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IN THIS ISSUE

FDA Panel Rebuffs Angel Medical's Guardian Implantable Cardiac Monitor

An FDA advisory committee has recommended against approving the premarket approval application for Angel Medical Systems' Guardian implantable cardiac monitor.

During a meeting last week, the Circulatory System Devices Panel of the Medical Devices Advisory Committee voted 8 to 4 that the device was not safe and 12 to 0 that the device was neither effective nor do the benefits outweigh its risks.

The AngelMed Guardian system is designed to detect rapid changes in the heart's electrical signal caused by a coronary artery occlusion, the precursor to a heart attack.

If an occlusion is detected, the system alerts patients to seek medical care by delivering a series of vibratory, auditory and visual warnings.

The panel reviewed data from a study of 907 high-risk subjects who had experienced a previous heart attack or acute

(See **Guardian***, Page 2)*

CDRH to Have 3 Divisions Under Program Alignment

CDRH soon will have three medical device divisions that are responsible for monitoring and managing the entire establishment inventory both domestically and globally, under its new program alignment.

That represents a significant change from the existing structure, said Sean Boyd, acting director of CDRH's Office of Compliance, during last week's FDAnews Medical Device Quality Congress in Rockville, Md.

Currently, the FDA's field operation is organized geographically with five regional offices — Pacific, Central, Northeast, Southwest and Southeast — and 20 district offices.

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Guardian, *from Page 1*

coronary syndrome event. All subjects were implanted with the AngelMed Guardian system and assigned to have the alerting feature of the device either turned on or off for a six-month period.

The trial's primary safety endpoint was met – demonstrating a greater than 90 percent freedom from system-related complications based on six months of data.

But, the trial failed to meet the primary efficacy outcome by reducing the rate of a composite of:

- Cardiac or unexplained death;
- New Q-Wave myocardial infarction, determined as being a new Q-Wave in the six-month ECG that was not present before subject randomization; or
- Arrival at a medical facility for a confirmed thrombotic event more than two hours after detection of ST segment changes exceeding the detection threshold by the Guardian.

In testimony at the meeting, Michael Carome, director of Public Citizen's Health Research Group, urged the panel to recommend that the FDA not approve the device.

Not only did the trial fail to show that the device was effective, but the conduct of the study was marred by serious protocol violations that undermined its integrity and validity, he said.

The FDA said the quality of the ECG data and the inconsistency of the Q wave results caused the sponsor to terminate the study earlier than the protocol required — a move that potentially caused bias.

The device also poses serious risks that are unacceptable given the lack of evidence of effectiveness, said Carome.

"The only reasonable course of action for the FDA is to reject the Guardian System. Allowing this device on the market would be a reckless decision," he said.

Following the meeting, Andrew Taylor, president and CFO of the company, expressed disappointment, but that the devicemaker believed the benefits of the device outweigh the risks.

The recommendation against approving the AngelMed Guardian System came a day after the panel voted to support Abbott's drug-eluting coronary stent Absorb — a device that, if approved, would become the first fully bioresorbable vascular scaffold in the U.S. (*see story, page 6*).
— Jonathon Shacat

CDRH*, from Page 1*

In the future, the U.S. will be one region instead of five. The three device divisions will be located in areas of the country where members of medical device industry are clustered, Boyd said.

"We are not looking to move investigators from one location to the next," he said. "There might be some instances where there is some more travel required where we don't have a device investigator in a particular area right now."

The FDA's Office of Regulatory Affairs is moving forward with its program alignment, and the agency plans to implement the new regulatory organizational model next year. Officials are working to finalize details, such as the job description of investigators, compliance officers or managers within ORA, he said.

"This the most dramatic change that ORA has experienced maybe in its history, so it will take time to communicate and ensure that people understand what is trying to be accomplished," he added.

The planned changes under program alignment come as new data shows the FDA has been conducting more quality systems inspections at foreign devicemakers (*see story, page 6*).
— Jonathon Shacat

FDA Cracks Down on Companies for Selling Zika Tests Without Approval

The FDA is taking aim at entities marketing Zika tests without approval, firing off letters to three companies so far this month.

In "it has come to our attention" letters, the FDA calls out MD Biosciences for marketing its Zika Virus RNA by RT-PCR Assay as well as Texas Children's Hospital and Houston Methodist Hospital for marketing their Zika Direct Test.

MD Biosciences made its test available on Feb. 29, saying the assay can be performed in a few hours. However, MD Biosciences later announced that testing services will not be offered, pending clarification with the FDA regarding "any pre-market approval requirements pertaining to this assay."

Eddie Moradian, CEO of MD Biosciences, says the company has no comment, "except that we welcome the discussion and will be fully cooperating with the FDA regarding our laboratory developed test."

Texas Children's and Houston Methodist announced Feb. 23 the release of "the country's first hospital-based rapid tests for the Zika virus." They say the tests were developed by pathologists and clinical laboratory scientists "in a matter of weeks."

The pair are working collaboratively with the FDA and sharing information regarding the tests' design, validation and performance characteristics, says spokeswoman Christy Brunton.

"The FDA has not asked us to discontinue use of our tests. Currently, our rapid Zika tests are only offered to our registered patients," she tells *IDDM*.

In a third letter, the FDA names First Diagnostic for marketing its ATFirst's One Step Zika Antibody Test, which is intended for simultaneous detection and differentiation of IgG and IgM antibodies to Zika virus in human serum, plasma or whole blood.

However, Jonathan Adam Barash, president of First Diagnostic, says its test is in the development phase and not being marketed.

"We were shocked to receive the letter, actually," Barash tells *IDDM*. He says he subsequently participated in a conference call with FDA officials, who later acknowledged that the agency mistakenly thought the company was marketing the test. However, the FDA would not confirm Barash's statement.

Tara Goodin, FDA spokeswoman, says the agency encourages laboratories to develop Zika tests, but the tests should not be used for clinical diagnoses without approval, clearance or authorization.

"Because of the serious public health impact of the Zika virus in certain populations, the FDA is requesting that those with tests for the detection of Zika virus in patient samples submit a request for emergency use authorization to the agency," she tells *IDDM*.

Read the letter to Texas Children's Hospital and Houston Methodist Hospital here: www.fdanews.com/03-14-16-Zika-Letter1.pdf, the letter to MD Biosciences here: www.fdanews.com/03-14-16-Zika-Letter2.pdf, the letter to First Diagnostic here: www.fdanews.com/03-14-16-Zika-Letter3.pdf. — Jonathon Shacat

NIH, FDA Release Draft Clinical Trial Protocol Template

The FDA and the National Institutes of Health are seeking comments on a new draft clinical trial protocol template for NIH-funded investigators.

The template is intended to be used for Phase 2 or 3 clinical trial protocols that require IND or IDE applications.

The template was developed to standardize clinical trial protocols to help investigators plan better protocols to avoid trial delays.

The guidance bridges definitions in the ICH E6 Good Clinical Practices guidance and the ISO Clinical Good Clinical Practice guideline (ISO 14155:2011).

Comments on the draft protocol template are being accepted until April 17 at: http://grants.nih.gov/grants/rfi/rfi.cfm?ID=54. — Tamra Sami

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FDA Offers Pointers for Labelers On Submitting Data for GUDID

While Sept. 24 might seem far off, the FDA is urging labelers not to be complacent in meeting that target date for submitting necessary information into the Global Unique Device Identification Database.

That message came loud and clear in a March 10 workshop put on by the agency on UDI deadlines. During the workshop, presenters noted that device identification information can be submitted manually via the GUDID web interface or as XML files using the HL7 SPL method.

Each option has its advantages, noted Indira Konduri, GUDID program manager. The web interface is easy to use and is suitable for smaller companies that don't have large volumes of records. SPL is better if a company has thousands of submissions; however, that process is more resource intensive and requires more upfront time.

The FDA is allowing labelers to get a GUDID account based on UDI compliance dates, which are being phased in by device class. The program took effect in 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 (*IDDM*, Jan. 29).

The GUDID database requires UDI-related data, including elements associated with the device label, packaging, lot, serial number and expiration date, said Mohan Ponnudurai, director at Sparta Systems.

Ponnudurai added that companies should look now for an automated way to gather these data elements for higher classification devices to get ahead and iron out any issues before the deadline for Class 1 submissions.

"When the EU brings [its] version of UDI, companies will be much more prepared technically and operationally to manage these processes effectively," he told *IDDM*.
— Jonathon Shacat

Sensimed Lands FDA Nod For 'Smart' Contact Lens

The FDA has given the green light to Switzerland-based Sensimed AG for its Triggerfish, a contact lens embedded with a sensor that detects changes in an eye's volume.

The FDA says the device could help identify the most critical time of day to measure intraocular pressure. Elevated eye pressure is associated with nerve damage common in glaucoma.

"IOP varies throughout the day and may not be abnormally high when the patient is at an eye care professional's office having an eye exam," the FDA says.

The Triggerfish is worn for a maximum of 24 hours, transmitting data wirelessly from the embedded sensor to an adhesive antenna that transfers information to a portable data recorder.

The device does not actually measure intraocular pressure, and is not intended to be a diagnostic tool.

The approval is based on clinical data showing an association between the device output and intraocular pressure fluctuation. The most common temporary side effects were pressure marks from the contact lens, red eyes and cornea irritation.

The FDA reviewed the data through the *de novo* premarket review pathway.
— Jonathon Shacat

Canon Acquiring Toshiba's Medical Unit for $6B

Canon has agreed to pay roughly $6 billion to acquire Toshiba's medical systems unit.

In December 2015, Toshiba announced plans to sell the unit — in part to improve the company's financial strength — following the resignation of its CEO over accounting irregularities.

The unit's portfolio includes diagnostic X-ray systems, magnetic resonance imaging systems, diagnostic ultrasound and diagnostic nuclear medicine systems. The transaction needs sign off from regulatory bodies. — Jonathon Shacat

FDA Inspections Rising at Foreign Facilities, Dropping Domestically

Newly released government data shows the FDA has been conducting more quality systems inspections at foreign devicemakers to keep up with rapidly growing inventory at those manufacturers.

From 2014 to 2015, foreign inspections climbed more than 4 percent to 620, while domestic inspections fell more than 8 percent to 1,484, the data show.

In time, the goal is to achieve parity in the number of foreign and domestic inspections that are performed by FDA investigators in any given year, said Sean Boyd, acting director of CDRH's Office of Compliance.

Meanwhile, overall inspections decreased nearly 5 percent to 2,104 from 2014 to 2015, according to the data.

The decrease in the number of surveillance inspections is the result of shifting resources from foreign to domestic inspections, Boyd said.

"There is more time required to plan and conduct foreign inspections compared to domestic, as well as shifting resources towards risk-based approaches and site selection of firms that we believe need more interaction with the FDA to resolve issues," he said.

CDRH sent 121 warning letters in 2015, the same amount as the year before. CRDH also issued 924 Form 483s, a decrease of more than 16 percent from the previous year. Those 483s contained 3,525 observations, a decrease of nearly 6 percent versus 2014.

Production and process controls and corrective and preventive actions continue to be the most frequently cited QS subsystems, the FDA says.

China led the way among the top five locations last year with 126 inspections, followed by 90 in Germany, 44 in Japan, 42 in Canada and 35 in United Kingdom, according to the data. The top three countries for 2015 remained the same as in 2014.

Read the data here: www.fdanews.com/03-17-16-FDAMDQS.pdf. — Jonathon Shacat

FDA Advisory Panel Supports Abbott's Absorb

An FDA panel last week threw its support behind Abbott's drug-eluting coronary stent Absorb, which, if approved, would become the first fully bioresorbable vascular scaffold in the U.S.

The Circulatory System Devices Panel of the Medical Devices Advisory Committee voted 9 to 0 — with one abstention — that the benefits of Absorb outweigh the risks. The panel also voted 9 to 1 that Absorb is safe and 10 to 0 that the device is effective.

The panel's review was based in part on data from a trial of 2,000 people that showed the investigational device is comparable to Abbott's Xience metallic drug-eluting stent.

If approved, Absorb will compete against Xience, Medtronic's Resolute and Boston Scientific's Synergy and Promus, says Lawrence Biegelsen, a senior analyst with Wells Fargo Securities.

He does not expect the product to capture significant market share, given its shortcomings, such as the difficulty to use, the numerically worse outcomes versus Xience and the higher rates of stent thrombosis.

In Europe, Absorb accounts for about 20 percent of Abbott's total DES sales, or $143 million, in 2015. "In the U.S., we estimate Absorb will capture about 5 percent of the total DES market, although our estimate may prove conservative if the post-approval data and experience with Absorb improves," Biegelsen adds.

Abbott submitted its premarket approval application for Absorb in mid-2015. Based on the panel's recommendations, Biegelsen says he expects approval of the device in mid-2016.
— Jonathon Shacat

Israeli Team Develops Device That Shortens Chest-Tube Insertion Time

A team in Israel has developed a device that shortens the amount of time it takes to insert a chest tube from 10 minutes to less than 30 seconds.

ThoraXS allows for quick access to the pleural space separating the lung from the chest wall. It was developed by a team from Hebrew University's Alexander Grass Center for Bioengineering, the Hebrew University of Jerusalem and the Hadassah Medical Center.

ThoraXS's market potential is estimated at $300 million annually, says Yaakov Nahmias, director of the Hebrew University's Alexander Grass Center for Bioengineering.

Innovations produced by the Biodesign program participants are commercialized by Yissum, the technology transfer company of the Hebrew University of Jerusalem, and Hadasit, the technology transfer company of the Hadassah Medical Center. — Jonathon Shacat

Olympus Issues Updated Reprocessing Instructions for Duodenoscopes

The FDA is calling on healthcare facilities to immediately implement employee training for updated reprocessing instructions for two Olympus duodenoscope models.

The updated instructions for the TJF-160F and TJF-160VF models include a more rigorous protocol for precleaning, manual cleaning and high-level disinfection procedures — specifically, additional flushing, brushing and increased flushing volume.

They also incorporate the use of an additional reusable brush to manually clean the distal end of the scope, including the elevator recess area. This new brush can be sterilized by autoclave following use, as outlined in the updated reprocessing manual.

Olympus and two other companies that make duodenoscopes — Pentax and Fujifilm — have faced intense scrutiny after reports of antibiotic-resistant infections in Chicago, Pittsburgh, Seattle and Los Angeles. Early last year, the FDA revealed that between January 2013 and December 2014, it had received 75 reports involving about 135 patients suffering from carbapenem-resistant Enterobacteriaceae transmissions linked to these devices.

All three companies received warning letters last year for a range of problems related to duodenoscopes, including failure to inform the FDA in a timely manner about patient injuries (*IDDM*, Aug. 21, 2015).

In January, the FDA granted Olympus with clearance for its TJF-Q180V duodenoscope with modifications to the device's design and labeling (*IDDM*, Jan. 18).

Read the FDA's notice here: www.fdanews.com/03-17-16-FDAOlympus.pdf. — Jonathon Shacat

Teleflex Recalls Intra-Aortic Balloon Pump Catheters

Wayne, Pa.-based Teleflex is recalling 47,140 units of its Arrow International intra-aortic balloon pump catheters and percutaneous insertion kits following reports of serious adverse events.

The company initiated the recall because the sheath body could disconnect from its hub. Separation may result in "significant blood loss or exsanguination" or "loss of intra-aortic balloon pump treatment," Teleflex says.

The recall — which the FDA has deemed Class 1 — follows 13 reports of adverse events, including six serious injuries and one death, according to an agency notice issued March 11.

The units were distributed to hospitals, clinics and medical centers worldwide. Teleflex initiated a worldwide recall on Feb. 9 and informed distributors and customers in a letter dated Feb. 11.

Teleflex could not be reached for comment by press time. Read the company's recall notice here: www.fdanews.com/03-14-16-Teleflex-Recall.pdf. — Jonathon Shacat

BRIEFS

BD, Apax to Form $500M Joint Venture

Becton, Dickinson and Company has entered an agreement to sell 50.1 percent of its Respiratory Solutions business to Apax Partners to form a joint venture. The joint venture, which will operate as an independent company, will consist of Respiratory Solutions in its entirety, including Ventilation, Respiratory Diagnostics, Vital Signs and Airlife. BD will maintain a non-controlling minority stake in the JV. The transaction falls just under $500 million and is expected to be completed by late fiscal year 2016 or early fiscal year 2017. BD expects a share reduction of $0.10 to $0.14.

Prism Medical Nabs CE Mark

Prism Medical has secured the CE mark for its ProteXsure Safety Capsule System, intended for the prevention of needle stick injuries. The approval is the first indication for the company's Prism platform. Globally, there are 3.5 million reported cases of NSI's every year.

Edwards Lifesciences Secures Approval

The Japanese Ministry of Health, Labor and Welfare has granted approval to Edwards Lifesciences' SAPIEN 3 transcatheter heart valve for the treatment of severe symptomatic aortic stenosis. The device is approved in 20-, 23-, 26 and 29-mm sizes and features an outer skirt seal to prevent paravalvular leak. The valve snagged commercial approval in the U.S. in June 2015 and in Europe in January 2014. A full product launch is expected toward the end of the year.

Roche Introduces DISCOVERY Yellow Kit

Switzerland-based Roche has launched the DISCOVERY Yellow Kit, the latest addition to its suite of VENTANA modular-based detection kits for uncovering cancer biomarkers and tumor cell populations. The kit features alkaline phosphatase-based detection chemistry and produces a yellow indicator that is not erased during alcohol dehydration, the company says. The kit is intended for use in combination with chromogens for identifying signal co-localization.

Greatbatch Completes Nuvectra Spin-Off

Greatbatch has completed the spin-off of QiG Group, which previously changed its name to Nuvectra. Under a long-term supply agreement, Greatbatch will manufacture Nuvectra's first implantable device, the Algovita spinal cord stimulation system, which is approved in the U.S and Europe. Nuvectra will focus on neurostimulation technology.

MHRA Warns of Hearing Aid Batteries

The UK's Medicines and Healthcare products Regulatory Agency is warning that certain ZeniPower mercury-free hearing aid batteries may explode. No injuries have been reported through the MHRA's Yellow Card Scheme safety monitoring system, the agency says. Due to a manufacturing fault, there is a low risk of the batteries exploding during use or if depleted, says John Wilkinson, MHRA's director of medical devices. The affected batteries have best before dates of August 2018 and September 2018. No other batches are affected.

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Cybersecurity, Privacy and Security Guidance for Medical Device Manufacturers

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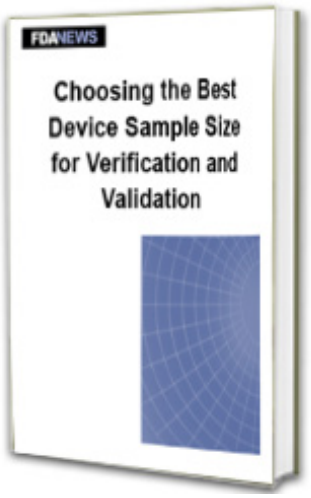

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