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IN THIS ISSUE

India to Expand Price Caps on Medical Devices

Despite ongoing pressure from the United States, Indian officials said they plan to cap prices for an increasing number of medical devices.

In September 2017, the U.S. Trade Representative urged India not to expand existing price controls to include additional medical devices. However, Indian officials told the USTR last month they would not to make such a commitment, Reuters reported.

The initial price caps, imposed in February 2017, capped prices of some high-end heart stents at less than $450. The same devices cost $3,000 prior to the introduction of the caps.

The NPPA is considering caps on three additional devices used to surgically treat heart conditions, saying in a Feb. 26 letter to the country's health ministry that the three devices—cardiac balloons, catheters and guide-wires—sometimes cost more than the stent itself.

(See **India***, Page 2)*

EU Regulators Release Updated Guidance on UDI Changes

The European Union's Medical Device Coordination Group released a trio of guidances that clarify devicemakers' responsibilities for implementing unique device identification systems under the EU's new Medical Device Regulations.

Along with guidance on the basic attributes for a device identifier (DI), the group released documents on the database and the architecture for the new UDI system.

The guidance clarifies that the Basic UDI-DI is a unique numeric or alphanumeric code specific to a model of device and allows the unequivocal identification of the device. As such, it is the main key in the database and includes relevant documentation to connect devices

(See **UDI***, Page 4)*

Abbott Yanks Xience Alpine Stents in India

In response to price controls imposed by India's National Pharmaceutical Pricing Authority, Abbott pulled its Xience Alpine drug-eluting stent from the Indian market.

The move comes in response to price caps that cut prices by as much as 75 percent for some drug-eluting stents.

Medtronic also notified the NPPA of its intent to withdraw its Endeavor Sprint coronary stent from the Indian market.

In response, the NPPA posted a notice on its website that said manufacturers wanting to withdraw products from the market must give six months notice and would need to issue a notice in at least two local newspapers.

Abbott, Medtronic and Johnson & Johnson control the lion's share of the drug-eluting stent market in India, and analysts had predicted that multinational devicemakers might stop offering their more innovative products if more price caps were imposed. Local media reported that Abbott said it also won't launch its next generation drug-eluting stent, the Xience Sierra, in India.

Abbott began notifying hospitals and healthcare providers in India of the planned discontinuation last year. The company said the price caps make it an "unsustainable business."

"We don't believe that price caps are a solution, and these will have a negative effect on the industry's ability to bring innovations to patients in India," Abbott said.

India, *from Page 1*

The NPPA also asked that intra-ocular lenses used during eye surgery be added to the list of devices with caps on the cost to consumers.

The USTR is considering ways to apply pressure to limit caps and is currently reviewing India's eligibility under its Generalized System of Preferences (GSP), a preference program that offers duty-free imports to developing countries. India is the largest GSP beneficiary nation, with $5.6 billion in annual duty-free imports.

According to the USTR, India was the United States' 18th largest goods export market in 2016, with exports of $21.7 billion, including $1.3 billion in medical and optical instruments.

India has traditionally been an attractive market for global medical device manufacturers. According to the U.S. International Trade Commission, an estimated 70 percent of India's medical device market is supplied by imports, 30 percent of which came from the United States in 2016. Imports make up 60 percent of India's stent market. The United States was the leading provider of stents to India from 2011 to 2016.

India's medical device market, estimated at $5 billion, has attracted several large U.S. healthcare companies, including Abbott, Boston Scientific, Johnson & Johnson and Medtronic, but the imposition of further price caps may scare those and other companies away from the previously lucrative Indian healthcare market.
— Donna Scaramastra Gorman

IMDRF Acts on Australia's Proposal for Personalized Devices

Following up on a proposal from Australia's Therapeutic Goods Administration, the International Medical Device Regulators Forum released a new consultation on personalized medical devices following its March meeting in Shanghai.

The aim of the consultation is to develop consistent definitions to describe devices intended for a particular individual.

"It is now possible to produce medical devices that are individualized, for example, using additive manufacturing (3D printing) methods based on CT scans, on a commercial scale," the document notes.

The draft makes a distinction between personalized medical devices and custom-made medical devices. It clarifies that patient-specific devices are made by an industrial manufacturing process according to the written request of an authorized healthcare provider but are not considered custom-made.

The guidance also suggests clear definitions for patient-specific devices and adaptable devices. Specific design characteristics refer to unique design specifications based on an individual's specific anatomy (*IDDM*, April 16).

TGA Conducts Product Safety Review of Ventilators

Australia's Therapeutic Goods Administration plans to conduct a product safety review on ventilators used in high-care hospital settings for long-term therapy of intubated patients.

The review will initially examine 18 of the most commonly used ventilators, but more will be added over time, the agency said. Products included in the initial review are manufactured by Draeger Medical Australia, GE Healthcare Australia, Getinge Australia, Medtronic, Philips Electronics, and Resmed.

The TGA has been collecting information since June 2017 on a range of safety issues such as unresponsive touch screens, unexplained spontaneous shut downs, auto-cycling or auto-triggering, power on and off difficulties, oxygen sensor malfunctions and issues related to software that include interface usability and data capture.

Long-term use is normally associated with integral or separate humidifiers, and the review does not include ventilators used to transport or in home settings, the agency said.

The TGA has asked sponsors to provide the following information:

- Evidence that the ventilators meet the ventilation delivery and monitoring specifications published in the Instructions for Use, which should include evidence that the breathing circuits recommended for use with this ventilator are valid;
- For ventilators that are intended for pediatric patients, a clear clinical justification and validation of why tidal volume delivery specifications are acceptable and safe;
- Post-market data; and
- Which breathing circuits are suitable for use with the ventilator.

Australia Forges Ties To Focus on Custom Devices

The Australian Research Council is launching a new research hub to focus on advanced manufacturing for medical devices.

The ARC Research Hub for Advanced Manufacturing of Medical Devices will be located at the University of Queensland and will look for opportunities to optimize designs of existing customized devices and investigate new ways to improve clinical outcomes.

The research hub's overall goal is to transform Australia's medical technology sector by developing cost competitive technologies, particularly customized devices tailored to individual patients.

ARC CEO Sue Thomas said the research hub will make the production of devices like endovascular stent grafts better, faster and more efficient.

(See **Research***, Page 4)*

UDI, *from Page 1*

with the same intended purpose, risk class and essential design and manufacturing characteristics.

The Basic UDI-DI is independent from the packaging/labeling of the device.

Technical documentation assessment certificates and product verification certificates are to be included with the Basic UDI-DI information as well as the name, model and type, the intended purpose of the device, manufacturer instructions for use and device risk classification. The conformity assessment declaration should contain the Basic UDI-DI and the product and trade name, product code, and catalog number to trace the device.

A new UDI-DI is required whenever there is a change that could lead to misidentification of the device. For example, a new UDI-DI would be needed if there were changes to the trade name, device version or model, label for single use, sterile packaging, quantity of devices or changes in color or other critical parameters.

Although not formally European Commission documents, the MDCG draft guidances were endorsed by the EU UDI Work Group. The European Commission is expected to issue a Q&A paper on the UDI requirements shortly.

The main provisions on establishing the UDI system under the new regulations for medical devices and in vitro diagnostics are contained in Chapter III of the MDR and Annex VI of the IVDR.

Database Requirements

Devicemakers must also provide additional information for the UDI database such as the quantity of devices per package; information for controlling devices such as expiration date, lot numbers and serial numbers; name and address of the manufacturer; the single registration number (SRN); the name and address of the authorized representative; the device nomenclature code, risk, class, trade name, electronic instructions for use; and labeling information, along with other requirements.

Additional database elements are required if devices are reprocessed single-use devices.

The guidance includes a table of definition and formats of core elements to be provided to the UDI database.

Read the guidance document here: www.fdanews.com/05-01-18-ECUDI.pdf.

Read the database guidance here: www.fdanews.com/05-02-18-UDIDatabase.pdf.

Research, *from Page 3*

ARC will commit AUS$2.8 million over five years for the research hub through its Industrial Transformation Research Program which brings together academic researchers and industry to solve specific challenges including for advanced manufacturing, cybersecurity, medical technologies and pharmaceuticals.

The project will investigate the feasibility of novel materials, design alterations and innovative manufacturing and processing technologies along with better understanding clinical problems through modeling, experimentation and discussions with clinicians. The project is expected to deliver pathways for future projects in the areas of design, materials development, manufacture and clinical delivery.

The hub's impacts "will extend from the obvious direct health outcomes for Australians through these advances, but also to job creation and economic benefits—providing small and medium enterprises with new technologies and skills that can be transferred to the manufacture of products for other sectors," Thomas said.

PEOPLE ON THE MOVE

Peter Macfarlane joined the clinical advisory board of electrocardiology device manufacturer **HeartSciences**. Macfarlane has spent over 40 years in the ECG interpretation field and is currently president of the International Society of Computerized Electrocardiology.

483 Roundup: Devicemakers Cited for Complaints, Quality

Grind Guard Technologies: The FDA hit Grind Guard Technologies with a Form 483 for failing to review all complaints, faulty procedures for suppliers and quality audit deficiencies.

After inspecting the company's Clarkston, Michigan facility in January 2018, the agency found that the firm did not properly deal with all complaints. Specifically, it did not evaluate any of a dozen complaints it received to see if they warranted an investigation after reviewing them. The quality system manager confirmed they had not been investigated, but gave no rationale for the reason why.

The agency observed that 4 of 12 complaints reviewed involved a device manufactured by the company getting stuck to the customer's teeth and in some cases requiring professional dental care. The company did not issue a CAPA request form to further investigate the issue.

The firm also had no agreement with suppliers and contractors to alert the company about changes in the product or service it received from them. The quality system manager confirmed the firm had not arranged any contracts with any of its suppliers to address relevant quality issues.

It also did not perform any quality audits. The firm confirmed it had never conducted an internal audit and did not have an audit plan in place.

Lannett Company: The FDA fired a Form 483 at Lannett Company for quality control procedures and batch production and control record shortcomings.

The agency cited its Seymour, Indiana facility, which it inspected in February 2018, for failing to follow responsibilities and procedures for its quality control unit. The firm did not open investigations for all low level complains within their 45 day deadline as dictated by a standard operating procedure in place.

It also had deficient batch production and control records, as not all of them include

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

Tips for Purchasing Controls

The FDA checks supplier purchasing controls during inspections of distributors of finished devices but doesn't inspect suppliers of device components, so some of the oversight is passed along to devicemakers.

There are several things to look at when taking a quick inventory of purchasing controls:

- Are you over reliant on third-party certification of suppliers? Certifying bodies have widely varying standards and FDA will not accept any quality system that does not satisfy its own QSRs;
- Do you have clear documentation that you are conducting performance reviews and supplier inspections and audits, prioritized by risk, when qualifying and monitoring suppliers;
- Do your vendor agreements require that the vendor will notify you of changes occurring at their facility? This should include changes to sub-suppliers and sub-tier components; and
- Do your purchasing controls cover your sister facilities and other companies that fall under the same corporate umbrella? Violations of purchasing controls regulations are actually more common when dealing with internal suppliers than with external suppliers. If sister facilities are under different quality systems, manufacturers must take the same quality control measures with them as they would with external suppliers.

An effective purchasing control system should address each of the following activities:

- Planning;
- Election of potential suppliers;
- Supplier evaluation and acceptance;
- Finalization of controls; and
- Delivery, measurement and monitoring, and feedback, including in the corrective and preventive action process.

Excerpted from the *FDAnews* management report: *Troubleshooting Your Quality System: A Guide to Five Devicemaker Quality Compliance Traps*.

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documentation of the accomplishment of each step in packing. For example, its general packaging procedure stated that the number of desiccants needed per bottle on the start-up fill check sheet should be reported on its production batch record. However, it gave no reason as to why desiccant start-up checks are only documented if more than one bottle is required.

In addition, the investigator observed production personnel wiping and removing an insect from a raw material as the material was being threaded through an oven. The firm's standard operating procedure — which requires the preservation of an area where a deviation or event occurs — was not followed in the observed situation.

SPR Therapeutics: SPR Therapeutics drew a Form 483 for inadequate complaint handling procedures.

The FDA inspected the firm's Cleveland, Ohio facility in February 2018. The firm claimed that it had contacted a supplier regarding a complaint and determined the cause was likely a manufacturing issue, but could provide no communication or investigation documentation of it.

It also did not properly establish its supplier qualification and monitoring procedure. It was unclear how its pre-audit questionnaires for suppliers are used and analyzed. One pre-audit questionnaire answered by a supplier included negative responses on specific quality questions, but the firm did not document its acceptance of the responses or put in place appropriate monitoring activities for the supplier.

Read the Grind Guard Technologies Form 483 here: www.fdanews.com/05-02-18-grindguardtechllc483.pdf.

Read the Lannett Company Form 483 here: www.fdanews.com/05-02-18-lannettcoinc483.pdf.

Read the SPR Therapeutics Form 483 here: www.fdanews.com/05-02-18-sprtherapeuticsinc483.pdf.

Wearable Fitness Monitors May Be Useful in Cancer Treatment, Study Says

Wearable fitness trackers — medical devices that monitor a person's steps taken per day — could be useful tools for assessing and treating cancer patients, a University of Texas Southwestern study suggested.

The pilot study, which appeared in the *Journal of Clinical Oncology: Clinical Cancer Informatics*, involved older cancer patients who wore physical activity monitors over a span of ten weeks or more and used them to measure their functional status, a key part of clinical encounters and a factor in treatment decisions, the researchers said.

The data collected from the monitors correlated well with clinician assessments of the patients, according to Arjun Gupta, the first author of the study.

"We found that patients could successfully use the wearable devices over a prolonged period. Measured steps per day differentiated performance status with great sensitivity, and correlated well with multiple quality-of-life surveys," he said.

Gupta said the attrition rate in the study was low, and patients reported a positive experience using the device, indicating the new-generation devices are adoptable "even in cancer patients, who may be elder and less technologically literate."

The study involved 24 patients being treated for a variety of cancers including lung, breast and gastrointestinal cancers. 23 of the patients met the goal set for feasibility for using the devices.

"My hope is that we can use wearable devices in large cancer clinical trials. That way, we can see what the true effect of different cancer treatments are on patients' physical activity," the study's co-author Muhammad Beg said. — James Miessler

APPROVALS

Gastrointestinal Pathogen System Receives CE Mark

Applied BioCode's MDx3000 gastrointestinal pathogen testing system received a CE Mark, allowing its distribution in Europe.

The MDx3000 automates the PCR amplification, hybridization and detection steps of molecular testing and can process up to 3,384 results in an 8-hour shift.

The system can process up to 3 different assay panels in the same session and can mask any test results within individual panels for tests not ordered by the patient.

Materialise Cleared For 3D Modeling Software

The FDA granted 510(k) clearance for Materialise's Mimics inPrint Software, which is used to create 3D anatomical models from medical image data.

The software outputs the models to a 3D printer at the point-of-care and is used to assist practitioners with consultation, patient diagnostics and planning for complex surgeries.

It is also used to enhance education and communication with the patient and between multidisciplinary teams.

Shockwave Wins CE Mark For Low-Profile Catheter

Shockwave Medical's Shockwave S4 peripheral intravascular lithotripsy catheter, used for treating calcified lesions in below-the-knee arteries, won a CE Mark.

The device uses sound waves to break up calcified lesions blocking vessels and is designed to minimize trauma to the artery.

The S4 includes a battery-powered generator and hand-held connector cable, as well as a catheter which houses the sonic emitters within an integrated balloon.

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

Approvals, *from Page 7*

Sandstone Diagnostics' Trak Volume Cup Cleared by FDA

The FDA gave 510(k) clearance for Sandstone Diagnostics' Trak volume cup, a new addition to its Trak male fertility testing system.

The volume cup allows patients to measure their semen volume and diagnose hypospermia.

The cup is coated with a liquefaction enzyme that breaks down sample viscosity and allows the user to funnel the sample into a graduate measurement compartment for an accurate reading of semen volume.

FDA Expands Indication For Drug-Coated Balloon

The FDA approved Medtronic's In.Pact Admiral drug-coated balloon for treating long superficial artery lesions in patients with peripheral artery disease.

The approval was based on data from complex lesion imaging cohorts from the company's global study.

The device can treat lesions up to 360mm and is suitable for treating lesions beyond 180mm, frequently involving in-stent restenosis and chronic total occlusions.

Blink's Neuromuscular Monitor Receives 510(k) Clearance

Seattle-based startup Blink Device Company received marketing clearance for its TwitchView monitor for neuromuscular blockade.

TwitchView is the first standalone electromyographic based monitor in the United States, according to the company. The quantitative monitor functions accurately regardless of patient positioning.

Elise Hyman, a former director at GE Healthcare specializing in perioperative care, is leading Blink's marketing and sales.

FDA Grants Clearance for Multi-Purpose Digital Imaging System

The FDA gave 510(k) clearance to Agfa for its Dr 800 multi-purpose digital imaging system, which covers radiography, fluoroscopy and advanced clinical applications.

The device comes with Dynamic Musica software that enhances noise suppression, brightness control and veiling glare reduction.

The device can handle a full range of radiography, including static exams and tilting exams, and fluoroscopy exams, including barium studies, arthrograms, cystograms, myelography and catheter placement.

Tandem Diabetes Care Gets CE Mark for Insulin Pump

A San Diego medical device company, Tandem Diabetes Care, received a CE Mark for its t:slim X2 insulin pump with Dexcom G5 mobile continuous glucose monitoring (CGM).

The device includes a large color touchscreen, watertight construction, USB connectivity and a rechargeable battery. It is the first CGM-enabled pump that lets users make treatment decisions without pricking their finger.

The company plans to launch the pump commercially in select global markets in the second half of 2018.

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EU MDR Compliance: *A Checklist for Meeting Manufacturing, Safety and Performance Requirements*

The new EU Medical Device Regulation is massive… complex… and confusing… and you must be ready to comply by May 26, 2020.

When the European Union revised its system of rules for medical device manufacturers in 2017, it replaced a longstanding set of directives on specific topics with one large document that covers all aspects of making devices in EU countries.

Not only did they consolidate all the rules, they gave them greater weight. Previously, medical device directives provided guidance but did not have the force of law. The new MDR, however, contains mandates that are legally enforceable by EU member countries.

The FDAnews report **EU MDR Compliance** can help. Our editors have combed through the regulations, picking out the most minute compliance points and building them into a checklist of 200+ requirements you can use to confirm that you are satisfying all the EU mandates for device manufacturing. The report provides:

- Definitions of key terms in the EU MDR
- Knowing where to find specific requirements in the 150+ page regulation
- Checklists that walk you through every aspect of manufacturing, safety and performance requirements
- A training tool for employees new to the regulations

EU MDR Compliance: *A Checklist for Meeting Manufacturing, Safety and Performance Requirements* is the tool that collects all the requirements, explains them and itemized them in an easy-to-use form to ensure compliance.

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Supplier Quality Metrics for Devicemakers: *Predicting and Selecting the Best*

Regulators are watching your supplier management practices closely. The FDA's Quality System Regulation (QSR), ISO 13485 and the international Medical Device Single Audit Program (MDSAP) all have specific requirements for purchasing controls and acceptance activities. They expect your suppliers to function as an extension of your quality system. So how do you choose the ones most likely to meet your standards?

An effective supplier evaluation system includes determining your expectations, converting them into measurable characteristics/metrics, defining the measurement method and setting the target you expect suppliers to hit.

In the **Supplier Quality Metrics for Devicemakers** management report you'll learn how to use predictive analysis of such metrics as delivery time, management efficiency and lot acceptance rate to identify suppliers you can count on and spot potential problems in the future. You'll learn:

- Requirements for receiving acceptance
- The difference between a contract manufacturer and a specifications developer and why it matters
- What aspects of your purchasing controls will be evaluated in an MDSAP audit
- How to create a supplier scorecard
- How to evaluate what you receive from suppliers
- Issues to look for in a supplier's complaint records
- How to analyze performance metrics to predict if a supplier is likely to create a problem.

Order your copy of **Supplier Quality Metrics for Devicemakers: *Predicting and Selecting the Best*** and gain a system for predicting and managing supplier conformance with FDA and international standards.

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