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House Panel Unveils Device Development Incentives, FDA Regulatory Overhaul

House and Senate lawmakers are teaming up to push the FDA to improve its regulatory processes and speed access to innovative medical technologies.

The two-pronged effort started Tuesday when the House committee that oversees the U.S. FDA proposed an overhaul of the agency's device procedures that would expand the use of third-party quality audits, streamline premarket notifications, promote more efficient use of FDA and industry resources during product reviews and expand humanitarian use for diagnostics.

The widely anticipated Energy & Commerce Committee proposal was released by Rep. Fred Upton (R-Mich.), the committee chair, and committee member Diana DeGette (D-Colo). It grew out of hearings the committee held last year under its 21st Century Cures initiative, which sought suggestions for improving the process of developing and approving new medical technologies.

The nearly 400-page draft 21st Century Cures Act includes numerous medical device reforms.

Use of Accredited Third Parties

To facilitate quality system assessments, the bill would allow the FDA to use accredited third-parties to certify minor manufacturing changes. Companies deemed to have a quality system by an accredited body would not need to submit a 510(k) or a supplement for the modification.

Third-parties would be accredited for two years and included on a list published in the *Federal Register*

In language aimed at speeding development of innovative devices, the bill would clarify that valid scientific evidence includes registry data and other well-documented case histories and studies published in peer-reviewed journals. Data collected outside the U.S. would be acceptable if it met the specified criteria.

The bill also would ensure that FDA reviewers are trained in the least burdensome means concept, and would direct the agency's

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ombudsman to audit presubmission units to assess their performance in implementing the concept. The audit should include interviews with devicemakers about their premarket review experience, the measure says.

Applicable Standards

To improve FDA recognition of applicable standards, the bill would require the FDA to make them available within 60 days of their publication by standards development organizations. The agency would also be required to train its reviewers on the use of the standards.

To streamline reviews of 5l0(k) submissions, the FDA would be barred from refusing an indication for use statement for a device if the predicate has the same indication statement. The agency also could not require 510(k)s to include information or data related to an indication not being requested.

The bill also would authorize the FDA to allow humanitarian device exemptions for in vitro diagnostics to address a public health threat impacting more than 4,000 people when no alternative test exists.

The bill also would require manufacturers of prescription devices to only use authorized distributors, beginning in January 2016. Wholesale distributors and third-party logistics providers would be subject to national licensing standards and user fees.

The proposal also includes efforts to improve the field of medical science, calling on the NIH to develop a strategic funding master plan. And it would expand CMS's authority for coverage with evidence development to include Medicare beneficiaries who participate in device clinical trials, addressing the costly process sponsors must go through to secure Medicare coverage.

The bill hints at regulatory relief in other areas as well, such as streamlining marketing notification for Class I devices and new, less-restrictive rules for promotion of devices via social media. And the proposal calls for the

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FDA to develop a management succession plan to minimize the impact of personnel changes at the agency.

Clinical Trials

On Thursday the Sens. Lamar Alexander (R-Tenn.) and Richard Burr (R-N.C.) joined the reform push with a report strongly criticizing the speed, cost and effectiveness of the FDA's device review process.

The report is especially critical of the FDA's clinical trial approval process for devices, saying it should require less premarket data and provide more clarity on trial design. The report also calls for a distinct division within the agency to handle combination products, saying it would eliminate confusion caused by cross-center communication under the current structure.

As in the House bill, the report notes concerns about FDA management. A growth spurt from 8.000 employees in 2001 to more than 12,000 today has "exacerbated management challenges," it says, and staff are further hobbled by a lack of efficient modern information technology.

The report says the FDA could use public-private partnerships to increase its technology expertise, and recounts a number of such initiatives. However, it notes that no one at the agency seems to be responsible for turning recommendations from the partnerships into real change.

Hearings on the issues outlined in the report are expected to begin in March.

AdvaMed praised the 21st Century Cures draft, saying the current "innovation ecosystem … is severely stressed."

The Energy & Commerce Committee has not produced a timeline for when it wants to file its bill, much of which is still loosely shaped. However, Upton has said he would like to put the bill on track to reach the president by the end of the year. The draft draws on a list of proposals from 40 representatives.

See the discussion draft here: www.fdanews.com/01-27-15-21st-Century-Cures.pdf. A separate white paper on the initiative can be found at www.fdanews.com/01-27-15-21st-Century-White-Paper.pdf. The Senate report is available at www.fdanews.com/01-29-15-senate.pdf. — Meg Bryant, Elizabeth Orr, Bryan Koenig

Clinical Trial Approval Times Improve, CDRH Review Shows

The U.S. FDA was much quicker to approve clinical trials in 2014 compared with the previous year, a new report shows.

According to an update on fiscal 2014-2015 strategic priorities, the Center for Devices and Radiological Health in 2014 met or exceeded all benchmarks it had set for improving the clinical trial system. Overall time to full approval of an investigational device exemption decreased by 53 percent over 2013, and the number of IDE studies requiring more than two cycles to reach an approval decision was down by 34 percent.

In addition, CDRH offered a teleconference with the submitter within 10 business days of the IDE decision for 100 percent of IDEs rejected in the last five months of 2014. "Overall, since this program started, CDRH has missed this goal only once," the report says.

However, one long-time industry insider who has noticed the friendlier approach is not convinced the swing toward a more efficient trial approval process will last.

Nancy Stark, president of the Clinical Device Group, expects devicemakers will have an easier time scheduling meetings and getting informal answers to questions about their IDEs over the next several years. But she's been working on device trial issues for more than 30 years and has seen similar cycles in the past. They tend to end when a device failure hurts or kills patients, and

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the adverse event is blamed on insufficient device testing, she says. "People start saying the FDA is too chummy with industry, and they crack down again."

Other trial-related achievements noted in the report include the establishment of a clinical trials program within the Office of Device Evaluation and appointment of its acting director in February 2014, and extensive education and training for CDRH review staff on IDEs and early feasibility studies. The center also developed a benefit-risk framework for IDEs and plans to issue draft guidance this year.

Other Progress Noted

The report also discusses progress CDRH has made toward two other goals, balancing premarket and postmarket data collection and "providing excellent customer service."

The center reviewed 69 percent of devices subject to a PMA in 2014 to determine whether some premarket requirements could be shifted to the postmarket setting, or whether the devices should be downclassified. A report on those findings is expected by April 15.

The FDA also issued draft guidance in 2014 on how the agency considers postmarket information in determining what data need to be collected in the premarket phase. A second draft guidance proposed a voluntary expedited access PMA program, which would shift certain premarket data requirements to the postmarket setting for devices that address an unmet public health need. Final guidance on both topics is expected in fiscal 2015, the report says.

Finally, CDRH implemented several tools to improve its customer service, including Customer Service Standards of Excellence and an online customer satisfaction survey.

CDRH also implemented a pilot program to collect, monitor and address feedback on the device center and published a quality management framework. In the coming year, the center will transition the feedback program from pilot to permanent, incorporating recommendations from an independent contractor.

View the priorities update at www.fdanews.com/02-02-15-priorities.pdf. — Elizabeth Orr

AED Makers Given 18 Months To Secure PMAs in the U.S.

Manufacturers of automated external defibrillators should let the U.S. FDA know by April 29 if they plan to file a premarket approval application for currently marketed devices. The deadline for obtaining PMA approval is July 29, 2016.

The final order, issued Wednesday, also requires manufacturers of AED accessories to submit PMAs by Jan. 29, 2020. The long timelines are to allow AEDs to remain available for use in emergencies while companies navigate the approval process, says William Maisel, deputy director for science in the agency's medical device center.

AEDs have long been a source of safety concerns. Between January 2005 and September of last year, the FDA received 72,000 adverse event reports involving the devices. During the same period, manufacturers staged 111 recalls involving more than two million AEDs, many of them due to design and manufacturing issues.

"We know AEDs save lives, but they also have a history of malfunctioning," Maisel says, citing multiple reports of AEDs not powering up when turned on.

The final order placing AEDs and accessories in Class III largely mirrors a March 2013 draft version, but offers greater clarity on the types of accessories that require a PMA. It also pushes back the compliance date for third-party accessories to account for industry concerns about their complexity and adds adverse tissue reaction to a list of AED-related health risks.

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The FDA defines regulated AED accessories as items that are necessary for the defibrillator to detect and interpret an electrocardiogram or deliver an electrical shock. Examples include pad electrodes, batteries, adapters and hardware keys for pediatric use. The agency included accessories in the final order because failures could lead to the same ill effects as if the AED itself failed.

The final order rejects comments submitted on the proposed order that claimed the FDA's adverse event data was flawed and that many AED and AED accessory failures were detected during routine maintenance checks.

The widespread distribution of these devices, their life-saving nature and the steady rate of MDRs support a call for PMAs, the agency says. Failures during maintenance checks only serve to underscore worries about design flaws that could make the device unusable when needed, the FDA adds.

Manufacturers that need to modify currently marketed AEDs before a PMA is approved, due to issues related to part obsolescence or specific risks to health caused by malfunctions, are instructed to contact the FDA.

View the final order at www.fdanews.com/02-02-15-AEDs.pdf. — Elizabeth Orr

Top Cardiologist to Oversee U.S. Policy on Medical Products

The U.S. Food and Drug Administration named prominent clinical researcher Robert Califf to be deputy commissioner for tobacco and medical products.

In his new role, Califf will provide executive leadership for CDRH, helping to advise the commissioner on priorities and policy setting for device and diagnostics oversight.

Califf will take on the long-vacant role at the end of February. He currently is a professor of medicine and vice chancellor for clinical research at Duke University, where he has worked for 33 years.

Because of the broad range of the deputy commissioner's duties and focus on administrative tasks, such as management and ensuring regulatory consistency, he's not expected to make broad changes, says Steven Grossman, president of HPS Consulting. However, Califf may make a personal priority out of improving clinical trial design, he adds.

Focus on Scientific Rigor

Steve Niedelman, lead quality systems and compliance consultant to the FDA and life-sciences practice team at King & Spalding, seconds that assessment. "I think he'll focus a lot on scientific rigor, including improving clinical trials," he tells *IDDM*. While most of Califf's medical product experience has been in the area of pharmaceuticals, his clinical expertise can be expected to also resonate with device issues, he says.

A 1978 graduate of Duke's medical school, Califf was a founding director of the Duke Clinical Research Institute — the world's largest academic research organization. He is principal investigator for the NIH Health Care Systems Research Collaboratory, a co-director of the National Patient-Centered Clinical Research network and serves on several Institute of Medicine panels.

Califf is editor-in-chief of the *American Heart Journal* and has authored or coauthored more than 1,100 articles. Recent topics include the ClinicalTrials.gov database and clinical studies in India.

The FDA established the Office of Medical Products and Tobacco in 2011. The last permanent deputy commissioner, Stephen Spielberg, left the agency in January 2013. Following his departure, the role was briefly filled by former Johnson & Johnson executive Leona Brenner-Gati. She left the agency in May 2013.
— Elizabeth Orr

Tests Could Double Diagnoses Of Heart Attacks in Women

New research suggests that high-sensitivity tests that measure the level of troponin protein in the blood may detect twice as many heart attacks in women as current standard tests, bringing rates in line with those of men.

Researchers from the UK and U.S. compared diagnosis rates from the ARCHITECT STAT high-sensitivity troponin-I assay with standard tests in 1,126 men and women admitted to an Edinburg, Scotland, hospital with chest pain. They found the higher-sensitivity test increased diagnoses rates of myocardial infarction from 11 percent to 22 percent in women, and from 19 percent to 21 percent in men.

The findings, published last month in the *British Medical Journal*, suggest that the difference in male and female diagnosis rates may be due to doctors using a threshold for troponin testing that is too high in women, says Anoop Shah, lead author and clinical lecturer in cardiology at the University of Edinburgh.

In September, the UK's National Institute for Health and Care Excellence published guidance recommending two assays as biomarkers for heart attack: Roche Diagnostics' Elecsys Troponin T high-sensitive and Abbott Laboratories' ARCHITECT STAT high-sensitivity troponin-I.

Read the *BMJ* article at www.fdanews.com/01-15-BMJ-Troponin.pdf. — Jonathon Shacat

Industry, Think Tank Disagree On Device Tax's Impact

The 2.3 percent medical device excise tax has cost the U.S. in the range of 195,000 jobs since it took effect in January 2013, new research by AdvaMed shows. But a recent analysis by a congressional policy group begs to differ.

The figure cited by AdvaMed includes an estimated 39,000 employees who were let go or never hired, as well as jobs lost by suppliers and other indirect costs. Fifty-five companies representing 49 percent of U.S. device and diagnostics revenues responded to the member survey.

The tax has had other negative effects as well, the survey shows. Fifty-three percent of respondents said the tax had led them to reduce R&D spending, while 58 percent said they would need to eliminate R&D spending altogether. In addition, 75 percent reported canceling, reducing or deferring opening new facilities, investing in start-up companies or raising employee salaries. Forty-six percent of companies said they would consider further staff reductions.

Little Elasticity in Device Market

In a separate survey conducted by the Medical Device Manufacturers Association, 72 percent of companies said they had slowed or suspended U.S. hiring to pay the tax.

A 2014 study by Ernst & Young concluded that the 2.3 percent tax rate had translated into a 29 percent increase in total manufacturer tax liability. However, that estimate was based on early projections of tax payments; actual receipts have been somewhat lower, according to an Internal Revenue Service report published last summer.

An economic analysis by the Congressional Research Service, issued earlier this month, also plays down the tax's impact.

CRS estimates industrywide job loss at 1,200 or fewer employees and a net profit decline of 0.9 percent. The office predicts that much of the tax's cost will ultimately be paid by consumers.

That assessment fails to account for the nature of device company customers, says David Nexon, senior executive vice president at AdvaMed. While consumer demand for health supplies isn't highly influenced by price, device-makers sell mostly to hospitals and group purchasing organizations. "This is a highly competitive market with little elasticity," he says. "CRS

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could never have come to the conclusion they did if they actually talked to anyone."

CRS' suggestion that companies will pass the tax on to consumers may not pan out, Jane Kiernan, president and CEO of Saltier Labs, told reporters on an AdvaMed media call on the device tax. Her 1,000-employee company saw its effective tax burden grow by 16 percent — or up to eight cents on every dollar — after the tax took effect.

The company discussed the possibility of higher prices to account for the difference with hospitals and GPOs. "To a person, they appreciated the fact that we approached them and engaged in a discussion around the new tax, and they appreciated us having the conversation instead of just passing the charge along," she says. "But they were quite insistent that they were not in a position to take on increased prices and refused to consider them."

With raising prices a nonstarter, Saltier Labs has relocated some manufacturing to Mexico and reduced its R&D spending, Kiernan says.

AdvaMed plans to share the survey results with lawmakers as part of its efforts to get the device tax repealed. — Elizabeth Orr

U.S. Clarifies GMP Requirements For Combination Products

In a 46-page draft guidance released Jan. 26, the U.S. FDA clarified a 2013 final rule that specifies how combination product manufacturers should meet both device and drug quality regulations and implement streamlined quality systems.

Under the guidance, combination product makers have two options for good manufacturing practice compliance: satisfy all device and drug GMPs, or implement a streamlined quality system that focuses primarily on one but incorporates elements of the other.

The guidance details what GMPs are applicable to a product, general methods for how to implement them, key definitions and how to make postmarket changes to a product's quality system.

The FDA also shows how to develop a streamlined system using three detailed product scenarios: a prefilled syringe, drug-coated mesh and drug-eluting stent.

Thirt-Party Manufacturers

Each scenario highlights certain issues that a combination product might raise. For example, in the drug-coated surgical mesh case, a manufacturer wants to coat the mesh in a drug made by another manufacturer.

Since the coated mesh is a single-entity combination product, the mesh maker is subject to GMPs for combination products.

The FDA also notes how to deal with third-party manufacturers, stressing that the sponsor of the combination product is responsible for ensuring its contractors meet GMPs. If a contractor only manufactures the device part of a combination product, then it only has to meet QS regulations. In addition, the guidance notes that if combination products are simply two products that are co-packaged after being made, combination product GMP requirements do not apply.

Monday's guidance also helps to clarify how combination product makers should work with the FDA. Each combination product will be accepted by the agency center that will oversee its premarket review, and that will be the lead center and primary point of contact for applicants.

The Office of Combination Products will offer assistance when needed for questions that are limited to the combination aspect of the application or to resolve disputes about which center takes the lead.

The FDA is seeking comments on the guidance, docket no. FDA-2015-D-0198, until March 30. To read it, visit www.fdanews.com/01-26-15-ComboGMPGuidance.pdf. — Robert King

Guidance Details Requirements For Nail Disease Treatment

Labeling for devices that treat fungally infected nails should clearly state whether they are indicated for the temporary increase of clear nail in patients with onychomycosis or for the treatment of that disorder, the U.S. FDA says.

Devices indicated for temporary increase of clear nail should result in a fully replaced, clear fingernail in about six months and a fully replaced, clear big toenail in 12 months, the agency notes.

Sponsors can continue to submit clinical performance data on use of the device with adjunctive treatments, except for oral antifungal drugs. Such drugs would likely confound the data, according to draft guidance issued Jan. 27. If adjunctive treatments are used in trials, this should be reflected in the Indications and Usage statement for the device.

The FDA is concerned that devices cleared for temporary improvement could be incorrectly used to treat onychomycosis, a common fungal infection of the nails. Labeling for those devices should clarify that they have not been proven effective in treating fungal infections and are cleared only for improvement in nail appearance, the guidance says.

"The distinction between aesthetic improvement of the nail and elimination of a fungal infection is of particular clinical relevance for vulnerable populations," as they could be at ongoing risk if they postpone treatment, the FDA says.

Efficacy Studies

For devices intended to treat onychomycosis, sponsors can use stains to assess the presence or absence of fungal organisms but should use cultures to determine if the organisms are viable and to identify the species, the FDA explains. The guidance defines mycological cure as a simultaneous negative stain and negative culture.

In slow-growing nails, there could be residual, nonviable fungal forms detected by staining, the agency notes. Therefore, two serial negative cultures from the same nail could be evidence of fungal cure.

As with temporary treatments, use of antifungal drug therapy in studies should be avoided as it could affect the assessment of the device. Debridement, or removal of damaged tissue, may be offered to improve use of the nail, but such interventions should be applied uniformly to study subjects with given severities and should be disclosed in labeling, the guidance says.

Effectiveness is particularly important for vulnerable populations, the FDA notes. "In these populations, trauma to the nail due to potential adverse events during the procedure may result in delayed wound healing or may predispose to severe or life-threatening infections," the guidance says.

For both types of devices, labeling should include the following text: "Warning: These devices should be used with caution in patients with diabetes, peripheral vascular disease, or immune-suppression, or with any other medical state which warrants definitive antifungal therapy." Devices that have not been studied in these populations should receive a similar warning.

The guidance also provides recommendations on clinical trial considerations for both indications.

Comments are due April 27 to Docket No. FDA-2014-D-1849. View the guidance at www.fdanews.com/01-27-15-Fungal.pdf. — April Hollis

Canada to Require Single-Audit Certificates, Starting in 2017

Devicemakers that market products in Canada will need to certify their quality systems through the International Medical Device Regulators Forum's single-audit program, beginning in 2017, regulators say.

Health Canada currently is accepting certificates issued through IMDRF's pilot Medical

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Device Single-Audit Program or the Canadian Medical Device Conformity Assessment System for companies seeking a new or renewed Class II, III or IV device license. But the agency plans to replace the CMDCAS program with MDSAP once the three-year pilot ends. It got underway in January 2014.

The agency is developing a transition plan to implement MDSAP fully, *IDDM* has learned.

Companies will have to comply with MDSAP regardless of whether they intend to market only in Canada, says Health Canada spokeswoman Maryse Durette. In such cases, only Health Canada-specific regulatory requirements would be assessed for the purposes of issuing a certificate. — Jonathon Shacat

Industry, FDA Communications Key to Speeding Reviews, Report Says

Better, more frequent communication with the U.S. FDA is helping large devicemakers clarify expectations and speed review of submissions, but smaller firms often fail to take advantage of these opportunities, a new report finds.

Forty-two percent of executives from large device companies reported always meeting with the agency at "key juncture points" before submitting applications, compared with just 23 percent of small company execs, according to PriceWaterhouseCoopers. Forty percent of small companies said they rarely meet with the FDA.

PwC recommends more FDA outreach to smaller companies and start-ups.

And despite improvements in communications, at least among large companies, PwC found widespread concern that outdated regulatory processes are limiting development of novel devices.

Executives "desire a more collaborative relationship, one marked by greater flexibility in product development and review," the report says. Companies may even agree to additional oversight as part of a faster, more predictable review process, PwC says.

To improve the review process, PwC recommends more use of public-private partnerships, such as the Medical Device Innovation Consortium, and other methods to facilitate an exchange of ideas to streamline product development.

MDIC, for instance, is working to streamline clinical trial design and hopes to publish case studies of alternative trial designs, PwC notes. While such initiatives take shape, companies should reach out to consumers through social media or online conversations, the report says.

There is not yet a fleshed-out, systematic process for incorporating that input into product development, but the FDA and lawmakers may work toward that goal in the near future, PwC says. "Negotiations prior to the reauthorization of the user fee programs in September 2017 may further codify consumer input as criteria for product approval."

User Fees

When asked about user fees, 32 percent of executive thought they brought shorter review times and 34 percent said they improved innovation. Still, "there is growing sentiment within industry that a more expedient and predictable regulatory process can no longer be obtained simply by increasing fees," the report says. "Industry leaders want the regulatory process reevaluated from start to finish with an eye toward advancing innovation."

In the meantime, PwC urges devicemakers to engage in high-quality dialogue with the FDA. This can help companies avoid multiple review rounds and enlighten them of agency-preferred testing methods.

The report also finds growing support among devicemakers for the FDA to evaluate device candidates on both their clinical and economic

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effectiveness, with 43 percent of execs supporting the concept versus 14 percent in 2010.

PwC attributes this change in part to multinational companies growing used to submissions that require a broad health technology assessment, as is required in many European countries.

The report is available at www.fdanews.com/01-28-15-PWC.pdf. — April Hollis

TreyMed Warned for Modifying Incoming Inspection Data

TreyMed, a contract manufacturer of sensors, received a warning letter from the U.S. FDA after modifying entries in its inspection data record for parts that resulted in failures.

The Sussex, Wis., company tested a lot of adult airway adapters in February 2014, and the testing "appears to have resulted in failures as the initial entry indicates" certain parts were rejected, according to the Jan. 9 letter posted online Tuesday. However, in March, the entries were modified to indicate there were no rejects and the lot was acceptable, the letter says.

TreyMed didn't produce a nonconforming material report for the initial test failures and indicated in the sample inspection data record that the adapters were okay to use. The adapters were released for use in production, despite the lack of a documented rationale for accepting them, the warning letter says.

Procedures for acceptance of incoming product also were lacking, according to the letter. Further, in three instances in February and April of last year, TreyMed performed an incoming inspection of adult airway adapters following an outdated version of a drawing for a part. And in July, the company performed an incoming inspection of triple tubing used on a Sensor following incorrect specification criteria.

TreyMed also failed to follow its standard operating procedure for nonconforming material. Five NMRs reviewed during the inspection

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lacked a determination of whether an investigation was required.

The NMRs also did not state the disposition authority of the nonconforming material. One indicates rework for adult airway adapters that were rejected, but there was no documentation of the rework instructions and no evidence to support the rework for the nonconforming airway adapters, the letter says. The final disposition status was unknown.

Other citations pointed to lapses in compliance with device history record procedures and corrective and preventive action procedures.

The company did not respond to a request for comment by press time. The warning letter is available at www.fdanews.com/01-27-15-IDDM.pdf. — April Hollis

Beware U.S.' Limited Definition Of Custom Devices: Expert

Companies hoping to bypass U.S. FDA premarket approval requirements with a custom device exemption need to grasp the narrow limits of that definition, an attorney says.

J. Mason Weeda, with Olsson Frank Weeda Terman Matz in Rockville, Md., says nine in 10 devices that manufacturers think are custom devices probably aren't. Custom device status is important because manufacturers are exempt from premarket approval and clinical trial requirements.

According to the FDA, a custom device is one that is not commercially available in the U.S. in its finished form and is intended to treat a disease or physical condition that couldn't be served by any other device. A product is also considered a custom device if it serves the needs of a specific doctor, such as a custom surgical tool for a physician with a hand deformity.

Weeda's practice has worked with multiple clients who believed that any device made to fit an individual patient is a custom device. "That really doesn't fit what FDA has in mind for this exemption," the attorney says. He spoke during a Jan. 20 *FDAnews* webinar on changes to the FDA's custom device policy under a September 2014 final guidance.

Under that guidance, custom devices may share standardized design or manufacturing practices with commercial devices and be produced in quantities of up to five units annually. If extra units are produced due to sizing concerns, ones that aren't used don't count toward the five.

Moreover, if multiple devices are made to treat the same patient for the same condition — for example, if someone needs two knee replacements — that counts as one unit, the guidance says.

Custom device makers must report annually to the FDA the number of patients who received a new device or a revision of a previous one, including multiple devices in one patient. The five-item limit applies only to new patients, Weeda notes.

QS Compliance

Devices that don't fit under the custom device heading but are produced in quantities too limited to support clinical trials may be cleared via the FDA's compassionate use pathway for patients with serious diseases for which no alternative treatment exists, Weeda says.

From time to time, manufacturers may make a single unit of an obsolete product to fill a specific patient need — for example, if a patient needs revision surgery to replace a device component that's no longer commercially available. In such cases, they should consider the FDA's compassionate use pathway, rather than seeking custom device status, Weeda says.

While they don't require clinical studies or premarket approval, custom devices must comply with FDA quality system regulations and listing requirements, Weeda notes.

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His final words of advice: Document everything. Have procedures in place so that employees know the limits of the exemption, and document the decisionmaking process the company went through to qualify the product as a custom device, Weeda says.

"If you can document in good faith that … you believe your product falls within the exemption, even if FDA disagrees, they're really not going to drop the hammer on you," he adds. —Elizabeth Orr

FTC Raps Software Firm for Making Unproven Health Benefit Claims

While recent U.S. FDA guidance widens the range of wellness products that can be sold without agency approval, that doesn't mean companies making dubious claims will escape federal intervention — as one software company recently found out.

Houston, Texas-based Focus Education advertised that its Jungle Rangers software product can permanently improve focus, memory, attention and behavior in children, including those with attention deficit and hyperactivity disorder, or ADHD. The ads also claimed that the benefits were "scientifically proven." Focus sold about $4.5 million worth of the software, at $214.75 a pop, between 2012 and mid-2013.

The U.S. Federal Trade Commission accused the company of making false or unsubstantiated claims and released a consent order Jan. 20 barring Focus and its co-founders from marketing any product implied to improve children's attention, memory or school focus unless there is scientific evidence to back up those claims. The evidence must be based on randomized, double-blind and controlled clinical trials conducted by qualified researchers, the order adds.

Focus must also get the FTC's sign-off on any marketing that makes medical claims, as well as the supporting documentation, for five years.

Guidance released earlier this month by the FDA says the agency won't regulate wellness products that make general claims about memory, mental skills or other aspects of health, or that mention a scientifically proven connection between a wellness activity and a chronic condition (*IDDM,* Jan. 19). It's unclear whether that policy would have applied to the Jungle Rangers product, says attorney Bradley Merrill Thompson of Epstein, Becker Green.

"The developer says the video game can be used by kids with ADHD and that is a disease or condition, and the FDA guidance says it is okay to promote products that help cope with a chronic disease or condition," Thompson tells *IDDM*. "But the claim has to be generally recognized as true, which according to the FTC these claims are not."

Thompson says the FDA probably could regulate the product, but avoided the debate by having the FTC take enforcement actions.

Focus Education could not be reached for comment. View the agreement at www.fdanews.com/ext/resources/files/01-15/01-26-15-FTC.pdf. — Elizabeth Orr

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You'll take home a jam-packed resource kit with **more than 20 templates, checklists, case studies, guidances and supporting information.** These are the tools that will help you effectively carry out the lessons you've learned over the two-day conference.

This workshop — **chaired by internationally renowned expert Fubin Wu** — has been specifically designed to provide you with industry best practices to achieve compliance and effectively assure medical device software safety.

In fact, it's a once-in-a-lifetime opportunity **to learn how the FDA expects you to manage the risks of your medical devices that contain software.**

In two days of intensive sessions, you will be brought up to date on the FDA's latest research on medical device software best practices, software risk management related standards and guidances and key success factors for effective software risk management.

Plus, in a special bonus, you'll find out more about assurance levels — and what it will take to convince regulators — in one of **our seven invaluable case studies**, always a popular and valuable way to learn. Our seven case studies cover:

Spread throughout the course will be lessons in applying these key software risk management related standards and guidances to your software development processes:

- ISO 14971:2007 and EN ISO 14971:2012, IEC 62304 Medical Device Life Cycle Process, IEC TR 80002-1 Application of ISO 14971 for Software
- FDA Guidance on Mobile Medical Applications, Cybersecurity in Medical Devices, Infusion Pump Total Product Life Cycle

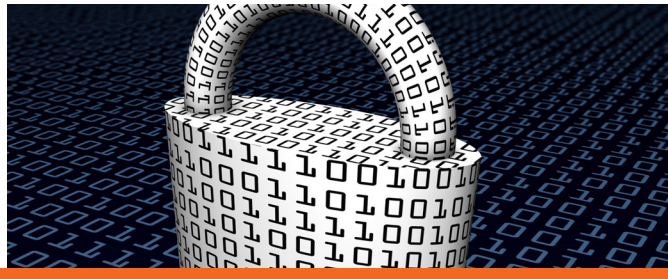
During each teaching session, Mr. Wu will share techniques and best practices on how to:

- Identify software related risks
- Identify software risk control and mitigation measures
- Assess and evaluate risk contributed/caused by software (premarket and post-market field issues)
- Assure the completeness and adequacy of risk management
- Communicate risk management information throughout the life of the product
- Key success factors for effective software risk management

Here's what you can expect to walk away with at the end of two intense days at **Software and Cybersecurity Risk Management for Medical Devices:**

- Understanding of how medical device manufacturers can overcome both technical and regulatory compliance challenges
- The resources and tools to help you succeed
- The medical device industry's best practices
- The FDA's latest updates on medical device software best practices

This conference has been pre-approved by RAPS as eligible for up to 12 credits towards a participant's RAC recertification.



Tuesday April 14

8:00 a.m. – 8:30 a.m. | **REGISTRATION AND CONTINENTAL BREAKFAST**

8:30 A.M. – 9:00 A.M. | **WELCOME AND INTRODUCTIONS**

9:00 a.m. – 10:00 a.m.

I. FDA's Research on Medical Device Software Best Practices

II. FDA's Analysis of Software-Related Recalls

10:00 a.m. – 11:00 a.m.

III. Overview of Recent FDA Guidances

a. Cybersecurity in Medical Devices (draft, June 2013)

b. Radio Frequency Wireless Technology in Medical Devices (August 2013)

c. Mobile Medical Applications (September 2013)

d. Total Product Life Cycle: Infusion Pump (draft, April 2010)

11:00 a.m. – 11:15 a.m. | REFRESHMENT BREAK

11:15 a.m. – 12:15 a.m.

IV. Key Relevant Standards

a. ISO 14971:2007 and EN ISO 14971:2012, IEC TR 80002-1 Application of ISO 14971 for Software

b. IEC 62304 Medical Device Software Life Cycle Process - Risk Management Section

c. IEC 80001-1 Managing Medical IT-Networks and relevant Technical Reports

d. NIST Framework for Improving Critical Infrastructure Cybersecurity, 2014

12:15 p.m. – 12:45 p.m.

Morning Summary of FDA Perspectives and Group Discussion

12:45 p.m. – 1:45 p.m. | LUNCH

1:45 p.m. – 2:45 p.m.

V. Risk Management Documentation to Support Regulatory Filings and Inspections

a. What is viewed as best practices to demonstrate safety

VI. Risk Management Documentation for Pre-market Submissions

a. Case study for risk traceability matrix. This study provides participants a template for and examples of best practices that are frequently requested for pre-market submissions or during establishment inspections

b. Case study for cybersecurity risk traceability matrix. This study provides participants a template for and examples of best practices that are frequently requested for pre-market submissions or during establishment inspections

2:45 p.m. – 3:00 p.m. | REFRESHMENT BREAK

3:00 p.m. – 4:30 p.m.

VII. Risk Management Completeness, Adequacy, Effectiveness and Reviewability

a. Introduction of assurance case concepts and how they are used in industry

b. Case study for medical device safety assurance case. This study illustrates how to document information in a story telling fashion and convince internal/external reviewers (e.g. ODE reviewers) that a risk analysis is adequate and complete

c. Case study for medical device cybersecurity assurance case. This case study illustrates how to document information in a story telling fashion and convince internal/external reviewers (e.g. ODE reviewers) that a cybersecurity risk analysis is adequate and complete.

4:30 p.m. – 5:00 p.m.

Day One Summary of FDA Perspectives and Group Discussion

Wednesday April 15

8:00 a.m. – 8:30 a.m. | CONTINENTAL BREAKFAST

8:30 a.m. – 9:00 a.m.

VIII. Characteristics for Medical Device Software

a. Understanding the difference between software and hardware

b. Understanding software quality and reliability engineering

c. Challenges of software risk management and cybersecurity

9:00 a.m. – 9:30 a.m.

IX. Emerging Methods and Techniques

a. Learn what new technical methods and techniques the FDA has been researching and looking into to improve the safety of software related medical devices

9:30 a.m. – 10:30 a.m.

X. Risk Identification

a. Preliminary hazard analysis

b. Top down analysis, fault tree analysis

c. Bottom up analysis – including design FMEA, function FMEA, process FMEA, usability FMEA, common causes of software failures

d. Connectivity analysis between top down and bottom up

e. Multi perspective analysis

f. Case study. This study provides participants an opportunity to apply techniques on how to identify and connect hazards, hazardous situations/causes using device examples.

10:30 a.m. – 10:45 a.m. | REFRESHMENT BREAK

10:45 a.m. – 11:45 a.m.

XI. Cybersecurity Risk Identification

a. Medical device cybersecurity basics

b. Asset profiling

c. Threat identification

d. Vulnerability identification

e. Software vulnerabilities

f. Connectivity between cybersecurity and safety risk analysis

g. Case study. This study provides participants an opportunity to apply techniques on how to identify and connect assets, threats and vulnerabilities using device examples.

11:45 a.m. – 12:15 p.m.

Morning Summary of FDA Perspectives and Group Discussion

12:15 p.m. – 1:15 p.m. | **LUNCH**

1:15 p.m. – 2:15 p.m.

XII. Risk Controls

a. Risk control basics

b. Software life cycle process control measures

c. Safety requirements identification

d. Cybersecurity capability and requirements identification

e. Special considerations for cybersecurity risk controls

f. Control measures implementation and effectiveness

g. Case study. This study provides participants an opportunity to identify, apply risk controls and establish traceability of its implementation using device examples.

2:15 p.m. – 3:15 p.m.

XIII. Software-Related Medical Device Risk Assessment and Evaluation

a. Pre-market risk assessment and evaluation

b. Post-market risk assessment and evaluation

c. Legacy product cybersecurity risk management

d. Maintenance and life cycle risk management

3:15 p.m. – 3:45 p.m.

XIV. Success Factors for Risk Management Programs

3:45 p.m. – 4:15 p.m.

Day Two Summary of FDA Perspectives and Group Discussion Plus Workshop Wrap Up

WHO WILL BENEFIT

- Software systems design engineers and managers
- Quality, reliability and risk management engineers and managers
- Project managers involved in design and development
- Medical staff evaluating risk, safety or effectiveness
- Quality managers
- Regulatory affairs specialists and managers
- Medical device app developers
- IT systems development managers
- Contract manufacturers
- General/corporate counsel

MEET YOUR INSTRUCTOR

Fubin Wu is the Co-Founder of GessNet. GessNet is a software and consulting company specializing in medical device risk management (www.GessNet.com). He designed and led the development of TurboAC™ risk management and assurance case software, in concert with the FDA, Association for the Advancement of Medical Instrumentation (AAMI), medical device manufacturers, hospitals and industry experts. Mr. Wu has spent more than 16 years in medical device quality management systems, hardware/software reliability engineering and risk management, serving various roles from quality engineer to quality director.

"All instructors were very knowledgeable and had expertise in the industry. Well done."

—May 2014 Workshop Participant

"The class had a good pace. It covered standard risk management well."

—May 2014 Workshop Participant

"[I liked the] small discussion groups and intimate setting"

—May 2014 Workshop Participant

COURSE BINDER MATERIALS

Each participant will receive a folder and flash drive packed with tools and reference materials in a combination of both electronic and hard copy format you can put to use right away, including:

- Copies of slides from PowerPoint presentations
- Interactive exercise worksheets
- Copies of case study examples
- Hazard analysis example
- Fault tree analysis example
- Example of FMEA analysis and connectivity with hazard analysis
- Risk traceability matrix example
- Cybersecurity risk analysis example
- Safety assurance case example
- Cybersecurity in Medical Devices (FDA draft guidance, June 2013)
- NIST Framework for Improving Critical Infrastructure Cybersecurity (Version 1.0, 2014)
- Software-Related Recalls: An Analysis of Records (by Lisa K. Simone of FDA, AAMI BI&T Nov/Dec 2013 Issue)
- Reducing Risks and Recalls: Safety Assurance Cases for Medical Devices (by Sherman Eagles and Fubin Wu, AAMI BI&T Jan/Feb 2014 Issue)
- Hazard Analysis for a Generic Insulin Infusion Pump (by Yi Zhang, Paul Jones, and Raoul Jetley of FDA, J Diabetes Sci Technol. Mar 2010)
- Total Product Life Cycle: Infusion Pump (FDA draft guidance, April 2010)
- Radio Frequency Wireless Technology in Medical Devices (FDA guidance, August 2013)
- Mobile Medical Applications (FDA guidance, September 2013)
- Risk Management in the Design of Medical Device Software Systems (by Paul Jones PL, Biomed Instrum Technol 2002 Jul-Aug; 36(4):237-66)

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UNDERSTANDING THE FDA'S POSITION AND BEST PRACTICES FOR COMPLIANCE

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Tuition rate is $1,797 per person and includes all workshop sessions, workshop materials, two breakfasts, two luncheons and daily refreshments.

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FDANEWS

How to Implement UDI: *A Guide for Devicemakers*

As of Sept. 24, 2014, many Class III devicemakers had to be in compliance with the new UDI requirements; deadlines for other manufacturers are approaching fast. And it's already clear that implementation and compliance with this new rule is a very big challenge.

That's why FDAnews developed the new management report How to Implement UDI: A Guide for Devicemakers.

It walks you step-by-step through the key portions of the UDI final rule, clearly pointing out the changes from the proposed rule and providing you with all the implementation and compliance details you need to know. You will learn:

- The difference between UDI and track and trace;
- The timetable for implementation for Class I, Class II and Class III devices;
- Which devices must comply with the rule and which are exempt;
- What information must be included on product labels;
- How to submit device identification information to the GUDID;
- About the accredited UDI issuing agencies, their roles (and how to become one);
- The benefits of UDI to industry, regulators and the public;
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Order your copy TODAY.

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