related to medical devices, with one group labeling it a "significant departure" from agency practices.

The comments came in response to draft guidance unveiled Dec. 31, 2015, on so-called emerging signals, which the agency defines as new safety information on a medical device used in clinical practice. The agency wants to communicate these signals at an early stage while it still is monitoring and analyzing the safety information and before it is validated or confirmed.

Specifically, the draft document addresses the criteria, timeframes, communication methods and agency follow-up on communications for emerging signals.

(See **Signals**, *Page 2)*

Signals, *from Page 1*

Many stakeholders express concern about the agency's intention to communicate information about these emerging signals early in the process, as it could cause undue patient alarm. The Medical Imaging & Technology Alliance even goes as far as to urge the FDA to withdraw the draft document.

If the agency moves forward with the document, the group says, it should consider the ramifications of sharing information with the public on an emerging signal that has not been properly evaluated. It highlights a section in which the agency acknowledges that a communication regarding an emerging signal "may lack certainty about the significance of the information." This lack of certainty could raise public concern needlessly, MITA says.

AdvaMed's Reactions

AdvaMed agrees, saying that the document "fails to articulate a reasonable basis to communicate emerging signals to the public." The group assails the agency over what it calls a stark departure from existing postmarket communication practices, adding that the propsal "may not, by FDA's own admission, be in the public interest."

Further, prematurely releasing emerging signal communications to the public could hurt the reputation of medical devices. Word of unconfirmed risks also could cause "frivolous litigation, class action lawsuits and other legal actions," AdvaMed says, adding that the agency acknowledges that these communications could be based on "incorrect, incomplete or misleading information."

The group even questions whether the agency has statutory authority to communicate emerging signals, as it is proposing "sweeping changes" to its postmarket communication policies. Such a proposal is more suitable for rulemaking and public comment, it maintains.

The FDA also doesn't spell out which of its staff will determine whether a communication is warranted. "Senior staff within FDA should be required to sign off on all early communications to ensure that decisions to issue such communications are consistent and scientifically appropriate," AdvaMed contends.

The 510(k) Coalition raises the question of what happens if the FDA determines no safety issue is posed by a device after issuing this communication.

In the draft guidance, the FDA says it will post updates on its website at least twice a year — or as often as it deems appropriate. It will do so until it can issue a formal safety communication with specific recommendations for affected parties.

However, the coalition doesn't believe the agency has provided enough clarification. "It is unclear, how, or whether, FDA would be able to adequately publicly announce that an Emerging Signal was a false one and to also undo any damage … to ensure that the product and/or company's reputation isn't forever tarnished," the group writes.

AdvaMed also takes aim on this aspect of the proposal, saying updates should be more frequent, and the agency should immediately notify the public if no causal relationship can be demonstrated between a safety issue and a device.

A MedWatch Approach

Not all commenters are so hard on the FDA's proposal. The American Society of Anesthesiologists says it is supportive of the general concept of emerging signals, but adds that some clarification is needed on how the process would work.

To that end, it recommends that communications be administered through a system akin to the agency's MedWatch alerts. The group also suggests identifying emerging signals by specialty and allowing organizations to subscribe to appropriate alerts.

To read MITA's comments, visit: www.fdanews.com/04-07-16-MITA.pdf. Read AdvaMed's comments here: www.fdanews.com/04-07-16-AdvaMedComments.pdf and the 510(k) Coalition's comments here: www.fdanews.com/04-07-16-510k.pdf. Get ASA's take here: www.fdanews.com/04-07-16-ASA.pdf. — Elizabeth Hollis

Medtronic's Micra Lands FDA Approval, As First Leadless Pacemaker in U.S.

The FDA gave the green light last week to what is now the world's smallest pacemaker: Medtronic's Micra transcatheter pacing system.

The Micra is a self-contained, inch-long device that is intended for use in patients who need a single-chamber pacemaker. It will allow patient data to be sent remotely to clinicians through the Medtronic CareLink Network. Remote monitoring is expected to be available later this year.

The approval is based on a 719-patient clinical trial in which 98 percent of patients had adequate heart pacing six months after the device was implanted. Complications occurred in fewer than 7 percent of participants and included prolonged hospitalizations, blood clots in the legs and lungs, heart injury, device dislocation and heart attacks.

The FDA has expressed concerns about the long-term safety of the devices. In February, the FDA's Circulatory System Devices Panel advisory committee recommended that long-term postapproval studies enroll a large number of patients for the devices (*IDDM*, Feb. 26).

The clinical trial will continue to follow patients for at least 12 months to evaluate long-term performance of the device, the FDA says.

More than 30 centers in the U.S. have experience with Micra implantation, as a result of participating in the clinical trial evaluating the device. A limited amount of product will ship in late April or early May to these sites, as physicians have satisfied training requirements through trial participation, says Medtronic spokesman Ryan Mathre.

"We will immediately begin scheduling training new physicians on the procedure which will occur after the Heart Rhythm Conference in May, with product shipment to these new accounts to follow soon after," he tells *IDDM*.

The Micra was awarded the CE Mark in April 2015 based on early clinical trial data.

Medtronic Seemingly Unconcerned About New Tax Inversion Rules

In the wake of the U.S. Treasury Department's move to combat inversion deals, Medtronic doesn't appear too worried — at least publicly.

Despite last week's issuance of temporary rules — which expire in April 2019 — that aim to stop domestic companies from buying smaller oversees firms to avoid paying U.S. taxes, Medtronic maintains that the move will "not have a material financial impact on any transaction undertaken by the company."

The regulations, which will apply to all deals made after April 4, address serial inverters — companies that have grown larger through inversions or acquisitions of U.S. firms — by disregarding their acquired American assets over the previous three years in determining their size.

Further, the regulations aim to tackle earnings stripping, whereby companies try to avoid U.S. taxes by paying deductible interest to a low-tax country. Under the new rules, Treasury can restrict related-party debt that does not finance new investment in the U.S.

That shines the spotlight on Medtronic's mega-$49.9 billion acquisition of Covidien in January 2015, through which the device giant moved its worldwide headquarters to Ireland for tax purposes.

Medtronic says it will study the regulations and "provide appropriate disclosure concerning any potential material impact on the company, if applicable."

Treasury's actions already have had an effect, with Pfizer and Allergan calling off their planned $160 billion merger last week. The two said the decision was driven by Treasury's actions.

Read the Treasury's temporary rules here: www.fdanews.com/04-06-16-FederalRegister.pdf.
— Michael Cipriano

Mesh, *from Page 1*

The petition cites internal, previously undisclosed Boston Scientific emails that say the company bought the stock in 2011 and 2012 from a suspected counterfeiter in China without fully testing it for its use as a vaginal implant.

The FDA posted a safety alert on April 1 saying it is examining the allegations. "FDA is not currently aware that the alleged counterfeit raw material contributes to adverse events associated with these products," the notice says.

The FDA says Boston Scientific will conduct additional testing that should be sufficient to determine whether the mesh manufactured from the alleged counterfeit raw material is equivalent to the mesh made from the original raw material supplier.

Attorney Amber Mostyn of Mostyn Law subsequently criticized the FDA for its "watered-down warning" of the risks of the mesh, adding "it is absurd to rely on testing by the company that is using it."

Boston Scientific says it stands behind its products and the materials used in them.

The company says samples of the resin underwent a rigorous battery of tests to demonstrate equivalency. It also conducted extensive mechanical tests to ensure that the mesh products manufactured with the newly sourced material met product specifications.

Earlier this year, the FDA issued two final orders requiring manufacturers to address safety concerns — including severe pelvic pain and organ perforation — through a PMA pathway to demonstrate safety and effectiveness (*IDDM*, Jan. 8).

Several companies — including Boston Scientific, Medtronic's Covidien, Johnson & Johnson's Ethicon and C.R. Bard — have faced legal action brought by women claiming personal injury while using their products (*IDDM*, June 26, 2015).

Read the petition here: www.fdanews.com/04-04-16-MLPetition.pdf. The safety alert is here: www.fdanews.com/04-04-16-FDASafetyAlert.pdf.

Canada Proposes Revisions to Classification System for IVDs

Health Canada is seeking stakeholder feedback on a revised plan to help manufacturers classify in vitro diagnostic devices based on risks.

The draft guidance document — which will replace a version released in 1998 — is intended to clarify how to apply the rules set out in the Medical Devices Regulations for IVDDs. The guidance was revised to provide greater clarity and updated examples, according to Health Canada.

The draft guidance spells out the rules and provides explanations and examples for several types of IVDDs, including those used for donor screening, patient management purposes and immunological typing, as well as those that determine disease status or immune status.

Included in the document is a flow diagram to help manufacturers apply the rules to determine in what class an IVDD belongs.

The revision follows Health Canada's release of guidance on the risk-based classification system for non-in vitro diagnostic devices last June, as well as guidance on supporting evidence for new and amended license applications for Class 3 and 4 devices not including IVDDs from July 2012.

Comments are due by May 31. Read the draft document *Guidance for the Risk-based Classification System for In Vitro Diagnostic Devices* here: www.fdanews.com/04-08-16-Canada.pdf.

FDA, NIH Propose Protocol Template For Phase 2 and 3 IDE Studies

With an eye toward making the conduct of clinical studies more efficient, the FDA and NIH have unveiled a template intended for investigators writing Phase 2 or 3 trial protocols that require IDE applications.

According to the agencies, the template aims to help investigators prepare protocols that are consistently organized and contain all of the information needed for proper review of trials. The proposed template follows the standard outlined in the *International Conference on Harmonisation Guidance for Industry, E6 Good Clinical Practice: Consolidated Guidance (ICH:E6).*

"We see the template as a way to facilitate creativity and innovation, not inhibit it," CBER Director Peter Marks said.

"Just as ICH E6 allows considerable flexibility in the actual operations of trials using quality by design principles, the template includes the appropriate elements to be considered, but does not dictate exactly how the trial should be done — that is the work of the investigators," he adds.

Comments are due by April 17. Access the draft template here: www.fdanews.com/04-06-16-INDIDE.pdf.

FDA Labels Cook Recall As A Class 1

The FDA has labeled the recall of Cook Medical's single lumen central venous catheters and pressure monitoring sets and trays as Class 1, meaning it could cause serious injury or death.

The recall — which is due to catheter tip fracture and/or separation — involves 12,516 devices distributed nationwide between April 24 and Oct. 23, 2015, according to a March 30 notice.

Cook sent letters on Jan. 6 instructing customers to quarantine unused products and return the affected items to the company. Globally, the recall involves 17,827 devices (*IDDM*, Feb. 11).

The recall is ongoing, according to company spokeswoman Moriah Sowders.

The action follows last year's recall of Cook's Beacon Tip catheters (*IDDM*, Oct. 14, 2015).

FDA Permits Marketing of System For Use During Morcellation

The FDA has given the go-ahead for Advanced Surgical Concepts to market PneumoLiner, the first containment system for use in conjunction with laparoscopic power morcellators to isolate uterine tissue that is not suspected to contain cancer.

PneumoLiner includes a containment bag and a plunger to deliver the device into the abdominal cavity. The tissue slated for removal is then placed in the bag, which is sealed and inflated. The device has been tested in laboratory settings and found to withstand forces in excess of what can expected during a surgical procedure.

Morcellators have received intense media scrutiny after the FDA issued a safety alert in 2014 saying the instrument's blades could spread unsuspected cancers in as many as one in 352 cases. Because of potential risks, the FDA is requiring the Ireland-based manufacturer to warn patients and healthcare providers that PneumoLiner has not been proven to reduce the risk of spreading cancer during these procedures.

William Maisel, deputy director for science and chief scientist at CDRH, said the device is intended for a limited patient population that has been appropriately informed of the risks of power morcellation.

The device was reviewed through the *de novo* classification process. — Elizabeth Hollis

CDRH Provides New Online Resources for UDI Program

The FDA has added new modules to its CDRH Learn online platform covering the Unique Device Identification program.

The tool now features a regulatory overview of the UDI system and the basics on submitting information to the Global Unique Device Identification Database.

In addition, devicemakers can learn about making a GUDID account request, requirements for the GUDID identifier record and submission options for GUDID HL7 SPL.

More information is available here: www.fda.gov/Training/CDRHLearn/default.htm.

Report Looks to the Future Of Device Evaluation System

A new report from the Duke-Margolis Center for Health Policy is offering an initial peek into a planned coordinating center intended to guide the development and implementation of a postmarket device evaluation system.

The future national medical device evaluation system — one of CDRH's 2016-2017 strategic priorities — is intended to capture and use real-world evidence to bolster regulatory decision-making. As envisioned, the coordinating center would create opportunities for better evidence generation and sharing with a network of partners.

The report — issued by the planning board for the national medical device evaluation system — provides suggestions on the objectives, tasks and capabilities a coordinating center would handle.

The center's primary objective would be "to optimize the cost of, access to, quality of, and the sharing of medical device real-world data for evidence development," the report says.

For example, the center could assist mid-size and small companies to identify analytic tools to run efficient pre- and postmarket trials, as well as studies to back up reimbursement and coverage decisions.

The center could also help solve some policy challenges, such as encouraging UDI adoption, standardizing informed consent and ensuring patient privacy.

The report comes a couple of weeks after a meeting hosted by the FDA and the University of Maryland's Center of Excellence in Regulatory Science and Innovation that discussed strategies to enhance postmarket data collection (*IDDM*, March 25).

The FDA has ramped up efforts towards a national evaluation system over the past couple of years.

In 2014, the FDA tasked experts from government agencies, healthcare delivery organizations and other entities to outline a national system. This planning board unveiled a February 2015 report, authored by experts from the Brookings Institution, to outline some of the proposed system's activities (*IDDM*, Feb. 27, 2015).

Late last year, the FDA asked the Duke-Margolis Center for Health Policy to reconvene the planning board to help lead the next phase for the system's coordinating center and governing body.

Read the report here: www.fdanews.com/04-06-16-NESReport.pdf. More information on the National Evaluation System is here: www.fdanews.com/04-06-16-FDANES.pdf. — Elizabeth Hollis

FTC, FDA Team Up on Guidance Tool For Mobile Health App Developers

The FTC has developed a web-based guidance tool for mobile health app developers, which links directly to information on federal regulations that may affect their apps.

The tool — which the FDA says could help make medicine more personalized for patients — asks developers questions regarding an app's purpose, data and services. After answers are received, the tool then directs the developer to more information intended to help them better understand the federal regulations that apply their apps.

Laws may include the FTC Act, the FTC's Health Breach Notification Rule, the Health Insurance Portability and Accountability Act and the Federal Food, Drug and Cosmetics Act.

"As the number of mobile health products available today continues to rise, it's important to clarify for developers how FDA and other agencies' regulations would apply to their app," says Bakul Patel, CDRH's associate director for digital health.

The tool was created under a partnership between the FTC and the Department of Health and Human Services' Office of National Coordinator for Health Information Technology, Office for Civil Rights and the FDA.

More information on the tool is here: www.ftc.gov/tips-advice/business-center/guidance/mobile-health-apps-interactive-tool. — Anisa Jibrell

BRIEFS

Stryker Wraps Up 3 Acquisitions

Stryker scored a hat trick last week, completing the acquisition of Physio-Control, Sage Products and Synergetics. The Kalamazoo, Mich.-based device giant bought Physio-Control in an all-cash transaction worth almost $1.3 billion, Sage for nearly $2.8 billion, and Synergetics for an undisclosed amount of money. The deals were announced in February (*IDDM*, Feb. 19).

Merck KGaA, Sysmex Inostics Gain CE Mark

Merck KGaA and Sysmex Inostics' jointly developed liquid biopsy OncoBEAM RAS CRC assay has garnered CE marking. Comparable to tissue-based testing, the test can identify which patients with metastatic colorectal cancer are more receptive to anti-epidermal growth factor receptor therapies, like Erbitux, according to a statement. The assay consists of a 34-mutation panel based on beads, emulsion, amplification and magnetics technology, and only requires a 10-ml blood sample.

Sterigenics to Acquire Nelson Laboratories

Sterigenics International has agreed to buy microbiology test developer Nelson Laboratories for an undisclosed amount. Upon completion of the acquisition, Nelson will merge with Sterigenics' microbiological and analytical testing and consultancy, SteriPro Labs. Both will market under the Nelson name. Additionally, Nelson will continue to operate in Salt Lake City, Utah, with Jeffery Nelson retaining his presidency. Sterigenics is a Deerfield, Ill.-based provider of contract sterilization services, gamma technologies and medical isotopes.

ResMed Finalizes $800M Brightree Deal

San Diego-based ResMed has finalized its acquisition of cloud healthcare software company Brightree for $800 million, the company reported last week in an SEC filing. The companies announced the acquisition in February. Brightree specializes in post-acute care-focused clinical software applications. The Atlanta-based company will keep its name and continue to operate as a separate entity.

NICE Backs ElectroCore's GammaCore

UK's National Institute of Health and Care Excellence has issued guidance backing electroCore's vagus nerve stimulation treatment gammaCore, intended to treat migraine and cluster headaches. The guidance noted five clinical trials in which patients experienced "substantial and meaningful benefit" from treatment. The CE-marked device is placed on the side of the neck over the vagus nerve, which is stimulated for two minutes. Treatment can last between four and six minutes and the device poses no serious side effects.

SpeeDX, Goffin Enter Distribution Agreement

Sydney-based SpeeDX has entered into a distribution agreement with molecular diagnostics company Goffin Molecular Technologies. Under the agreement, Goffin will distribute SpeeDX's PlexPCR and ResistancePlus qPCR kits — for the detection of pathogens and antimicrobial resistance markers, respectively — in Belgium, Netherlands and Luxembourg. The agreement expands SpeeDX's presence in Europe in molecular diagnostic markets.

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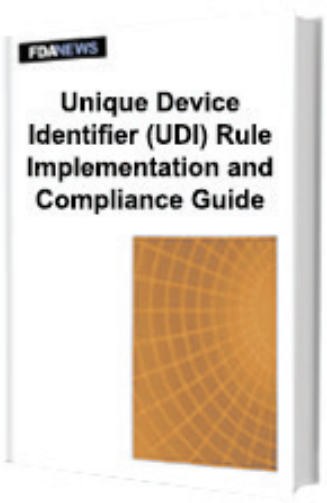

Unique Device Identifier (UDI) Rule Implementation and Compliance Guide

The rush to compliance is in full swing. By Sept. 24, 2015, all implantable, life-saving or life-supporting devices must comply with the new UDI requirements. By 2018 all devicemakers must be in compliance.

You'll need to understand what UDI is … who it applies to … what the exceptions to the rule are … what deadlines you must meet … what UDI issuing agencies are ... and how to work with them. Thankfully, help is here.

With **Unique Device Identifier (UDI) Rule Implementation and Compliance Guide**, you'll gain a clear understanding of this complex new rule and learn to work with it more successfully. You will learn:

- The timetable for implementation;
- Which devices must comply with the rule and which do not;
- What information must be included on product labels;
- How to submit device identification information to the GUDID;
- About the accredited UDI issuing agencies and their roles;
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Unique Device Identifier (UDI) Rule Implementation and Compliance Guide is fully updated to reflect the final rule, chapter by chapter the report includes the critical information you need to get down to the real nitty gritty of complying with the UDI rule.

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