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CDRH Seeks Participants for Manufacturing And Product Quality Pilot Program

CDRH is looking to enroll a total of nine participants in its new pilot program aimed at identifying best practices for quality product manufacturing.

The center, which began accepting applications for the Case for Quality Voluntary Medical Device Manufacturing and Product Quality Pilot Program on Jan. 2, intends to select manufacturers that can represent the medical device industry.

Participants must have remained in good FDA compliance during the last five years, and they must agree to: Appraisals conducted by the CMMI Institute; collecting and submitting metric data; being available for real-time consultations; participating in monitoring activities; and allowing the institute to report performance data analyses to the FDA.

Data collected throughout the duration of the pilot, which will run until Dec. 28, may also be used "to help determine if changes to the

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China FDA to Require Registration, Training of Medical Reps

China FDA released draft regulations that would require medical representatives in China to register, and mandate that medical device marketing authorization holders provide adequate training.

Medical representatives are defined as professionals, rather than sales persons, who perform academic promotion and technical consultancy work, so it is "not surprising that the CFDA requires medical representatives to have certain qualifications and/or related experience," Katherine Wang, partner at law firm Ropes & Gray in Shanghai, tells *FDAnews.*

Under current CFDA regulations, medical representatives are not required to be registered. The draft regulation spells out qualification requirements for medical reps, including a two-year junior college degree or higher with a major in life sciences.

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pilot program need to be made, de-identify data for benchmarking and trending, and to adjust any benefits to the firms where appropriate," FDA spokesperson Deborah Kotz told *FDAnews*.

Participants will work in collaboration with the institute, agency staff, and the Medical Device Innovation Consortium (MDIC), which collectively developed the Capability Maturity Model Integration (CMMI) system, a maturity and appraisal program for the medical device industry.

The CMMI system's goal is to "help organizations discover the true value they can deliver by building capability in their people and processes," the FDA said. It has been "successfully used in various industries, including information technology, healthcare, automotive, defense, and aerospace to consistently deliver high quality products and reduce waste and defects," the agency said.

According to the MDIC, there are several benefits for participating companies, such as having products reach the market at a faster pace, as well as improving resource allocation. Boston Scientific estimated participating in this program could have allowed it to redeploy $500,000 of resources assigned for the 69 30-day notices it submitted in 2016, the consortium said.

The CfQ Program was also designed to benefit the FDA by potentially reducing the allocation of resources, as participating firms can get inspection waivers.

"The idea of just routinely going out to do an audit for a company doing quite well...is probably not the best utilization of the agency's limited resources," Robin Newman, director at CDRH's Office of Compliance said during the 2017 CfQ program workshop.

"It would be much better to go out and use those resources in areas where situations are not under control" (*IDDM*, Oct. 13, 2017). — Ana Mulero

CFDA, *from Page 1*

China's State Council announced in January 2017 that medical reps would be required to register on a government website, but the draft regulations introduce much broader requirements, and medical device companies in China "should closely monitor the legislation's progress and implementation," according to law firm Sidley Austin.

The marketing authorization holder (MAH) will need to provide comprehensive training for medical reps, including information on laws and regulations, professional ethics and product knowledge. MAHs are responsible for the training of any third-party sales force they authorize, the law firm said.

The draft regulation also requires MAHs to get prior approval from hospitals before medical reps can conduct any activities targeting physicians, either inside of outside of hospitals. In addition, the regulation prohibits medical reps from providing donations, sponsorship or grants to individual physicians or internal departments of hospitals, Sidley said.

Violations of the draft regulation by medical representatives or MAHs will be published online and reported to the agency in charge, Wang said. The CFDA or local FDA may order the marketing authorization holder to arrange mandatory off-job training for its medical representatives who violate the draft regulation.

The CFDA may also transfer cases to other enforcement agencies if medical reps or MAHs violate other regulations, Wang said.

"For example, besides the CFDA, the PRC State Administration for Industry and Commerce and its local counterparts (collectively known as the SAIC) are key enforcement agencies overseeing medical representatives. The SAIC may step in and impose penalties on medical representatives and/or marketing authorization holders if they are involved in bribery, illegal advertising or promotional activities, Wang said.

The CFDA draft regulations are less harsh than the first draft registration document released by the Shanghai FDA, Sidley said, noting that the Shanghai FDA regulation held that companies could be de-registered and medical reps could lose their jobs.

Comments on the draft regulation are due by Jan. 19.

Australia Clarifies Criteria For Priority Reviews

Australia's Therapeutic Goods Administration issued new guidance on the priority review pathway for medical devices including IVDs.

The regulatory authority set three criteria that devices must meet to be considered in its "front-of queue" priority list: The new device's intended use must be for treatment of a serious health condition; the expectation must be for it to "fulfil a major or urgent unmet medical need"; and it must be associated with a breakthrough technology.

IVD sponsors should include a justification for how early market availability in the country will result in improved health of the Australian population, TGA said.

The justification should be supported by documented evidence of the new IVD's improved sensitivity and specificity compared to existing products, and an estimation of the patient population that could benefit from the treatment it is designed to provide.

As of this year, the priority review designation application fee is AU$9,660 ($7,574). The TGA must reach a final decision within 20 working days, and a successful applicant will then have no more than six months to submit an additional application for approval, after which the designation would lapse and the company must reapply to regain a priority review status. — Ana Mulero

Device Industry Groups Nix Direct Sponsorships of Health Professionals

Member medical device companies at four of the top industry trade associations worldwide have made a major change in how they support healthcare professionals' education and training.

In a Jan. 3 joint statement, AdvaMed, APACMed, Mecomed, and MedTech Europe announced a new revision to their codes of ethics in China, Europe, the Middle East and North Africa as well as in the Asia-Pacific region — the removal of direct sponsorships, such as registration fees or expense reimbursements, for healthcare professionals' attendance at third-party educational events including medical conferences.

The revision was made with the goal of striking a balance between transparent interactions and the need for healthcare professionals to "make independent decisions regarding patient care and treatment," which could be unintentionally influenced via direct sponsorships, the organizations explained.

The decision to stop providing this kind of support "follows a global trend that began…some time ago, as in the U.S., Australia, and other countries, such as Sweden and Russia," they said.

Member companies may instead offer educational grants and sponsorship to aid conference organizers, healthcare institutions and/or professional associations in supporting the attendance by professionals. But they will continue to provide training and host educational meetings on the use of complex products.

"With the end of direct sponsorships, we anticipate that companies will have more resources to devote to high-impact HCP training and education opportunities based on companies' individual educational strategies," the organizations wrote in the joint statement. — Ana Mulero

Korean Government, Devicemakers Agree on Fast-Track for New Devices

The South Korean government reached an agreement with the nation's medical device industry to adopt accelerated approval procedures for certain devices.

The Korean Fourth Industrial Revolution Committee — a state committee chaired by Korean President Moon Jae-in — led a marathon policy discussion to determine strategies for regulating devices. Participants in the discussion included government agencies such as the Ministry of Drug and Food Safety and the Ministry of

(See **Korean***, Page 4)*

Pakistan Approves First Medical Device Rules

Pakistan's government approved new rules regulating the sale of medical devices for the first time.

The rules, approved in a Dec. 26 cabinet meeting, will apply to all medical devices. Prior to their approval, the country's only law regulating trade for medical devices was the 1976 Drugs Act.

The new rules come after years of complaints about lower quality devices being sold as higher-quality ones, according to local media reports.

The new rules will reform the device fee structure and simplify requirements for technical documentation during the registration process for devices imported from key reference countries, including the United States, Japan, Canada, Australia and the European Union.

The rule also harmonizes device classifications to better align with guidelines established by the World Health Organization, the Asian Harmonization Working Party and the International Medical Device Regulators Forum. — Zack Budryk

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Health and Welfare, along with medical technology companies based in the country.

One of the group's key concerns was devices whose success depends on entering the market before the competition. Under the consensus reached, the government will establish a fast-track approval path for next-generation devices for which a first-entrant advantage is vital.

The committee also will create a value-based evaluation pathway that factors potential clinical and societal benefits into the approval process along with clinical evidence. Devices approved based on this assessment will be granted a clinical usage period of three to five years followed by a re-evaluation, according to the committee.

South Korea's Ministry of Food and Drug Safety has joined the International Medical Device Regulatory Forum. The ministry has determined the forum's Medical Device Single Audit Program, a common set of audit requirements for all member nations, could be applied in Korea. — Zack Budryk

483 Roundup: FDA Cites Four Device Firms

The FDA issued Form 483 reports to devicemakers in Oregon, California and Colorado.

Dental Components: A devicemaker's manufacturing facility in Oregon was cited for closing customer complaint investigations without documenting the changes identified for addressing the issues or verifying their effectiveness.

An FDA investigator reviewed eight complaints of Dental Components' distributed medical devices during a September 2017 site inspection and found that four of them listed corrective actions, but their effectiveness had not been documented. Issues reported in the complaints include a barb coming out of the Autoclavable Premium Saliva Ejector swivel assembly, and threaded tips not screwing off.

The facility also lacked certain adverse event reporting procedures and requirements. It had not specified situations that would reasonably suggest a device malfunction would be likely to cause or contribute to a death or serious injury if it were to reoccur, as well as requirements for ensuring timely MDR submissions to the FDA. Out of the eight closed complaints, five had not been evaluated to determine whether they met the criteria as MDR-reportable events.

The agency also found deficiencies in the firm's procedures for maintaining device history records. A total of 11 records out of 13 selected did not include required information, including initials and dates, from personnel who released the devices for distribution.

Zeus-MJB: An FDA site inspection at Zeus-MJB's manufacturing facility in California revealed several noncompliance issues associated with its quality management systems.

As of late September 2017, the firm did not have procedures for executive management to conduct routine reviews of its quality system in order to ensure compliance with established policies. The facility also lacked procedures for performing internal quality audits.

There was also no plan defining the practices, resources, and activities for designed and manufactured devices to meet quality requirements, and management had not established policies and objectives for committing to quality manufacturing, the agency said.

In addition, the firm had "not completed any evaluations to select potential suppliers, contractors, and consultants on the basis of their ability to meet specific requirements, including quality requirements," and did not maintain records for those deemed acceptable.

The facility also lacked procedures for complaint handling, acceptance and verification activities, as well as adverse event reports.

Multisource Manufacturing: Multisource Manufacturing drew a Form 483 for failing to adequately establish or validate various procedures at its Colorado medical device facility, the FDA found in a November site inspection.

The FDA investigator observed that the facility had not validated its automated milling and lathing processes. In addition, the instruments, which the firm used to manufacture its blunt tips and linear probes, did not have all of their parts verified.

The firm was also cited for inadequately establishing procedures for accepting and controlling in-process product. Specifically, it had been using an inadequate procedure for monitoring and measuring products. The firm had not documented in-process inspection requirements, and failed to perform an in-process measurement for length as required by established specifications.

CAPA procedures were also flagged as they lacked requirements for work operations, analyzing processes and other sources for obtaining quality data, and an analysis of data used to track quality management system effectiveness was found to have a lack of defined limits or actions taken to correct issues.

Good Clean Love: Complaint handling and CAPA procedures were flagged at Good Clean

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

Electric Power at All Baxter Facilities In Puerto Rico Finally Returns

Following several months of efforts in Puerto Rico to recover from the widespread destruction from recent hurricanes, all three of Baxter's IV saline and amino acids manufacturing facilities on the island are back on the power grid.

"All facilities will continue to have backup diesel generation in case of power interruptions, which still occur intermittently," Baxter spokesperson Bill Rader told *FDAnews*.

The FDA had been working with Baxter to help restore production as the previously existing shortages of IV saline and amino acids for injections had been exacerbated when Hurricane Maria struck.

FDA Commissioner Scott Gottlieb reported the power returning all of the Baxter's facilities "means that the shortage situation is anticipated to continue to improve in the coming weeks." The company expects "more normal supply levels" in the next few weeks, Rader confirmed with *FDAnews*.

Steps the FDA took to help mitigate the shortage included allowing Baxter to temporarily import its amino acids for formulating IVs from its facilities in the United Kingdom and Italy, among other countries. "These imported products began reaching healthcare providers in late October and product continues to enter the supply pipeline," Rader said.

"We also continue to work with the FDA to explore opportunities to leverage other Baxter manufacturing facilities to help address product demand," Rader added.

Other devicemakers had also been affected. Edwards LifeSciences' manufacturing facilities on the island, which had been impacted by a limited supply of diesel, strong winds and floods, are back to pre-storm capacity, quality manager Richard Rodriguez told *FDAnews*.

But the recovery is not over yet. The FDA remains concerned with the production situation, with Gottlieb noting the commercial power grid is still unstable in several parts of the island.

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Love's Oregon manufacturing facility during a September 2017 FDA site inspection.

A total of 20 customer complaints that the firm had marked as investigated since 2016 were reviewed by an agency investigator. Seven of them did not include a lot coding for each device and the firm lacked documentation of any attempts to obtain the coding.

None of the 20 complaints had any documentation on whether they had been evaluated to determine if they should be reported to the FDA as adverse events.

The investigator observed that CAPA procedures were inadequate at the time of the inspection in that they did not include processes for analyzing quality data that could help to identify any issue other than nonconforming product. One in three of the firm's CAPA actions that had been implemented since 2015 "was not fully implemented and the effectiveness of the activities was not documented."

The firm also failed to document complaint analyzes for the Almost Naked Lubricant device until Sept. 22, 2017.

Other Form 483 observations related to inadequate procedures controlling documentation and design verification, as well as a lack of procedures for design changes and a device master record.

Read the Dental Components Form 483 here: www.fdanews.com/01-05-18-dentalcomponentsllc483.pdf.

Read the Zeus-MJB Form 483 here: www.fdanews.com/01-05-18-zeusmjbinc483.pdf.

Read the Multisource Manufacturing Form 483 here: www.fdanews.com/01-05-18-multisourcemanufacturingllc483.pdf.

Read the Good Clean Love Form 483 here: www.fdanews.com/01-05-18-goodcleanloveinc483.pdf. — Ana Mulero

China's 3rd Batch of Exemptions From Clinical Trial Requirements

Grace Fu Palma, founder and CEO of Boston-based China Med Device, LLC, a firm specializing in commercialization and funding for medtech companies entering China, considers the China Food and Drug Administration's moves to speed registrations and approvals of medical devices and IVDs.

CFDA will continue to add more medical devices and IVDs to its clinical trial exemption list this year to keep up with international standards and to further speed registrations and approvals.

In the U.S., the medical device and IVD approval process is mature and well-developed, and 80% of medical devices and IVDs can find referred predicate products and get exempted from a clinical trial. But in China, 50% of medical devices/IVDs require clinical trials to complete their registration.

To keep up with western countries, the CFDA decided to issue several updates of the Medical Device/IVD Clinical Trial Exemption List. On Oct. 31, the CFDA released its third batch of medical devices exempt from clinical trial requirements, including 37 Class II, 11 Class III and 116 Class II in vitro diagnostic devices.

For new device registrations in China, the manufacturer must first determine the device classification within the CFDA's classification catalog. U.S. FDA classification does not correspond to that of CFDA. For example, an exempt device in the U.S. could be a Class II device in China.

Generally, a Class I device only needs to be filed with the CFDA. But most Class III devices require a clinical trial, especially if they are listed in the Catalog of Class III Medical Devices that Need Clinical Trials.

After you know the classification of your device in the CFDA's system, check first to see if your device is on the clinical trial exempt list. Make sure you refer to the newly updated 3rd batch of the clinical trial exempt lists.

If your devices/IVDs are on a clinical trial exemption list, you only need to submit the following clinical evaluation materials:

- A comparison of your product information and the related content in the clinical trial exemption list; and
- A comparison of your product and approved predicate product(s).

This year will be a big year for healthcare reform in China. Based on the new policy from China's 19th CPC National Congress aimed at building an efficient healthcare system, CFDA announced the new Opinions on Deepening the Review and Approval System Reform and Encouraging the Drug and Medical Device Innovation. This guidance document includes the State Council's policies to reform the clinical trial system, such as accepting overseas clinical data and expanding regulatory resources for clinical trials.

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APPROVALS

Avinger Image-Guided Atherectomy Device Gets CE Mark

Avinger received a CE Mark for its image-guided Pantheris Lumivascular atherectomy system for treatment of peripheral artery disease.

The new device features a simplified single balloon system for the occlusion of blood flow and device positioning, the company said. It enables surgeons performing atherectomy to see from inside the artery during the procedure via Avinger's Lightbox console instead of using x-rays.

FDA Clears Spectral Medical Stand-Alone Pump

The FDA granted 510(k) clearance to Spectral Medical's Spectral Apheresis machine for use in therapeutic plasma exchange and continuous renal replacement therapy.

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Approvals, *from Page 7*

The stand-alone pump was initially developed for use in intensive care units to septic shock patients without requiring third-party CRRT machines.

The company said it will seek clearance for use of the Apheresis as an open platform hemoperfusion delivery device once an FDA-approved hemoperfusion cartridge is available on the market.

FDA Clears Biotricity ECG Remote Monitoring Device

Medical diagnostic firm Biotricity received 510(k) marketing clearance for Bioflux, its ECG remote monitoring device.

The device detects and transmits diagnostic heart information, including probable arrhythmias, to physicians to allow for remote monitoring and diagnosing of patients with cardiovascular coronary heart disease.

Shire Web-Based Dosing Software Achieves FDA Clearance

Shire received 510(k) marketing clearance for its web-based dosing software for patients with hemophilia A treated with ADVATE.

The mPKFit estimates a patient's pharmacokinetic profile using just two measurable blood samples — compared to the 9 to 11 samples recommended by the International Society on Thrombosis and Haemostasis — enabling clinicians to tailor treatments to the individual patients.

The severity of hemophilia A is determined by assessing the amount of factor in the blood, with more severity associated with lower amounts of factor.

Prescient Surgical Scores FDA Clearance For Wound Retraction and Protection System

The FDA cleared Prescient Surgical's Clean-Cision wound retraction and protection system for use in abdominal surgery.

Developed by surgeons and infection control experts, the device combines wound protection and irrigation with an easy-to-use retraction system.

The system features active cleansing technology to continuously suction harmful bacteria from an incision throughout a surgical procedure to help prevent contamination of the wound.

Sanuwave's Diabetic Foot Ulcer Device Gets FDA Marketing Clearance

The FDA signed off on marketing authorization for Sanuwave's Dermapace system, a shockwave device used to treat diabetic foot ulcers. The system uses energy pulses to mechanically stimulate wounds in adult patients whose ulcers last longer than 30 days.

The agency based the approval on clinical data from two multi-center studies with a total of 336 patients.

Abbott Gets CE Mark for Alinity Hematology Testing System

Abbott received a CE Mark for its Alinity h-series hematology testing system.

The solution is intended to be combined for use with the Alinity hq standalone hematology analyzer.

Its reagent bottles were designed "to work like a lock and key to ensure that the right reagents can only be inserted into the right location, preventing costly mistakes and time delays in the lab," the company said.

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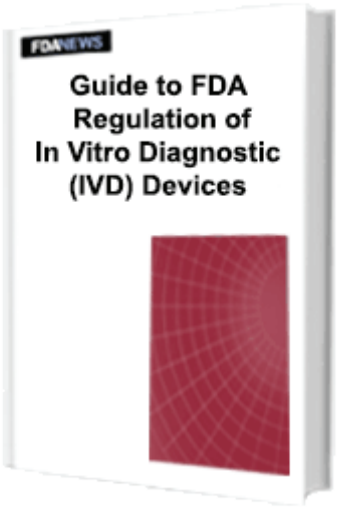

Guide to FDA Regulation of In Vitro Diagnostic (IVD) Devices

Devicemakers, IVD marketers and clinical labs struggle often with FDA regulation — and it's no wonder. The rules governing IVDs are scattered throughout the CFRs, and exceptions, special cases and pitfalls abound. Some hapless firms have even followed the wrong set of rules — and endured 483s or warning letters as a result.

Guide to FDA Regulation of In Vitro Diagnostic (IVD) Devices brings together all the disparate parts of IVD regulations and guidances and provides an expert interpretation of requirements, including:

- Clear technical and practical definitions of different types of IVDs, including multivariate index assays, analyte-specific reagents, research use only IVDs, investigational IVDs and laboratory-developed tests
- How to apply UDI rules to IVDs, especially in convenience kits
- How to develop and label companion devices
- The FDA's enforcement policy for premarket notification
- Rules on calibrating IVD instruments

This first-of-its-kind guide has all the regulatory resources you need:

- 21 CFR parts 801, 803, 806, 809, 812 and 820;
- 21 CFR Part 211.166, the only drug regulation that impacts IVDs;
- 42 CFR Part 493 on laboratory-developed tests;
- And more…

Guidance documents are few and far between, and new ones are not expected any time soon. **Guide to FDA Regulation of In Vitro Diagnostic (IVD) Devices** is your opportunity to clear up regulatory confusion.

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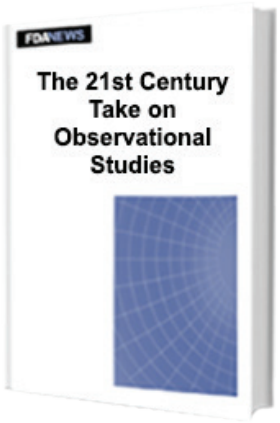

The 21st Century Take on Observational Studies: *Using Real-World Evidence in the New Millennium*

Passage of the 21st Century Cures Act reaffirmed Congress's and the FDA's commitment to using real-world evidence to supplement or even replace traditional clinical trials.

More flexible, faster and cheaper research methods, including observational studies, are now acceptable in the FDA's approval process.

Observational research requires an entirely different set of procedures and careful planning to ensure the real-world evidence collected is valid and reliable.

The 21st Century Take on Observational Studies walks you through everything you need to know about the opportunities and pitfalls observational studies can offer. The report looks at the growing trend toward observational research and how provisions in the 21st Century Cures Act create even more incentives to rely on real-world evidence in the development of medical products. The report covers:

- Provisions of the 21st Century Cures Act related to observational studies and gathering of real-world evidence
- The evolution of patient-focused research
- How observational studies can be used in the preapproval and postmarket stages
- The potential for saving time and money
- New data sources that make observational studies a viable alternative to clinical trials
- How drug- and devicemakers view observational research and how they are using it

Order your copy of **The 21st Century Take on Observational Studies: *Using Real-World Evidence in the New Millennium*** and learn effective uses of observational studies in both the preapproval and postmarket phases; how to identify stakeholders and determine what kind of data they needed, and how the FDA's view on observational research is evolving.

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