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Booz Allen: More Time Needed to Show Effects of CDRH's Device Review Reforms

CDRH is making significant progress to improve its medical device review program, but it's too early to tell if the efforts will have long-term effects, Booz Allen Hamilton says in an independent assessment report.

The report, released by the FDA last week, says the agency has successfully completed Stage 1 for each project in its December 2014 *Plan of Action* to address 11 recommendations made by Booz Allen in June 2014.

"If supported and sustained, these improvements implemented are expected to yield meaningful progress toward the shared goals of greater consistency, transparency and predictability in the review process, as well as shorter review times to get products into the hands of patients sooner," Booz Allen says.

(See **MDUFA**, *Page 4)*

Sen. Murray Proposes Bill that Aims To Improve Scope Safety

Sen. Patty Murray (D-Wash.) introduced a bill last week that would give the FDA additional tools to review and ensure the safety of medical devices, such as duodenoscopes.

The legislation, called the *Preventing Superbugs and Protecting Patients Act*, follows an ongoing investigation into contaminated devices linked to antibiotic-resistant infections at Virginia Mason Medical Center in Seattle and nationwide.

The legislation:

- Gives FDA the authority to refuse or deny a 510(k) submission based on whether the manufacturer's cleaning instructions work in real-world conditions, and whether the manufacturer can provide satisfactory data showing the device can be reliably decontaminated between uses; and

(See **Scopes**, *Page 4)*

Nontraditional Methods Of Sterilization in FDA Spotlight

With the FDA continuing to see nontraditional methods of sterilization, the agency is advising sponsors on what to include in their 510(k)s for devices labeled as sterile.

The update comes in the form of guidance titled "Submission and Review of Sterility Information in Premarket Notification (510(k)) Submissions for Devices Labeled as Sterile." Once final, the document would apply to 510(k)s for devices that are subject to industrial terminal sterilization processes based on microbial inactivation.

The document says the FDA is seeing a range of new methods other than steam, dry heat, radiation and ethylene oxide. "FDA has experience with other methods, such as hydrogen peroxide, ozone and flexible bag systems, and now considers them to be established methods," according to the guidance document.

However, these newer methods are sometimes altered, and the agency has some concerns about these novel methods, as they could provide inadequate sterility assurance. To mitigate any risks, the agency says compliance with GMP should be carefully assessed. It adds that it intends to inspect a manufacturing facility before clearing a device sterilized with a novel method.

The document lists some of the novel methods the FDA has encountered, including vaporized peracetic acid, high-intensity light or pulse light, microwave radiation, sound waves and ultraviolet light.

In addition, the document recommends what specific information about these processes sponsors should include in their 510(k)s:

- A comprehensive description of the sterilization process;
- The method used to validated the sterilization cycle;
- The validation protocol; and
- The sterilization validation data, identifying applicable published literature.

Issued Jan. 21, the guidance document comes a little more than seven years after the release of the draft version. It will supersede an August 2002 document titled "Updated 510(k) Sterility Review Guidance K90-1."

Read the guidance here: www.fdanews.com/01-16-FDASterility.pdf. — Elizabeth Hollis

Abbott Scoops Up Alere, Kalila in Shopping Spree

Abbott is on an acquisition spree, shelling out $5.8 billion for Alere and an undisclosed amount of money for Kalila Medical last week.

By purchasing Alere, Abbott says it will become the leading diagnostics provider of point-of-care testing. Abbott's total diagnostics sales will exceed $7 billion after the close.

"Alere's complementary portfolio of products will provide Abbott access to new channels and geographies, including entry into fast-growing outlets, such as doctors' offices, clinics, pharmacies and at-home testing," says Abbott.

Abbott expects the transaction to be completed by the end of 2016, company spokeswoman Darcy Ross tells *IDDM*.

Overall, Abbott appears attracted by Alere's potential with its expansive product offering and strong presence in both hospital and retail markets, says Lawrence Biegelsen, a senior analyst with Wells Fargo Securities. Abbott plans to leverage its own operating platform to streamline processes and costs to improve profitability, he adds.

Meanwhile, with the acquisition of Kalila, Abbott gains technology to expand its portfolio of tools to treat atrial fibrillation and other heart rhythm disorders, the company says.

Kalila, headquartered in Campbell, Calif., has developed a novel steerable sheath that helps physicians access and perform catheter-based electrophysiology procedures. Kalila obtained 510(k) clearance from the FDA for its steerable introducer sheath in 2014 and received the CE Mark in December 2013. — Jonathon Shacat

Arkray Recalls Test Strips Due to Inaccurate Readings

Arkray is recalling certain test strips due to inaccurate blood sugar readings.

The recall, designated as Class 1 by the FDA, involves 99 boxes of Spotchem II Basic Panel-1 Reagent Test Strip and Spotchem II Glucose Reagent Test Strip. The strips are intended for use with the Spotchem EZ analyzer.

The products were recalled in Florida, Illinois, Kentucky, Michigan, North Carolina, New York, Ohio and Tennessee.

They were manufactured from November 2014 to September 2015 and distributed from Feb. 18, 2015 to Oct. 13, 2015.

The test strips are reporting falsely low blood glucose levels. As a result, when the true levels are above 265 mg/dL, there is a risk that a healthcare provider would not diagnose hyperglycemia in a timely manner.

No illnesses or injuries have been reported from the use of the strips, but the issue may cause serious injury or death, the FDA says.

Arkray declined to comment. Read the recall notice here: www.fdanews.com/02-16-ArkrayRecall.pdf. — Jonathon Shacat

Two Sentenced for Medicare Fraud at Medical Equipment Supply Company

The former owner of JC Medical Supply, a durable medical equipment supply company based in Long Beach, Calif., will serve four years and three months in prison, the Justice Department announced late last month.

Vladislav Tcherniavsky, 46, was convicted of one count of conspiracy to commit healthcare fraud and five counts of healthcare fraud by a federal jury on Oct. 15, 2015. His wife, Amalya Cherniavsky, 41, who co-operated the company, was found guilty of the same offenses. She was sentenced to a term of probation.

U.S. District Judge Terry Hatter Jr. of the U.S. District Court for the Central District of California also ordered the defendants to pay $614,418 in restitution.

Between 2006 and 2013, the defendants submitted more than $1.5 million in claims to Medicare and received $783,756 in reimbursement, according to evidence presented at trial.

Evidence showed the defendants paid illegal kickbacks to patient recruiters for referrals and physicians for fraudulent prescriptions — primarily for expensive, medically unnecessary power wheelchairs. — Jonathon Shacat

Stryker to Buy Sage Products For Nearly $2.8B in Cash

Stryker has agreed to pay almost $2.8 billion in cash to Madison Dearborn Partners for Sage Products, aiming for growth of disposable products targeted at reducing "never events," primarily in intensive care and medical-surgical hospital settings.

The deal is expected to close in the second quarter of this year. The transaction includes an anticipated future tax benefit exceeding $500 million, Stryker says.

Sage develops, manufactures and distributes a range of products, covering oral care, skin preparation and protection, patient cleaning and hygiene, turning and positioning devices and heel care boots.

Sage, headquartered in Cary, Ill., had sales of $430 million in 2015, representing 13 percent organic growth over the prior year, says Lawrence Biegelsen, a senior analyst with Wells Fargo Securities.

"We see the deal as somewhat expensive, but think the strategic rationale makes sense and fits within Stryker's M&A strategy. Ultimately, we think that the purchase price is justifiable if Sage can maintain double-digit growth as part of Stryker," he adds. — Jonathon Shacat

MDUFA, *from Page 1*

The assessment showed that three of the projects and part of another project were completed in time to allow for data collection and analysis of initial results, including:

- The use of a new online issue reporting and tracking system on the QM program site;
- Completion of mandatory training on premarket review systems, and awareness of a newly designated cadre of IT experts;
- Deployment and collection of Kirkpatrick metrics; and
- Awareness of new informal training policies and procedures.

However, there was insufficient time to assess both the initial results of most of the implementation projects, as well as the long-term outcomes of any of them.

The assessment was part of FDA's performance commitments under the 2012 reauthorization of the Medical Device User Fee Amendments. Read Booz Allen's report here: www.fdanews.com/02-16-FDAReport.pdf. — Jonathon Shacat

Scopes, *from Page 1*

- Requires the agency to prioritize updates to its guidance that will clarify when manufacturers are required to seek FDA clearance to market modified devices.

Last month, an investigation led by Murray determined that the FDA's regulatory system for monitoring the safety of devices failed to quickly identify and resolve the spread of antibiotic-resistant infections linked to the duodenoscopes (*IDDM*, Jan. 18).

Murray said the investigation also found evidence that certain manufacturers failed to properly test whether the device could be cleaned reliably between uses. Further, there was evidence that certain manufacturers failed to seek necessary FDA clearance before marketing devices with modifications that affected the safety and effectiveness of those products.

Following the investigation, Olympus recalled the scopes, and the FDA then cleared a newly redesigned duodenoscope (*IDDM*, Jan. 18). — Jonathon Shacat

Kenya's Nairobi County to Buy More LuViva Devices From Guided

Guided Therapeutics is planning to sell five LuViva advanced cervical scans to the Nairobi County Health Services Sector in Kenya for use in the agency's cancer screening program.

The planned purchase — expected to ship in the first quarter of this year — brings to six the number of LuViva devices purchased by Nairobi County.

An additional seven units are slated for purchase this year, says Guided. When fully implemented, more than 12,000 women a month will be able to be screened.

Gene Cartwright, CEO and president of Guided, says the company will work with Asian and Latin American governments to expand usage of the device to help detect cervical cancer.

Cervical cancer ranks first in cancers affecting women in Kenya. More than 10.3 million women in that country are at risk of developing the disease, according to the World Health Organization and International Cancer Organization Information Centre.

Annually, 2,454 women are diagnosed with cervical cancer, and 1,676 die, according to WHO/ICO. An estimated 15 new cases of cervical cancer are diagnosed each week in Nairobi County. — Jonathon Shacat

White House's Cancer 'Moonshot' Draws Praise From Imaging Industry

President Barack Obama has established a new task force as part of an initiative that aims to support cancer research and enable progress for treatment of the disease.

As part of the effort — to be led by Vice President Joe Biden — the FDA will be tasked with developing a virtual Oncology Center of Excellence to leverage the combined skills of regulatory scientists and reviewers. The center will speed the development of companion diagnostic tests, as well as the use of combinations of drugs, biologics and devices to treat cancer.

Also, the National Institutes of Health will invest in developing and evaluating minimally invasive screening assays to enable more sensitive diagnostic tests for cancer. Recent advances in genomic and proteomic technologies have increased the sensitivity of methods to detect markers of the disease.

In an open letter sent to Biden last week, Nelson Mendes, chairman of the board at the Medical Imaging & Technology Alliance, committed to help with the "moonshot" initiative.

"Imaging provides doctors with otherwise impossible views into the anatomy and function of the body, allowing for confident decisions to be made about the best course of treatment. As these technologies advance, they will only become more critical to detecting, treating and ultimately curing cancer," he says.
— Jonathon Shacat

Companies Take Aim At Zika With New Tests

With Zika poised to strike in more and more countries, companies are responding by developing new tests that can identify the virus.

For example, Rockville, Md.-based GenArraytion has developed a polymerase chain reaction-based molecular test to identify the Zika virus. It analyzes samples for dengue, yellow fever, Chikungunya, as well as multiple signatures for the Zika virus in a single test. The test will list for $75 with an initial offer of buy three, get one free, says company spokesman Brad Wills.

Meanwhile, Genekam, a German biotechnology company, has developed a highly sensitive DNA test to detect Zika. The test kit — which can detect this virus in human samples and in mosquitoes — costs roughly $6.

(See **Zika***, Page 6)*

3M to Retain, Invest in Its Health Information Systems Business

3M has decided to retain and invest in its health information systems business after a review of strategic alternatives, including spinning-off or selling the business.

Retaining the business and investing more in it as a part of 3M provides the best opportunity for 3M Health Information Systems to derive greater long-term value, says 3M chief executive officer Inge Thulin.

The unit is rapidly growing. Sales increased 11 percent in 2015 to $760 million, and the business has delivered more than 10 percent compounded annual growth over the past decade.

The unit's portfolio focuses on computer-assisted coding, clinical documentation improvement, performance monitoring and quality outcomes reporting. — Jonathon Shacat

Zika, *from Page 5*

Currently, no therapy or vaccine is available for the Zika virus, which is spread by *Aedes aegypti* mosquitos. Prevention is one possible way to stop spread of the virus, Genekam points out.

"The Zika virus has the potential to become a serious epidemic, with as many four million people risking exposure in the next year if the mosquito population isn't controlled, according to the Pan American Health Organization," says R. Paul Schaudies, CEO of GenArraytion.

PAHO says it anticipates the Zika virus will continue to spread and will likely reach all countries and territories of the region where *Aedes* mosquitoes are found.

The World Health Organization declared a global public health emergency for the spread of Zika last week, calling for a coordinated international response to expedite the development of diagnostic tests. — Jonathon Shacat

The FDA Is Watching: What You Need To Know about Nonconforming Products

Dan O'Leary, president of Ombu Enterprises, explained the requirements for handling nonconforming products during an FDAnews webinar last month. The following is adapted from that event.

When companies investigate product nonconformity, what should they be looking for?

O'Leary: What's the nature of the nonconformity, and why did it happen? Presumably, you've implemented adequate procedures, so this shouldn't have happened. This is going to lead to an understanding of the cause of the problem — that's going to have many of the elements of corrective action.

What are some appropriate statistical tools other than trend analysis?

O'Leary: One of the things that you might be interested in is Pareto analysis, which can help you analyze why these problems are happening, based upon their frequency or the nature of the problems.

You could do a scatter plot, for example. If you think there's a relationship between nonconforming material and some of the nonconforming product and some of the parameters in the production process.

You also might conduct some kind of analysis to determine if there's a difference between shifts. For example, is there a statistically significant difference between the nonconformance rate on first shift versus the second, or summer versus winter, or Monday versus Friday?

When using a contract manufacturing organization for a finished product, what suggestions would you have for managing nonconforming product when the CMO is responsible for its own manufacture and quality system?

O'Leary: If you're using their quality management system, you need to ask how they're going to handle nonconforming material. So, you want to look at all of their procedures.

You want to be very careful that you clearly specify what dispositions they're allowed to make. If they're making nonconforming material, it's probably OK for them to make a scrap disposition, because it's not going to end up in your company. On the other hand, they should not be making use-as-is or concession disposition without your explicit approval.

If they're doing rework or repair, then you have a somewhat similar situation. There's an obligation to document it in the device history record. You need to be clear who's managing the device history record. All of this is usually going to be spelled out in a quality agreement of some sort.

I would look at all of these dispositions, decide which ones the contract manufacturer is allowed to make on its own, as well as which ones require your approval. You need to write it all up — typically in a supplier agreement.

In a procedure for nonconformity and defect awareness, what should be included in defect awareness?

O'Leary: The people doing this kind of work need to have a clear understanding of how to tell the difference between what's conforming and what's nonconforming.

One way is to — on a periodic basis — figure out what kinds of problems you're having and make sure the people who are doing verification and validation activities are aware of, for example, the most recent nonconformances in the last six months.

In some companies, there may be photographs of what nonconforming material looks like, or even there samples of conforming and nonconforming products. We used to do this when I was involved in a lot of work that required hand soldering. We had photographs and models of what a good solder joint looked like and what a bad solder joint looked like. And that's how we trained the inspectors and the people who were doing the job.

BRIEFS

TE Connectivity to Acquire the Creganna

Switzerland-based TE Connectivity is acquiring Creganna Medical for $895 million in an all-cash transaction. Creganna, headquartered in Ireland, designs and manufactures minimally invasive delivery and access devices serving original equipment manufacturers. The acquisition establishes TE as a leading supplier to the fast-growing minimally invasive interventional medical device segment, the company says. Creganna, which is owned by Permira Funds, reported sales of roughly $250 million in 2015.

LivaNova Snags Japanese Approval

Japan's Pharmaceuticals and Medical Devices Agency has approved LivaNova's new generation of full-body magnetic resonance imaging-conditional pacemakers, according to the company. KORA 250 SR and DR pacemakers allow patients to undergo MRI scans on any region of the body. KORA 250 also features the automatic MRI mode, which makes scans safe for patients with pacemakers. It automatically detects the MRI scanner's magnetic field and ensures appropriate pacemaker operation during the scan. After the scan, the device automatically returns to its initial configuration. As a result, KORA 250 minimizes the amount of time that patients experience MRI mode.

Intersect ENT Lands Designation

InEk, the German Institute for the Hospital Remuneration System, has assigned NUB Status 1 for reimbursement of Intersect ENT's mometasone furoate implants for 2016, the company announced. The purpose of the NUB process is to support the introduction of innovative medical products by allowing a limited number of participating hospitals to receive reimbursement. NUB Status 1 is the highest priority designation available, and was only assigned to a minority of product submissions for 2016, Intersect ENT says.

Mauna Kea Expands Deal With Fujifilm China

Mauna Kea Technologies has expanded its partnership with Fujifilm China to commercialize the Cellvizio confocal laser endomicroscope for gastroenterological and pulmonary applications. With the recent Chinese FDA clearance for Cellvizio 100 series, Fujifilm China now is positioned to launch Cellvizio for bilio-pancreatic applications as part of its leading endoscopic ultrasound range of products, Mauna Kea says. "With our recent agreement with Cook Medical for urologic applications, we continue to further expand our strategic partnerships for a wide range of therapeutic applications for our unique endomicroscopy platform," says Sacha Loiseau, founder and CEO of Mauna Kea.

Insulet to Divest Diabetes Supplies Business

Insulet is selling its Neighborhood Diabetes supplies business to mail order medical supply company Liberty Medical for $5 million in cash. The deal is expected to close in the first quarter of the year. Insulet adds that the transaction will enable the company to direct its resources toward driving continued growth of its OmniPod insulin management system. Danielle Antalffy of Leerink Research says in a note that the move is a positive one, as it allows Insulet to focus on Omnipod while shedding a slower growth business.

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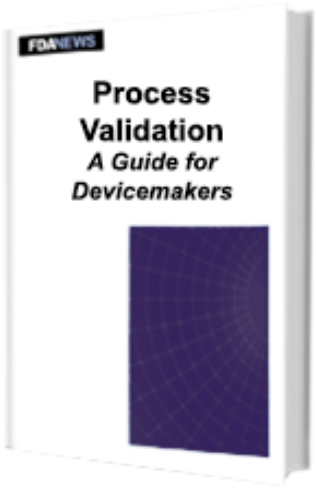

Process Validation
A Guide for Devicemakers

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.

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