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CMS Report Cites Theranos For Deficiencies at California Lab

The once-hot startup Theranos got more bad news last week — this time in the form of a letter from the Centers for Medicare & Medicaid Services.

In the letter, CMS details several deficiencies at Theranos' Newark, Calif., laboratory, following a Nov. 20, 2015, onsite survey.

Of particular note is a finding of "immediate jeopardy" level in hematology. As a result, the company needs to take corrective action immediately, as the laboratory's noncompliance poses risks to patient health and safety.

"To be clear, that finding does not apply to the whole lab, and none of these findings relate to our Arizona lab, where we currently process over 90 percent of our tests," Theranos says in response to the CMS report.

Further, there are three condition-level deficiencies related to personnel, such as documentation and oversight. One of the deficiencies is related to analytic systems. CMS found that within hematology,

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FDA Issues Draft Guidance on Design, Labeling for Interoperable Devices

With an eye toward ensuring the safe exchange of patient information between connected systems, the FDA is offering its thinking on ways to develop and design interoperable devices and providing recommendations on the content of premarket submissions and labeling.

As the agency notes in draft guidance issued Jan. 26, interoperability in healthcare can lead to enhanced patient care. "[However,] the failure to establish and implement appropriate functional, performance, and interface requirements during product development may lead to the exchange of inaccurate, untimely, or misleading information," according to the draft guidance issued Jan. 26. "It may also lead to device malfunction, including the failure to operate, and can lead to patient injury and even death."

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Theranos, *from Page 1*

certain policies, procedures and associated events did not meet the relevant standards.

"It's important to note this particular survey was conducted months ago and is not a reflection of the current state of our lab in Newark, CA. As the survey took place we were simultaneously conducting a comprehensive review of our laboratory's systems, processes and procedures to ensure that we have best-in-class quality systems," Theranos explains.

The company says that it has made policy and personnel changes at the Newark lab, including adding a new Clinical Laboratory Improvement Amendments lab director and a new clinical consultant.

CMS issued no findings covering certain allegations that were mentioned in recent media coverage, Theranos points out, including proficiency testing "cheating," manipulating data to make proprietary machines seem more accurate, and improperly hiding the existence of the lab holding its proprietary technologies.

Theranos says it is continuing to take corrective action, and it will submit a full plan of correction to CMS soon.

Despite the company's assurances, not everyone is satisfied, including Walgreens. The company told the startup that it must stop sending any clinical laboratory tests provided through Theranos Wellness Centers at Walgreens to the Newark lab for analysis. In addition, Walgreens is halting Theranos laboratory services at its Palo Alto, Calif., store.

Further, no patient samples will be sent to the Newark lab until all issues are resolved, Walgreens says.

This isn't the first time Theranos has faced criticism. Last year, the FDA hit Theranos with two 483s, one of which took the company to task for shipping an uncleared device (*IDDM*, Oct. 30, 2015). — Jonathon Shacat

Interoperability, *from Page 1*

To ensure proper information exchange, the agency encourages members of industry to consider the information model (data attributes), functional model (role played within the interoperable system) and architectural model (how the device is connected within the system) during the design and development phase.

Manufacturers should conduct testing that considers the risks associated with interoperability, reasonably foreseeable misuse, and reasonably foreseeable combinations of events that can result in a hazardous situation, says the draft guidance.

In addition, manufacturers should consider the following as they design their devices:

- The purpose of the electronic data interface;
- The anticipated users, e.g., biomedical engineers or IT professionals;
- Ways to mitigate risk;
- Verification and validation; and
- Labeling considerations.

The guidance document also provides the agency's thinking on the contents of premarket submissions for interoperable medical devices. Submissions should describe how each interface is meant to be used and detail any limitations. They also should contain information to support claims that a device exchanges and uses information from other devices, technologies or products.

In addition, the document says labeling should include information on how to connect to the device. For a device that is meant to interact with only a few specific devices, the labeling should also explicitly state which items are and aren't compatible.

Comments are due by March 28. Read the draft guidance "Design Considerations and Premarket Submission Recommendations for Interoperable Medical Devices" here: www.fdanews.com/01-16-FDAInteroperability.pdf. — Jonathon Shacat

St. Jude Recalls Optisure Dual Coil Defibrillation Leads

St. Jude Medical is recalling its Optisure dual coil defibrillation leads due to a manufacturing error that may have caused damage to the insulation layer of one of the shock coils.

The recall, designated as Class 1 by the FDA, involves 447 devices manufactured from March 12, 2014 to March 22, 2015, and distributed from April 9, 2014 to Oct. 20, 2015.

An investigation revealed that a variation in the process to remove excess medical adhesive used in the assembly of the superior vena cava shock coil could result in cuts to the insulation of the lead, potentially causing an electrical malfunction. However, the company says there is a low probability for this problem and that any associated risks can be prevented with device reprogramming.

"Depending on device programming and the depth of the cut, this could result in the inability of the defibrillator to deliver electrical therapy to the patient," says the FDA's notice.

The use of affected products may cause serious adverse health consequences, including patient injury or death. However, St. Jude says it has received no reports of lead malfunction or patient injury.

The company's original advisory stated that 281 of the devices were distributed in the U.S. Since issuing its "Dear Doctor" letter in November 2015, St. Jude Medical clarified with the FDA that three of the leads were never implanted in patients, bringing the total U.S. population of implanted leads to 278, company spokesman Justin Paquette tells *IDDM*.

In addition to the U.S., the devices were distributed in Belgium, Switzerland, Germany, France, the UK, India, Italy, Japan, Luxembourg, the Netherlands, Saudi Arabia and Sweden.

Read the recall notice here: www.fdanews.com/01-16-StJudeRecall.pdf. — Jonathon Shacat

Baxter Recalls IV Solutions for Potential Leaking Containers, Particulate Matter

Baxter International is voluntarily recalling four lots of intravenous solutions due to the potential for leaking containers and particulate matter.

Baxter says it was made aware of the issue as the result of two complaints for leaking containers and one customer complaint for three lots for particulate matter. No adverse events associated with these incidents have been reported to Baxter to date, the company says.

The company adds that leaking containers were confirmed in 11 units of one lot of 0.9 percent sodium chloride injection, 100 mL in Mini-Bag Plus Container, and a subsequent investigation identified the root cause as a mechanical issue that affected one machine during a single shift. The mechanical issue has since been remedied.

The company says a fragment of cardboard particulate matter was found in single unit in a separate lot of 0.9 percent sodium chloride injection, 100 mL in Mini-Bag Plus Container. A unit of metronidazole injection 500mg/100mL was found to contain cloth fiber particulate matter. Also, a unit of Clinimix E 5/15 was found to contain a small fragment of dried skin particulate matter.

Read the recall notice here: www.fdanews.com/01-16-BaxterRecall.pdf. — Jonathon Shacat

Indian Device Industry Pushes for Certification Requirement Options

India's medical device industry is urging the country's government to do away with the insistence on U.S. FDA approval in the tendering process for the public healthcare system and to replace it with more democratic options.

Insistence on an exclusionary FDA certification requirement is a discriminatory clause, as it favors large U.S. companies in the domestic

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CDRH Accepting GUDID Account Requests for Class 2 Devices Feb. 1

On Feb. 1, labelers of Class 2 devices can begin requesting accounts for the FDA's Global Unique Device Identification Database.

Requests should be submitted by April, but definitely no later than June, Linda Sigg, associate director of informatics at CDRH's Office of Surveillance and Biometrics, said during a Jan. 27 FDA webinar.

The timeframe should help labelers meet the Sept. 24 compliance date.

Labelers must include a UDI on device labels and packages — except if an exception or alternative exists — and submit device identification information to the GUDID, according to a final rule issued in 2013.

The FDA is allowing labelers to get GUDID accounts based on UDI compliance dates, which are being phased in by device class, said Chris Diamant, UDI program analyst for CDRH's Office of Surveillance and Biometrics.

The program took effect September 2014 for Class 3 devices, and last September for implantable, life-supporting and life-sustaining devices. The compliance date for Class 1 devices is in 2018.

GUDID is designed to make device identification information available for everyone, including patients, caregivers, healthcare providers, hospitals and industry. — Jonathon Shacat

Califf's Nomination Faces Obstacles From 3 More U.S. Senators

The road to grabbing the title of FDA commissioner keeps getting tougher for Robert Califf, with senators from both sides of the aisle putting hurdles in front of his path.

Last week, two lawmakers — Sens. Bernie Sanders (I-Vt.) and Edward Markey (D-Mass.) — put holds on his nomination, with both voicing concerns over the FDA's handling of opioid addiction. On Jan. 26, Markey announced that he was placing a hold on Califf's nomination unless the agency implemented measures to make advisory committees involved in the opioid approval process.

In addition, Sen. Joe Manchin (D-W.Va.) has announced he will filibuster the nominee, citing his strong ties to the pharmaceutical industry. He also said he does not believe that Califf is the right person to handle the opioid epidemic.

Sen. Lisa Murkowski (R-Alaska) also expressed her intent to block the nominee's approval until she has reassurances from the agency on mandatory labeling requirements for genetically modified salmon. She gave her thumbs up to him during the Senate HELP committee vote, but said she would block him if her concerns about the salmon are not addressed. — Michael Cipriano

IsoLux Cited for Procedural Failures in FDA Warning Letter

IsoLux has earned a warning letter from the FDA for several procedural failures related to its A/C powered illuminators.

The Jan. 8 warning letter follows an inspection of the company's manufacturing facility in Naples, Fla., from Nov. 4 through 6, 2015.

In the warning letter, the FDA says IsoLux failed to keep documents related to an investigation for uniformity and homogeneity of its fiber optic cable illumination and misalignment of its Isovu Headlight Camera System in March 2011. The company also failed to implement conformity procedures to adequately qualify the new supplier of fiber optic cables in 2011.

Both failures are continued observations from previous inspections in January 2010 and August 2005, the FDA says.

In addition, the warning letter dings IsoLux for failing to ensure that incoming products meet

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public healthcare procurement process, says Rajiv Nath, forum coordinator of the Association of Indian Medical Device Industry.

"This insistence is a pure absurdity and has resulted in exclusion of domestic manufacturers and manufacturers from other countries from bidding and hiking up the healthcare costs," Nath says.

Nath points out that India has very competent manufacturers with European Certification or the CE Mark. An additional option could be ISO 13485 certification from a reputable, competent and accredited certification body, while the FDA could be an alternate option, he adds.

Amending the technical specifications would make the bidding process more competitive and democratic, and manufacturers from all over the world could participate in the public healthcare procurement process, Nath says.

"In no country of the world do medical institutions demand that manufacturers meet foreign standards and specification, and invariably have technical certifications to encourage local job creation and local manufacturing industry," says Mala Vazirani, director of Transasia, a large diagnostic company in India.

"Every government's mission is to lower healthcare cost and to do away with discrimination against domestic manufacturers. This protectionist policy is particularly the trend for decades in Europe, the USA and Japan, so why not India?" she adds. — Jonathon Shacat

IsoLux, *from Page 5*

specifications, failing to maintain design change procedures and failing to establish a design history file for 1180 XSB Xenon Light Source devices.

IsoLux sent a letter to the FDA on Dec. 1, 2015, regarding observations in a Form 483, but the agency says the response did not provide adequate supporting evidence that the company had implemented corrections and planned actions.

Read the warning letter here: www.fdanews.com/01-16-IsoLuxLetter.pdf. — Jonathon Shacat

Novartis Seeks to Revamp Struggling Eye Care Unit

Novartis is looking to breathe new life into its flagging Alcon business by transferring the unit's drug products to the pharmaceuticals division.

The move, according to Novartis, will allow Alcon to focus on its core surgical and vision care business.

Alcon's annual surgical sales have declined as a result of weaker performance in intraocular lenses and cataract equipment. Its vision care business has declined, due in part to slower contact lens sales.

Michael Ball has been tapped as the division head and CEO of Alcon, effective Feb. 1. Ball, who was CEO of Hospira until it was bought out by Pfizer, will replace current Alcon head Jeff George.

Ball's expertise in ophthalmology — as well as medical devices — will be instrumental in accelerating innovation and growth at Alcon, said Joseph Jimenez, CEO of Novartis.

In a research note, Larry Biegelsen of Wells Fargo says Novartis thinks Alcon's performance will "remain challenged" during the first half of the year, but could turn around in mid-2016. — Michael Cipriano and Jonathon Shacat

UK Dentist Sanctioned for Using Counterfeit, Noncompliant Equipment

A UK dentist has received sanctions on his dentistry registration for using counterfeit and noncompliant dental equipment, the country's Medicines and Healthcare products Regulatory Agency announced last week.

During a Jan. 18 General Dental Council hearing, the Professional Conduct Committee determined that Fizan Tahir's misconduct impaired his fitness to practice.

The MHRA conducted an extensive investigation following an Oct. 31, 2013, incident involving the use of a counterfeit dental hand-piece on a patient in the Worthing Tooth Booth Practice. The agency subsequently seized more than 100 counterfeit and noncompliant items of dental equipment from 14 tooth booth practices.

Read the full determination and conditions here: www.fdanews.com/01-16-PCCHearing.pdf. — Jonathon Shacat

FDA Warning Letter Dings LAR MFG For Procedural, Validation Failures

LAR MFG has received a warning letter from the FDA citing several procedural and validation failures regarding its ceramic dental brackets.

The Dec. 9, 2015, letter follows an inspection at the company's manufacturing facility in Port Richey, Fla., from Aug. 31 to Sept. 1, 2015.

The warning letter says the company failed to validate the manufacturing process for ceramic orthodontic brackets.

Also, the company failed to establish and/or maintain procedures for:

- Corrective and preventive action for nonconforming product;
- Calibration of the optical comparators, micrometer and dial calipers;
- Acceptance activities for the incoming raw component;
- Device history records; and
- Quality audits and quality systems.

In addition, the company failed to develop, conduct, control or monitor production processes to ensure that a device conforms to its specifications. For example, LAR MFG does not have any documented instructions or manufacturing procedures concerning the production of ceramic orthodontic brackets, the warning letter says.

LAR MFG sent a letter to the FDA on Oct. 5, 2015, regarding a Form 483, but the agency says the response was inadequate because the company failed to outline specific steps for each observation to comply with regulations.

Read the warning letter here: www.fdanews.com/01-16-LARMFGLetter.pdf. — Jonathon Shacat

BRIEFS

Ireland Issues Warning for MRI Systems

Ireland's Health Products Regulatory Authority is warning of the potential for incorrectly installed quench lines for superconductor magnets in Siemens Healthcare's Magnetom MRI system. In a Priority 2 warning, the HPRA says an improperly installed quench line may cause helium gas to be blown directly into the magnet room or other areas, potentially leading to the displacement of oxygen and cold burns. Siemens will inspect all sites with a Magnetom system to ensure that the quench line was installed in a manner that ensures safe operation, HPRA says.

Jan Medical Lands Funding

Mountain View, Calif.-based Jan Medical has scooped up $7.5 million in Series C funding from Brainlab for activities related to BrainPulse. Jan Medical has earmarked the funds for wrapping up clinical trials, as well as submitting a regulatory filing with the FDA and obtaining the CE Mark in the EU for BrainPulse. The device aims to detect abnormal neurological conditions — including concussion and stroke — quickly and accurately. BrainPulse works by capturing a novel, noninvasive, physiological signal that utilizes the cardiac output to measure vasculature and brain tissue conditions, according to a Jan Medical statement. Munich, Germany-based Brainlab also has committed to assist with the clinical research, regulatory filings and commercialization activities, as well as provide expertise in R&D.

Centinel Spine Scores Home Run

Ahead of the winter storm that blanketed the East Coast, New York-based Centinel Spine received FDA clearance for its Altos posterior cervical thoracic stabilization system. The system is indicated for use in either the lateral masses of the cervical spine or the pedicles of the cervical-thoracic spine. The first patient already has been implanted with the device. According to the company, Altos is the first FDA-cleared posterior cervical thoracic system intended for implantation into either the cervical lateral masses or the cervical-thoracic pedicles.

Panasonic, Kyoto University Team Up

Panasonic and Kyoto University want to make it easier to monitor the vital signs of people on the go. To that end, the two have developed a new remote sensing technology for vital signs — such as heart rate and heartbeat interval — all without placing sensors on the body. It works by combining millimeter-wave spread-spectrum radar technology and an analysis algorithm that identifies signals from the body. "Heartbeats aren't the only signals the radar catches," says Toru Sato, professor of communications and computer engineering at Kyoto University, in a prepared statement. "The body sends out all sorts of signals at once, including breathing and body movement. It's a chaotic soup of information. Our algorithm differentiates all of that." As Hiroyuki Sakai, a researcher at Panasonic, notes in the release, going sensorless allows people to monitor their health in a relaxed environment. Further, it might encourage patients to be more proactive in monitoring their own vital signs.

Correction

The Jan. 25 issue of *IDDM* erroneously stated Kim Trautman's new employer. She is working for NSF Health Sciences. We regret the error.

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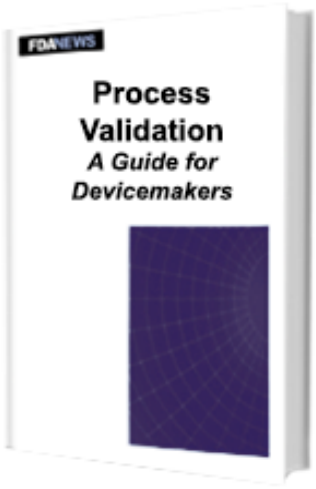

Process Validation
A Guide for Devicemakers

When must a process be validated? That is the first crucial question devicemakers must answer. But with no clear guidance from the CDRH, finding the answer can be difficult.

The new FDAnews management report — **Process Validation: *A Guide for Devicemakers*** provides you with the answers. This report will walk you through each point in the decision-making process, including how to determine if a product can be "fully verified," and how FDA inspectors define that term.

In it, you'll also find a valuable in-depth overview of all of the currently applicable regulatory guidelines that have an impact on process validation for devices, including those from three key sources: the FDA, the International Organization for Standardization (ISO) and the Global Harmonization Task Force (GHTF).

Process Validation: *A Guide for Devicemakers* teaches the proper application of the regulatory requirements that lead to successful process validation, and also offers advice on the practical issues confronting validation compliance by using real-life anecdotes and scenarios.

You also get invaluable extras, such as checklists for IQ, OQ and PQ — and hundreds of pages of appendices, including the invaluable *Medical Device Quality Systems Manual: A Small Entity Compliance Guide*, which is no longer available from the FDA.

But, most importantly, throughout the report, you'll find real-life examples that illustrate relevant concepts … show when processes need to be validated … identify the kinds of evidence you need to collect and maintain to demonstrate proper validation … and actual FDA warning letters to help you learn from others' mistakes.

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