International Devices & Diagnostics Monitor

Vol. 3, No. 17
April 24, 2017

IN THIS ISSUE

Senate Committee Sets April 26 For Gottlieb's FDA Confirmation Vote

The Senate Health, Education, Labor and Pensions (HELP) Committee has scheduled April 26 for its vote on the confirmation of Scott Gottlieb to be the next commissioner of the FDA.

At his confirmation hearing earlier this month, Gottlieb said the agency should pursue alternative chronic pain treatments and look toward medical devices as therapy options (*IDDM,* April 10).

He was also grilled over his financial ties to the industry he would be charged with regulating, including former ties with a venture capital firm, New Enterprise Associates, that invested in a company marketing devices for treating chronic pain.

Gottlieb has pledged to recuse himself from agency decisions related to companies where he previously had a financial interest, including GlaxoSmithKline, Daiichi Sankyo and Bristol-Myers Squibb (*IDDM*, April 3).

MHRA Includes Device Regulatory Goals in Pre-Brexit Work Plan

The U.K.'s Medicines and Healthcare products Regulatory Agency laid out its top 10 priorities for 2017 and 2018 — including developing a model for the agency's future, post-Brexit.

The MHRA is planning to propose a five-year plan encompassing national and international strategies for collaboration, as well as a model for the future regulation of the country's medical products after leaving the European Union.

Regarding the EU's new medical device and in vitro diagnostic regulations, the MHRA plans to revise its processes by the end of the fourth quarter. Other major goals include securing global supply chains for medical devices.

The agency also plans to help expand the International Medical Device Regulators Forum with new working groups — and

(See **MHRA**, *Page 2)*

MHRA, *from Page 1*

establish a separate working group of European regulators to develop a consistent approach to combination products.

MHRA plans to play a leadership role by:

- Driving the implementation of the Competent Authorities Medical Devices (CAMD) strategy as a member of the CAMD executive;
- Being a lead partner for EU joint action on market surveillance; and
- Providing EU leadership on IMDRF initiatives, including the Medical Devices Single Audit Program, the Medical Device Nomenclature Working Group, and the Registration working group.

Additionally, the agency plans to liaise with the FDA and observe its implementation of the 21st Century Cures Act and real-world evidence initiatives.

The MHRA's full business plan is available here: www.fdanews.com/04-21-17-MHRA-2017BusinessPlan.pdf. — Conor Hale

Ivoclar Vivadent Alleges Patent, Trade Violations by GC and GC America

The U.S. International Trade Commission (USITC) announced it will investigate, for patent infringement and tariff violations, certain dental ceramics and related products, and methods of making them.

Dental ceramics maker Ivoclar Vivadent, of Schaan, Liechtenstein, filed the USITC complaint and a related lawsuit against GC of Tokyo as well as GC America, Alsip, Ill.

Ivoclar Vivadent asserts that GC's products infringe U.S. patents protecting its lithium silicate glass ceramics technology. USITC has not yet made any decision on the merits of the case. — William Schulz

Firms Urge FDA to Develop Guidance On Combination Product Reviews

Manufacturers and industry groups urged the FDA to develop guidance on its processes for assigning a lead center for the review of a combination product.

In a comment to the agency on topics to be considered by the agency's Combination Product Policy Council, Johnson & Johnson suggested focusing on on aligning approval requirements among CDRH, CDER, and CBER.

J&J also asked for further clarification of the data needed for combination product approval, and on the types of products and manufacturing processes that may require changes in GMP and inspection requirements.

J&J and other industry commenters also urged the agency to outline methods for resolving scientific and regulatory disagreements among reviewing centers.

Cures Act Leaves Combination Product Issues Unresolved

Two prominent Washington D.C., attorneys believe the 21st Century Cures Act did not go far enough to fix a bias against devices in the classification of combination products – although another device law expert has a different perspective.

In almost every case, a combination product involving a chemical action is automatically referred to the Center for Drug Evaluation and Research regardless of the device component, said David Fox, a partner with Hogan Lovells — a former counsel to FDA's combination products programs and former associate chief counsel for drugs — in an *FDAnews* webinar.

The Cures Act codified the FDA's guidance on primary mode of action (PMOA), but also established that simply having a chemical action was not sufficient grounds to automatically refer a product to CDER.

Going forward, an additional legislative solution, perhaps as part of the upcoming reauthorization of FDA user fees, is more likely than FDA action to make up for the Cures Act's shortcomings, Fox said.

Predictability

A separate provision in the Cures Act is the law's best opportunity for combination product manufacturers to "get some predictability" on regulation, according to Fox.

It gives manufacturers the option after a PMOA decision to request a meeting to hammer out how their product will be reviewed.

The Cures Act's provisions on combination product GMPs provide another opportunity to lighten the regulatory burden on such products, according to Robert Church, also of Hogan Lovells, and a former associate chief counsel at the FDA.

Under the law, within 18 months, the FDA must identify types of combination products that may use alternative GMP guidelines.

By December 2020, FDA must issue a final guidance document including:

- A structured process for providing feedback during pre-submission interactions;
- FDA best practices for providing feedback during pre-submission interactions;
- Information that must be submitted with a meeting request for a combination product.

Alternate View

James O'Reilly, professor at the University of Cincinnati College of Medicine, takes a different view in an upcoming report from FDAnews titled Drug or Device? How the 21st Century Cures Act Impacts Combination Products.

O'Reilly sees no bias against devices in the Cures Act. Rather, he says the law has created a loophole that will compel the FDA to classify combination products as devices from the very start.

CDER is already overburdened, O'Reilly says, giving reviewers great incentive to move products off their docket whenever possible—that is, deciding that the PMOA is that of a device.

If the FDA should decide a combination product is a drug, he says, the law allows the sponsor to demand the agency provide scientific evidence for its conclusion.

Savvy product developers will win most debates about the approval process, O'Reilly says.

The recorded webinar is available here: www.fdanews.com/products/53803.

The new report, Drug or Device? How the 21st Century Cures Act Impacts Combination Products, will be available in May from www.fdanews.com/products/category/101-books.
— Zack Budryk and William Schulz

Industry Seeks a More Device-Specific Off-Label Communications Guidance

Devicemakers say FDA's draft guidance on off-label communications is a good start, but is focused too much on drugmakers.

AdvaMed wants additional, device-specific examples in the guidance "that recognize the unique nature of medical devices, to promote understanding of how the guidance applies to medical devices."

The industry group also requests that FDA outline additional types of communications that are consistent with FDA-required labeling and do not introduce a new intended use. Examples could include information regarding the use of a medical device in a specific anatomical location, subset patient population, or surgical procedure where the device has been approved or cleared for a general use.

The FDA issued the draft guidance for public comment in January, along with a memo ruling that the First Amendment does not exempt manufacturers from FDA oversight of off-label communications (*IDDM*, Jan. 23). It received 13 comments by the close of the comment period on April 19.

AdvaMed asks that, in discussing communications consistent with FDA-required labeling, FDA give clear guidance that it is the overall study and presentation of data that is primary, not individual data points.

"We believe that this approach of focusing on the overall study…would promote the use of real-world data/evidence," AdvaMed says.

The group also recommends that the FDA allow communications based on meta-analyses of clinical studies, if appropriately presented.

Sub-analyses of data derived from FDA-approved studies should also be acceptable, AdvaMed says, provided observations are fair and balanced, describe data limitations "and do not draw or suggest conclusions regarding safety or effectiveness unless the study was adequately powered to do so."

Read AdvaMed's comment here: www.fdanews.com/04-21-17-AdvaMed.pdf. — William Schulz

What are the Requirements for CERs In CFDA Medical Device Registration?

Grace Fu Palma, founder and CEO of Boston-based China Med Device, a firm specializing in commercialization and funding for U.S. medtech companies entering China, offers some tips for submitting Clinical Evaluation Reports in the CFDA registration process.

China introduced new requirements for clinical evaluation reports in 2015.

The CER must summarize the data from clinical literature, clinical experience, and clinical trials, etc. This requirement applies to clinical evaluations of Class II and III medical devices for registration and declaration but does not apply to IVDs. The CER may also require specific technical information for particular products.

CERs must comply with CFDA Technical Guidelines for the Clinical Evaluation of Medical Devices (No. 14 of 2015). For low risk, mature devices where there is an established manufacturing process and a large amount of available safety and clinical effective data, a CER is a viable option.

One key requirement that most often blocks approval of a CER is proof of equivalency with the predicate device in China. Equivalency must be shown in terms of the product's basic principle, structure, manufacturing materials, production processes, performance requirements, safety evaluation, alignment with national / industry standards, intended use, and other aspects of basic equivalency.

You need sufficient technical and clinical information for the predicate device. The predicate device must have been approved by CFDA and must be within its validity period (all devices in China must be renewed every 5 years in order not to lose their validity). If a manufacturer does not have its own predicate device approved by CFDA to show equivalency, the manufacturer must obtain the authorization of a third-party manufacturer with a similar device. Getting this authorization can be very challenging.

In addition to searching the common English clinical literature database, you must also search the Chinese clinical database and also demonstrate that you have performed sufficient search and analysis in the local Chinese database.

You will also need to show that the clinical trial data is sufficient in terms of the sample size, indication, coverage, and the Asian/Chinese data subgroup.

A CER typically takes 3 to 4 months and costs $40,000 to $100,000 in China.

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FDA Posts Evaluation Summaries For More Than 100 De Novo Devices

FDA has posted evaluation summaries for more than 100 medical devices classified as de novo with low to moderate risk.

The list includes summaries for such devices as a noninvasive nerve stimulator, an esophageal cooling system, a hearing aid and a strep throat assay.

There are two options for de novo classification for novel devices of low to moderate risk.

Option 1: Any person who receives a not substantially equivalent (NSE) determination in response to a 510(k) submission may, may submit a de novo request within 30 days for the FDA to make a risk-based evaluation for classification of the device into Class I or II. Option 2: Any person who determines that there is no legally marketed device upon which to base a determination of substantial equivalence may submit a de novo request for the FDA to make a risk-based classification of the device into Class I or II, without first submitting a 510(k) and receiving an NSE determination.

The agency says the de novo summaries can also serve as a resource for the types of information device manufacturers may wish to use as a predicate for future 510(k) submissions.

See the summaries here: www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHTransparency/ucm232269.htm.

483 Roundup: FDA Targets Three Device Facilities

The FDA has cited three device firms for a range of compliance issues including inadequate design and device validation procedures as well as inadequate procedures for receiving, reviewing and evaluating complaints.

Following a Jan. 23 to Feb. 3 visit to Signal Medical, Marysville, Mich., FDA inspectors determined that the company had not validated the packaging design for the firm's hip implant system to ensure that it met specifications, including maintenance of sterility. The agency noted a risk analysis the company performed in 2015 but said it failed to consider, among other issues, the packaging used, in part, to maintain sterility of the hip system components.

According to a Form 483, results of validation testing in 2016 for several of Signal's hip system components showed the following: failures of the inner and outer pouches for dye penetration, seal strength and internal pressurization (bubble) testing. A complaint filed in 2016 described a hip stem component found to have perforated both the inner and outer pouches when opened in the operating room. FDA says Signal continued to ship hip components even after being notified of the packaging failures.

The FDA said Signal failed to take preventive and corrective action including for a rust-colored patch or staining issue affecting its implants. The agency said the company did not validate a cleaning process to remove from its devices excess iron deposits implicated in the staining issue. In addition, Signal did not review, evaluate or investigate complaints involving instrument disassembly, instrument fracture or compromised sterile barrier of an implant.

Kindara: FDA inspectors visited Kindara's Boulder, Colo., facility Jan. 25 to Feb. 8, and determined that the firm could not provide documentation of software validation for the Kindara mobile app, which is designed to interface with the Wink Digital Fertility Monitor for fertility prediction based on basal body temperature.

The device transmits biometric data via Bluetooth to the Kindara mobile app. The FDA inspectors found the firmware that performs the device functions was not validated according to an established protocol. Kindara first marketed the Wink device in May 2016 and the firmware has not changed since, FDA says. Inspectors found that while Kindara received software defect reports from customers, these were not logged or evaluated for medical device reporting procedures.

Wieland Designs: During a February visit to medical furniture manufacturer Wieland Designs, Goshen, FDA inspectors found no documented investigators or corrective action reports for 1,439 out of 1,500 complaints received by the firm since July 2015.

Complaints included the following: a missing brake lever for locking the brake on a wheelchair, a chair missing brake pedals, device brakes on casters that allowed the wheels to slide on the floor, and a nonworking brake paddle.

The FDA inspectors, according to a Form 483, also found that procedures have not been established to control product that did not conform to specified requirements, that rework and re-evaluation activities had not been documented in the device history record and that a correction or removal in order to reduce a health risk posed by a device was not reported in writing to FDA as required.

The companies did not return requests for comment.

Read the Signal Medical Corp. Form 483 here: www.fdanews.com/04-20-17-signalmedicalcorp483.pdf.

Read the Kindara Form 483 here: www.fdanews.com/04-20-17-kindara483.pdf.

Read the Wieland Designs Form 483 here: www.fdanews.com/04-20-17-wielanddesignsinc483.pdf.

AdvaMed Weighs in on Pre-Request For Designation Program

AdvaMed is calling for changes to the FDA's draft guidance on the preliminary request for designation (Pre-RFD) program for combination products.

The guidance, issued in January, lays out the content and format sponsors will be expected to follow. The Pre-RFD process has fewer requirements than the full RFD program, and can be helpful if a product is very early in its development, or if the product's classification — or the agency center it would be assigned to — is unclear or in dispute.

For AdvaMed, the guidance's 15-page limit for Pre-RFD submissions is "insufficient" for sponsors to provide enough detail to obtain a definitive designation and requests modification "to allow for a more robust background documentation package."

AdvaMed also noted concerns that analysis for a product's primary mode of action (PMOA) is denoted as optional for the Pre-RFD process. The group points out that the official designation of the product is dependent on the PMOA. "The decision to optionally omit the PMOA analysis would seem to be counterproductive to industry members who are working towards an official designation," AdvaMed says.

Applications can be submitted to the FDA's Office of Combination Products, which will conduct a preliminary assessment for the application's completeness within five business days and alert the sponsor before beginning the full review.

BIO also commented on the draft guidance, saying that optional sponsor recommendation of classification "puts the FDA classification decision at the starting point" and "may dissuade sponsors from using the structured and documented Pre-RFD process."

After a PMOA designation has been made, BIO says, the FDA should consider revising the draft guidance to include the alternative regulatory appeal process outlined in the 21st Century Cures Act.

The draft guidance recommends including a list of claims sponsors intend to make or have made regarding a product as part of basic information in the Pre-RFD, AdvaMed says. "However, we feel that the determination should be made on the intended use/indications for use rather than the intended claims," the group says.

The guidance recommends paying special attention to the product description, why it would be used, and how it works — and in the case of combination products, the relative contribution of each component. In addition, the sponsor should include any marketing claims planned for the product, and whether the combination product will be marketed as a whole or by its constituent parts.

Finally, Bio wants specifics on how FDA will protect proprietary information and it asks the agency to provide clarity on how confidentiality of the data and information provided under the Pre-RFD process will be protected.

A Pre-RFD application must include a listing of all components and ingredients, as well as instructions for the product's use.

Read the guidance here: www.fdanews.com/04-20-17-PreRFDDraftGuidance.pdf.
— William Schulz

BRIEFS

FDA Clears Lifetrack Medical Systems Next Generation PACS for Distributed Radiology

Philippines–based Lifetrack Medical Systems has won FDA marketing clearance for its Lifesys picture archiving and communication system. Widely available in Asia, the product is now being rolled out in the U.S. and in other global markets.

Medtronic Updates Faulty HVAD Pump Controller

Medtronic is replacing a faulty controller for its HVAD pump for heart failure, which was linked to a Class 1 product recall.

The updated controller—approved by the FDA on April 7—addresses several, previously reported potential safety issues, Medtronic says.

(See **Briefs**, *Page 8)*

Malaysia Issues Guidance on Combination Product Registration

The Malaysian government has released guidance for registration of drug-medical device and medical device-drug combination products.

The government agency for registration of combination products is based on the primary mode of action by which the claimed effect or purpose of the product is achieved. A medical device that does not achieve its primary mode of action in or on the human body by pharmacological, immunological or metabolic means would be regulated by the Medical Device Authority (MDA).

A drug, with a PMOA based on pharmacological, immunological or metabolic action in or on the body, would be regulated by the National Pharmaceutical Regulatory Agency (NPRA).

In cases where the NPRA is the primary regulator, a combination product must first obtain certification from a Conformity Assessment Body (CAB), then endorsement from the MDA, and finally apply for registration with the NPRA before commercialization.

For combination products whose primary regulator is the MDA, obtaining an NPRA endorsement is the first step, followed by CAB certification and finally MDA registration.

Malaysian regulators have set July 1, 2018 as the registration deadline for any unregistered combination product.

Read the guidance here: www.fdanews.com/04-21-17-MinistryHealthMalaysia.pdf.
— William Schulz

Briefs, *from Page 7*

Esophageal Cooling Device Wins FDA 510K Approval

Chicago-based Advanced Cooling Therapy has won FDA pre-market approval for its esophageal cooling device.

FDA Clears Additive Orthopaedics Locking Lattice Plating System

New Jersey–based Additive Orthopaedics has received FDA marketing clearance for its 3D printed Locking Lattice plating system. The device is designed to assist in stabilization and fusion of fractures, osteotomies and arthrodesis of small bones.

gammaCore Receives FDA Clearance For Treating Cluster Headache Pain

New Jersey–based electroCore has gained FDA clearance for gammaCore, a non-invasive vagus nerve stimulator for the acute treatment of pain associated with episodic cluster headache in adult patients.

The company expects to market gammaCore in the U.S. early in the third quarter of 2017.

Monitored Therapeutics Wins FDA Clearance for Home-Use Spirometer

Ohio–based Monitored Therapeutics has received FDA marketing clearance for its GoSpiro Home Spirometer.

Ethicon Receives FDA Clearance For Echelon Circular PowerEd Stapler

Cincinnati–based Ethicon has received FDA marketing clearance for its Echelon circular-powered stapler. The device is designed to reduce anastomotic complications in colorectal, gastric and thoracic cancer surgeries.

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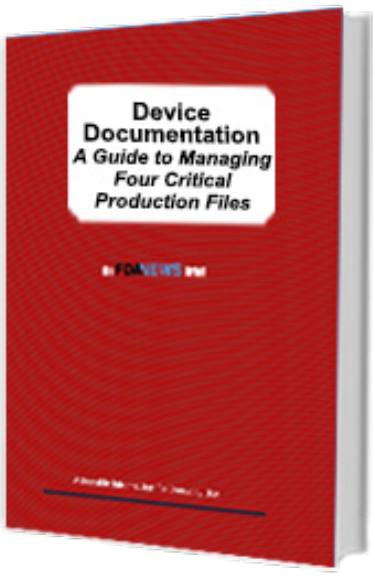

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