INTERNATIONAL DEVICES & DIAGNOSTICS MONITOR

Vol. 1, No. 33
Aug. 24, 2015

IN THIS ISSUE



## FDA Hits 3 Endoscope Makers With Warning Letters

Olympus is facing tough questions from the FDA following inspections conducted in April and May of four facilities that manufacture endoscopes. The company — along with Pentax and Fujifilm — is facing scrutiny after their complex endoscopes were linked to patients becoming sick or dying.

In a warning letter posted to the agency's website last week, the FDA says Olympus failed to inform the agency within the required time period that its TJF Type Q-180V had caused patient injuries. That particular model has been linked to at least two deaths at UCLA Ronald Reagan Medical Center in Los Angeles.

*(See* **Endoscope***, Page 2)*

## Innovation, Transparency Take Center Stage in China Device Reforms

China's State Council has unveiled new guidelines intended to make the medical devices approval process more science-based and efficient.

The guidelines, which also affect pharmaceuticals, look to raise the review standards to those of international levels while helping enhance transparency throughout the device approval process. To that end, the council is aiming to improve registration, technical review, product testing and field inspection conditions.

A key goal of the guidelines is to enhance the quality control system. To accomplish this, the government will work to improve review mechanisms and standardize procedures to reduce inconsistency in regulatory decisions.

Qing Shen, a quality and regulatory consultant at NAMSA China, tells *IDDM* that this standardization will improve the efficiency and transparency of China Food and Drug Administration processes to ensure that review is impartial and scientific. A big challenge for companies has been the variability in technical opinions from differ-ent lead reviewers, Shen says.

To encourage the development of innovative devices, the government also is looking to cut companies a break on pricing policies for

*(See* **China***, Page 4)*

**Endoscope,** *from Page 1*

The letter cites one complaint referencing 16 patients who contracted a *Pseudomonas aeruginosa* infection after being treated with one of the company's endoscopes. Some of those treated experienced abscesses. According to the FDA, the company submitted one MDR to account for all of the patients — roughly three years after the events occurred.

"Your firm became aware of the event on May 16, 2012," the agency says. "The referenced MDR and all additional MDRs associated with the event were received by FDA in 2015, which is beyond the 30 calendar day frame."

The FDA received a response from an Olympus official addressing the concerns, but says its adequacy can't be determined at this time. Further, while the response described corrective actions, it didn't provide evidence of implementation to the FDA.

In addition, the agency found fault with the company's MDR procedures, saying there is no internal system for the timely transmission of complete reports.

An Olympus spokesman tells *IDDM* that the company is reviewing the letter so it can respond in a timely manner. He adds that Olympus already has taken steps to make improvements, including working on its MDR system.

Regarding the multipatient MDR, he says Olympus submitted an MDR report on the incident on May 25, 2012, following up in 2015 with additional MDR reports to 'unbundle' the 2012 report on the 16 patients and include additional information.

TJF Type Q-180V was launched in the U.S. market in 2010 and was based on an existing device, but it was never formally cleared by the FDA. The company says it thought it didn't have to submit a 510(k), but did so in 2013 (*IDDM*, March 6).

Like Olympus, Pentax also was rebuked for not reporting patient injuries in the required timeframe. In this case, patients developed difficult-to-treat *Carbapenem-resistant enterobacteriaceae* infections.

The FDA cites the company for not having adequate MDR procedures. Other issues include failure to establish and maintain design validation procedures to ensure devices conform to user needs and intended uses. According to the agency, the company failed to include testing of production units under actual or simulated use conditions or document the results of design validation in the device history file.

"The validation studies conducted to support the Ethylene Oxide (EtO) sterilization and cleaning and high level disinfection (HLD) Instructions for Use (IFUs) for the currently marketed device, ED-3670TK, were conducted using different model/series endoscopes. Your firm failed to document why design validation results for the different model/series endoscopes are valid and applicable to the ED-3670TK devices," the warning letter says.

Pentax says it is reviewing the contents of the letter and will respond within the timeframe required by the agency. The company tells *IDDM* it has been working with federal authorities, providers and industry leaders to address concerns related to the devices.

Fujifilm took heat for, among other problems, not having a proper reprocessing validation for the ED-530XT duodenoscope by not including an evaluation of the effects of reprocessing on the O-ring. Also, the company failed to verify that the LT-7F manual air leak tester could adequately perform the required task. The ED-530XT model also lacked FDA clearance.

"The health and safety of patients is Fujifilm's number one priority, and we have been actively working with the FDA to ensure that our products and processes meet FDA requirements," the company says. That includes filing a 510(k) application for the ED530-XT on Aug. 10, a Fujifilm spokeswoman tells *IDDM*.

The Olympus warning letter is available at www.fdanews.com/082415-olympus-warning-letter.pdf. Read the Pentax letter at www.fdanews.com/082417-hoya-warning-letter.pdf and the Fujifilm letter here: www.fdanews.com/082415-fujifilm-warning-letter.pdf. — Elizabeth Hollis

## Whistleblower Apologizes for Error In Lawsuit Against Unilife

York, Pa.-based Unilife has scored a big win after a whistleblower acknowledged that he was wrong in alleging the company failed to comply with FDA requirements.

Talbot (Todd) Smith made the admission in a federal court in Philadelphia Aug. 18, nearly three years to the day after bringing suit against Unilife. He had accused the company of retaliatory termination for disclosing protected disclosures related to shareholder fraud and noncompliance with FDA requirements.

"I now understand that there were no violations of FDA regulations during my tenure at Unilife," Smith said during the dismissal of the suit, according to a Unilife release.

"In addition, in the summer of 2011, Unilife issued press releases, which stated that they had begun shipments of validated Unifill product to customers. I now understand that the production process was, in fact, validated."

### Validation Suspicions

Smith served as vice president of integrated supply chain at Unilife from September 2011 through August 2012. In his amended complaint, Smith alleged that the company had lured him to join with false assertions that the Unifill prefilled syringe had been validated and that shipments had been made to Sanofi, which had acquired exclusive rights to negotiate the purchase of the product in 2008.

However, despite company press releases in the summer of 2011 saying shipments and sales of the product had begun, Smith alleged that the required FDA validation process was not completed until March 30, 2012. That meant the company either was shipping products before they were validated or it was shipping samples and not making the sales it had claimed in the press releases.

Smith became increasingly concerned, airing his misgivings to his supervisor, Ramin Mojdeh. Rather than listen to his concerns, Mojdeh allegedly told Smith he "was following the rules and procedures established by the FDA too closely," and thus slowing down production.

Undeterred, Smith kept making complaints and, in one instance, opened a CAPA when unreleased product was allegedly shipped to an external laboratory for testing without proper procedures being followed.

Smith also accused the company of misleading investors by overstating customer demand and manufacturing capacity.

After what he saw as more violations, Smith made an anonymous report to the Unilife board of directors alleging unethical activities, including stock fraud, suppression of negative information, compromise of the quality system and retaliation against whistleblowers. The latter charge related to Smith's allegation that a reduction in workforce as a result of a lack of customer demand for Unilife products included many employees who had refused to participate in the company's unlawful activities.

His supervisor was provided a copy of the allegations, and Smith ultimately was terminated.

### Counterclaims

Unilife denied all of Smith's allegations and filed counterclaims. The company accused him of secretly recording a conversation with Mojdeh in violation of the Pennsylvania Wire Tapping and Electronic Surveillance Control Act.

As part of the case's dismissal, Smith has agreed to pay to settle Unilife's claims against him.

The case, *Talbot (Todd) Smith v. Unilife Corporation, Unilife Medical Solutions, Inc., Alan Shortall and Ramin Mojdeh*, was filed in the U.S. District Court for the Eastern District of Pennsylvania. — Elizabeth Hollis

**China**, *from Page 1*
registration and approvals. Shen notes this will apply only to small and startup domestic companies developing innovative products.

As it tries to boost innovation, the government is also looking to crack down on bad actors. Sponsors and research institutions that falsify sections of their submissions — such as incorrect clinical trial data or quality standards — will be punished severely, the council says.

The council has requested that relevant laws and regulations be amended throughout the country as soon as possible. — Elizabeth Hollis

## Japan, Brazil Look for Common Ground on Device Regulations

The Japan External Trade Organization and that country's Pharmaceuticals and Medical Devices Authority are looking to enhance ties with Brazil's Agência Nacional de Vigilância Sanitária on medical products regulations.

With this goal in mind, the three groups have scheduled a seminar for Sept. 10 in Tokyo where medical device experts will discuss their respective country's regulations. It marks the second time representatives from the two countries will conduct such a seminar — the first occurring last year in São Paulo, Brazil.

Ahead of last year's event, Japanese Prime Minister Shinzō Abe met with Brazilian President Dilma Rousseff to promote cooperation in the medical and healthcare fields. The seminar that followed included sessions in which participants discussed solutions for efficiency in the review process of medical devices.

Topics for this year's seminar include international cooperation related to quality management and good manufacturing practices, as well as enhancing review efficiency. For more information, visit www.pmda.go.jp/english/symposia/0081.html. – Elizabeth Hollis

## Group to FDA: Cozy Relationship With Industry Taints Draft Guidance

A consumer advocacy group is calling on the FDA to retract draft guidance on patient preference information and end its relationship with a consortium that it maintains is dominated by medical device manufacturers.

In comments on *Patient Preference Information — Submission, Review in Premarket Approval Applications, Humanitarian Device Exemption Applications, and De Novo Requests, and Inclusion in Device Labeling*, Public Citizen asserts that members of industry have had undue influence in developing a strategy to incorporate PPI in regulatory decision-making.

The group specifically highlights the relationship between the FDA and the Medical Device Innovation Consortium, a public-private partnership that, according to its website, is dedicated to advancing regulatory science.

Public Citizen sees this relationship as too cozy, "resulting in an approach to regulatory development that is centered on industry interests, rather than patient and public health interests."

The group points out that of the 23 members of the MDIC steering committee, 11 represent the medical device or affiliated industries and seven are FDA officials. Only one member is from a patient group. However even that group is funded by industry.

"This extensive involvement between members of the medical device industry and the officials who regulate them is inappropriate, particularly when presented as an effort to develop a 'patient-centered' approach to product development and regulation," the group asserts. "Device manufacturers and affiliated industries have an inherent conflict of interest: In seeking to incorporate patient views into the regulatory process, these companies are necessarily motivated by the desire to increase the sales of medical devices, and thus their own profits."

Issued in May, the draft guidance discusses the main factors sponsors and other stakeholders should consider when collecting PPI that may be used in reviewing premarket approval applications, HDE applications and *de novo* requests.

Submitting this information is optional, but the FDA says it can help when multiple treatment options exist and none is clearly superior, or if patients' views on a product's benefits and risks are significantly different from those of healthcare providers (*IDDM*, May 15).

Public Citizen doesn't see the draft guidance as helping patients. If the document is finalized, it will effectively lower the standards of regulatory approval, potentially allowing unsafe, ineffective medical devices on the market, the group says.

To bolster its claims, Public Citizen notes that hypothetical examples used in the draft guidance suggest using PPI when evidence backing the safety and effectiveness of a device is inconclusive.

"Out of all the examples used in the draft guidance, only example C indicates that the FDA might deny approval of the device under consideration, and this denial is made in spite of patient preference information, not because of it," according to group.

The group also cites a real-world example, EnteroMedics' Maestro Rechargeable System, as an example of how the FDA's approach is flawed.

The FDA gave the green light to the device, despite a majority of advisory committee members voting against its effectiveness. The agency cited information from the Center for Devices and Radiological Health's Patient Preference Weight Loss Study as the basis for its decision, saying patients would accept the risk associated with the implanted device.

Public Citizen says there wasn't enough transparency of how the agency used the data from the study, adding that the MaxR-MinB

*(See* **PPI***, Page 6)*

**PPI**, *from Page 5*

calculator tool, which is intended to aid in regulatory decisions related to obesity devices, has not been made public.

"We urge the FDA to include steps for greater transparency in any subsequent version of the guidance, including a pledge to publish individualized results generated by regulatory tools developed using patient preference information, such as the tool developed based on data from the CDRH Patient Preference Weight Loss Devices Study," the group writes.

### A Different View

Most of the other 17 comments were positive and congratulated the FDA for its efforts.

The National Psoriasis Foundation, for example, says it backs the FDA's commitment to capturing PPI and suggests the agency do more by developing a meaningful definition of patient engagement and establishing a system for gathering patient-reported data.

AdvaMed says the document is informative, but should be less repetitive and more concise.

Further, the trade group disagrees with the FDA's assertion that patient preference studies considered in a premarket application should generally be described in the labeling.

"Very few preference studies have been done thus far, so it is not clear what impact, if any, including PPI in the labeling would have," AdvaMed says.

Study data could prove helpful in determining the impact, the group adds, citing MDIC's ongoing efforts to determine how to effectively communicate the risks and benefits of medical procedures to doctors and patients.

To read Public Citizen's comments, visit www.fdanews.com/082415-public-citizen.pdf. AdvaMed's comments are available at www.fdanews.com/08-24-15-AdvaMed-Comments.pdf, while NPF's are at www.fdanews.com/08-24-15-NPF-comments.pdf. — Elizabeth Hollis

## FDA to Shine Spotlight On PCLC Systems

The FDA is seeking feedback on the design and development of devices that deliver life-saving therapies in critical-care environments.

The issue — physiological closed-loop controlled devices used to deliver anesthesia, vasoactive drugs and fluids and mechanical ventilation — will be the focus of an Oct. 13-14 workshop at the agency's White Oak campus in Silver Spring, Md.

"Recent advances in medical device technology and control system science have increased the development of PCLC medical devices," according to an Aug. 17 *Federal Register* notice announcing the meeting. "This may or may not introduce new risks to patients, but could introduce new medical device hazards that, considered during device design and development, can be mitigated throughout the device life-cycle."

PCLC devices help clinicians and patients by automatically making adjustments to therapeutic delivery — something that could prove highly beneficial during mass casualty events, for example.

Potential areas of discussion slated for workshop include:

- Benefit-risk considerations;
- Design and development challenges;
- System performance analysis for different controller types;
- Fault detection and fallback modes;
- User interfaces and operational transparency;
- Knowledge gap between clinicians and system engineers;
- Clinician involvement in system design;
- Control system terminology;
- Preclinical evaluation;
- Evidence needed to demonstrate a stable and robust controller;
- Use of computer simulations, including verification, and validation;
- Real-time bench testing;
- Clinical evaluation;
- Clinical validity of sensors;
- Patient populations;
- Environments of use;
- User-related level of expertise; and
- Human factors.

The deadline to submit comments on all aspects of the workshop is Sept. 1.

To learn more, visit www.fdanews.com/082415-PCLC-workshop.pdf. — Elizabeth Hollis

## Security Vulnerability Triggers UDI Compliance Extension

The U.S. FDA has extended until Oct. 24 the deadline to submit required labeling and data to the Global Unique Device Identification Database, following the discovery of a security vulnerability.

The extension applies to implantable, life-supporting and life-sustaining devices, which had an original compliance deadline of Sept. 24.

In Aug. 14 guidance, the agency says it took the GUDID system offline on Aug. 7 until a patch could be implemented. The issue was fully resolved as of Aug. 19.

Class III labelers that requested and received an extension that would have expired between Aug. 7 and Sept. 24 also may take advantage of the deadline delay.

An FDA spokeswoman tells *IDDM* that the vulnerability was identified July 24, and the agency began an immediate investigation.

With implementation of the UDI program, devicemakers must include an identifying code on the product's label to make it easier to track postmarket data. The data are submitted to the GUDID.

The UDI final rule was issued in 2013, and the program took effect for high-risk devices in September 2014.

To read the guidance document, visit www.fdanews.com/08-24-15-gudid-extension.pdf. — Elizabeth Hollis

## FDA Seeks Volunteers For MDR Pilot Program

Attention devicemakers: The FDA wants you.

Beginning Sept. 1, the agency will accept nominations for a pilot program for submitting medical device reports for malfunctions occurring in Class I and Class II devices that are not permanently implantable, life-supporting or life-sustaining.

The agency intends to use the information to develop malfunction reporting criteria for these device types, which are subject to Section 519(a) of the Federal Food, Drug, and Cosmetic Act. Class III and permanently implantable, life-supporting or life-sustaining Class II devices are ineligible for participation.

In an Aug. 18 *Federal Register* notice, the FDA provides specifics on the program, through which participants submit Form 3500As on a quarterly basis, summarizing malfunction reports received for a unique device problem code.

Data provided by devicemakers should be detailed enough to understand any malfunction, summarizing the event, the result of the investigation and any remedial action taken by the company. If a firm decides against taking remedial action, it should be prepared to explain why.

The agency also gives case samples illustrating the format for the reports, which, among other details, should include the manufacturer name, city and state, type of reportable event and a summary narrative.

The FDA will add all summary MDR reports to the Manufacturer and User Facility Device Experience Database. The pilot will run until all participants have completed two consecutive quarter cycles.

Due to resource issues, the agency is capping the number of pilot participants at nine. Devicemakers may withdraw from the pilot at any time.

Read the *Federal Register* notice announcing the pilot program here: www.fdanews.com/082415-pilot-malfunction.pdf. — Elizabeth Hollis

## Devicemakers to Shell Out More for Export Certificates

Medical devicemakers in the U.S. will have to pay more for their follow-on export certificates. A lot more.

In an Aug. 19 *Federal Register* notice, the FDA says it is raising the price of subsequent export certificates from $15 to $85 — an increase of about 466 percent.

This marks the first time that costs for these types of certificates, which are issued for the same products as part of the same request, have gone up since 2003.

"These changes are necessary to ensure that the program remains self-sustaining and to cover FDA's increased costs, which are currently being covered by appropriated funds," according to the notice. The total cost of the export certification program for devices in FY 2014 was $5.7 million.

As the agency notes, the volume of certificate requests has grown 369 percent since FY 1997, when 11,140 were issued. In FY 2014, 52,193 were issued. Adding to the strain is that devicemakers are permitted to include multiple devices on a single certificate, rather than having to file separate ones.

While the FDA will continue to allow multiple devices to be included on a single certificate, it has cut the maximum number of pages from 50 to 25. That number includes the certificate page and a maximum of 24 more to allow for any attachments. The notice provides additional details on how the agency will determine the total cost of certificates.

Original certificates will continue to cost up to $175. The increased fees for subsequent certificates take effect Sept. 1.

Read the *Federal Register* notice at www.fdanews. com/082415-export-certificates.pdf. — Elizabeth Hollis

## GAO: Less than Half of Companies Know Source of Conflict Minerals

A new Government Accountability Office report has found that most companies don't know the origin of their so-called conflict minerals — tantalum, tin, tungsten and gold — meaning they could be acquiring them from countries rife with humanitarian abuses.

According to a sampling of firm filings examined by the GAO, 94 percent of companies report doing their due diligence in tracking the chain of custody of conflict minerals. However, 67 percent could not determine whether the minerals came from the Democratic Republic of Congo, or neighboring countries that fund armed insurgents that practice human rights abuses within the DRC.

Devicemakers are among those that have had trouble sourcing these minerals. In filings covering 2013, both Medtronic and Integra LifeSciences confirmed they could not identify the country of origin. Both said the complexity of the supply chain makes doing so difficult.

The report comes as part of the 2010 Dodd-Frank Wall Street Reform and Consumer Protection Act, which requires the Securities & Exchange Commission to collect data on companies' use of these minerals from the DRC, Central African Republic, South Sudan, Zambia and Angola. Only 1,321 companies filed the forms, far fewer than the SEC estimate of 6,000 that could be affected by the rule.

Even as the SEC collects this information, the U.S. Court of Appeals for the D.C. Circuit ruled Aug. 18 that forcing companies to state on their websites that products have "not been found to be 'DRC conflict free'" violates the First Amendment, covering corporate speech. The ruling puts the future of the rule in doubt.

In May, European lawmakers voted 402 to 118, with 171 abstentions, to require devicemakers that use conflict minerals to certify that the minerals aren't sourced from certain zones (*IDDM*, May 22). Parliament also voted to enter into talks with member states to agree on a final version. No date has been set for final adoption.

To read the GAO report, visit www.fdanews.com/082415-SEC-minerals.pdf. The appeal court ruling is at www.fdanews.com/082415-decision.pdf. — Elizabeth Hollis

## Medical Device Funding Jumps For All Areas in Second Quarter

More details have emerged about investments in the medical device sector during the second quarter of 2015, with the official release of a report from PricewaterhouseCoopers and the National Venture Capital Association.

According to the PwC/NVCA *MoneyTree* report, based on data from Thomson Reuters, medical device investments jumped 22 percent in terms of dollars over the same period last year.

Medical diagnostics funding saw the biggest gain, 88 percent to $140 million, while medical therapeutics rose 29 percent to $500 million.

Medical/health products, however, saw a decline of 16 percent to $174 million versus the same period last year.

### Funding Stages

Early-stage Funding for devices rose 59 percent to $264 million in 33 deals. That compares with $167 million in 24 deals for the same time period last year.

Late-stage funding also grew — 10 percent to $549 million in 42 deals. During the second quarter of 2014, the total was $500 million across 53 deals.

### Growing Confidence

The report notes that the average deal size for late-stage medical device transactions was $13.1 million versus $8 million for early-stage deals.

"In the second quarter early-stage investments grew significantly year-over-year for both biotechnology and medical devices," says Greg Vlahos, life sciences partner at PwC.

"It's another sign of confidence in the sector."

Vlahos sees a lot of investor optimisim about the device arena, particularly as more companies look to file initial public offerings.

"We've seen a strong medical device IPO market over the past few quarters in addition to an increase in VC investing," he says.

"We expect that VC investing in medical device companies will at least match the dollars invested in 2014, if not exceed it."

The two firms released figures in July, showing that investors pumped more than $800 million into private companies.

That figure represents an increase of about 70 percent over the first quarter of the year.

For the two quarters, medical device companies have taken in about $1.29 billion — slightly ahead of the halfway mark of 2014, when the total stood at $1.26 billion (*IDDM*, July 24).

### More Cash

Overall, second-quarter investments in the life sciences sector — biotechnology and medical devices combined — accounted for about $3.1 billion going into 201 deals, a 41 percent increase in dollars, but flat in terms of deals, versus the first quarter of the year.

Calhoun Vision, a Pasadena, Calif.-based company that is developing a light adjustable intraocular lens, was the leader, bringing in nearly $69 million in financing.

The next largest monetary injection went to San Jose, Calif.-based Outset Medical, which reeled in $51 million, according to the company.

The report attributes the uptick in funding to changes in the investor ecosystem. New sets of investors are stepping in, such as private equity firms that have evolved into venture capitalists.

That has led to billion dollar rounds — a reality that didn't exist in early 2014.

To read the life sciences section of the report, visit www.fdanews.com/082415-pwc-report.pdf.
— Elizabeth Hollis

# BRIEFS

## MDIC to Hold Annual Public Forum

The Medical Device Innovation Consortium is inviting stakeholders to join industry peers in learning about recent activities by the public-private partnership, which focuses on medical device regulatory science. Scheduled for Sept. 25 in Washington, D.C., the event will examine, among other topics, the FDA's regulatory science priorities. It will feature a talk by CDRH Director Jeff Shuren, as well as former Medtronic CEO Bill Hawkins, who now is the lead director at Immucor. Register to attend in person or by webcast at http://mdic.org/2015-annual-public-forum/register/.

## Roche to Buy GeneWEAVE BioSciences

Swiss healthcare giant Roche has inked a definitive agreement to acquire GeneWEAVE BioSciences for $190 million upfront and up to $235 million more if certain milestones are met. The deal gives Roche access to GeneWEAVE's Smarticles technology, designed to identify multidrug-resistant organisms and assess their antibiotic susceptibility directly from clinical samples. An initial product, the vivoDx, is being evaluated in a multicenter clinical trial in the U.S. GeneWEAVE will be integrated into Roche Molecular Diagnostics upon the deal's close.

## Action Taken Against Infusion Product

Brazil's Agência Nacional de Vigilância Sanitária has asked Descarpack of Brazil Ltd. to suspend marketing and distribution of Equipo Macrogotas for intravenous infusion, lot SEML 024-SET / 2013, with an August 2018 expiration date. The product — used to infuse sterile parenteral solutions — yielded unsatisfactory results in tests by the Adolfo Lutz Institute. ANVISA has advised the company to take back unused products in this lot from customers in the state of São Paulo.

## CareFusion Recalls 7,000 Alaris Pumps

CareFusion is promising to take corrective action in the wake of recalling 7,481 units of its Alaris Syringe pump. The FDA has deemed it a Class I recall, saying in a notice that "the channel error will cause an audible and visual alarm on the Alaris PC unit and a channel error on the Alaris Syringe." The recall covers model 8110, which was manufactured between March and September 2014. The model was distributed in Australia, New Zealand, South Africa, Canada, the Middle East, Malaysia and Taiwan. This marks CareFusion's ninth Class I recall of an Alaris device since 2010.

## Regulatory Bodies Warn on Rib Supports

Johnson & Johnson has alerted health authorities around the world about a design issue with its Vertical Expandable Prosthetic Titanium Rib (VEPTR) caudal rib supports that could lead to potential adverse events in patients with thoracic insufficiency syndrome. J&J subsidiaries are recalling unused stock as a result of a partially formed hole in the supports that could lead to mechanical failure if the system is fully lengthened. There are no confirmed reports of breakage directly related to the partially formed holes. However, there have been eight cases of extension bar breakage when the VEPTR system was fully extended since 2004.

FDANEWS

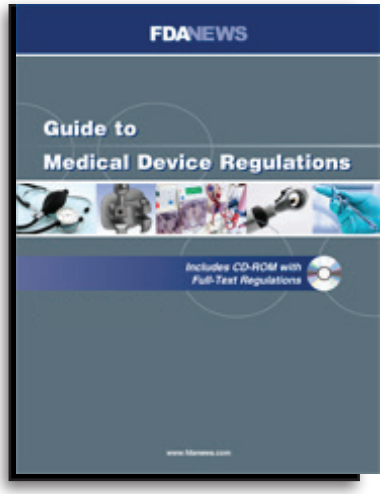
**Customer Service**
(888) 838-5578 • +1 (703) 538-7600
customerservice@fdanews.com

**Editorial:** Elizabeth Hollis
(703) 538-7639
ehollis@fdanews.com

**Ad Sales:** Jim Desborough
(703) 538-7647
jdesborough@fdanews.com

300 N. Washington St., Suite 200 • Falls Church, VA 22046-3431 • Phone: (888) 838-5578 • +1 (703) 538-7600 • Fax: +1 (703) 538-7676
www.fdanews.com

**Reporters:** Kellen Owings, Jonathon Shacat, Michael Cipriano
**President:** Cynthia Carter; **Editor-in-Chief:** Meg Bryant; **Managing Editor:** John Bechtel




# Guide to FDA Medical Device Regulations: *2015 Edition*

Whether you need to help your company convince the FDA to accept a predicate device in a simple 510(k) filing or you're responsible for implementing UDI across a family of high-risk implantable devices, there's one thing all regulatory professionals need. The most up-to-date, latest FDA regulations available.

That's why the **Guide to FDA Medical Device Regulations** is an FDAnews best-seller.

The 2015 **Guide** includes full texts of every device-related regulation and guidance — included on a fully searchable CD — plus executive summaries and analyses that will help your company avoid regulatory missteps, get to market faster and improve profitability. For newcomers and veterans alike, this is a must-have quick-reference encyclopedia.

Discover the changes and best practices regarding:

- Determining substantial equivalence of predicate devices
- Home use devices
- Cybersecurity requirements
- UDI
- De Novo classifications
- Expedited access for devices addressing unmet medical needs
- New Policy on General Wellness Devices
- Labelling
- And much more

Stay up-to-date on key medical device regulation changes with the 2015 edition of **FDAnews' Guide to FDA Medical Device Regulations** — the most authoritative and comprehensive guide ever assembled.

**FOUR EASY WAYS TO ORDER**

1. **PHONE:** Toll free (888) 838-5578 or +1 (703) 538-7600
2. **WEB:** www.fdanews.com/49166
3. **FAX:** +1 (703) 538-7676
4. **MAIL:** FDAnews
   300 N. Washington St., Suite 200
   Falls Church, VA 22046-3431

☑**Yes!** Please send me ____ copy(ies) of ***Guide to FDA Medical Device Regulations*** at the price of $397 each for the format I've selected: ❑ Print ❑PDF

Name _____

Title _____

Company _____

Address _____

City_____ State _____ Zip code _____

Country _____

Telephone _____

Fax _____

Email _____

METHOD OF PAYMENT

❑ Check enclosed (payable to FDAnews)

❑ Bill me/my company. Our P.O.# _____

❑ Charge my credit card:
❑ Visa ❑ MasterCard ❑ American Express

Credit card no. _____

Expiration date _____

Signature _____
(Signature required on credit card and bill-me orders)

Add $10 shipping and handling per book for printed books shipped to the U.S. and Canada, or $35 per book for books shipped elsewhere. Virginia customers add 6% sales tax.

15FLYR-N

FDANEWS PRESENTS THE

**Space Is Limited, Register Today!**

# SOFTWARE AND CYBERSECURITY RISK MANAGEMENT FOR MEDICAL DEVICES

## UNDERSTANDING THE FDA'S POSITION AND BEST PRACTICES FOR COMPLIANCE

**AN INTERACTIVE WORKSHOP PRESENTED BY FDANEWS AND GESSNET**

**OCT. 14-15, 2015**

HILTON WASHINGTON DC/ROCKVILLE HOTEL & EXECUTIVE MEETING CENTER • ROCKVILLE, MD

### YOUR INSTRUCTORS

**FUBIN WU**
Workshop Leader and Co-Founder of GessNet — software and consulting company specializing in medical device risk management

**LISA SIMONE, PH. D.,**
Software Review Team Lead and Policy Advisor, Office of Blood Research and Review, CBER, FDA

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 **four class exercises**, always a popular and valuable way to learn. Our four class exercises cover:

1) risk analysis for medical device mobile apps

2) risk assessments and risk controls for software hazards

3) cybersecurity risk analysis

4) cybersecurity risk assessments and risk controls

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 and Dr. Simone 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

### Special Take-Home Resource Kit:

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.

## DAY ONE

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. Software Characteristics Comparing to Hardware

a. Understanding the difference between software and hardware
b. Understanding software quality and reliability engineering
c. Challenges of software risk management and cybersecurity

### II. FDA's Analysis of Software Recalls

a. What kinds of software issues causing recalls
b. What kinds of devices have more software issues
c. What are the common types of causes for software calls

10:00 a.m. – 10:15a.m. | **REFRESHMENT BREAK**

10:15 a.m. – 11:00 a.m.

### III. Overview of FDA Software & Cybersecurity Related Guidance

a. Mobile Medical Applications (Feb 2015)
b. Medical Devices Data Systems, Medical Image Storage Devices and Medical Image Communications Devices (Feb 2015)
c. Total Product Life Cycle: Infusion Pump (Dec 2014)
d. Content of Premarket Submissions for Management of Cybersecurity in Medical Devices (Oct 2014)
e. FDASIA Health IT Report – Proposed Strategy and Recommendations (April 2014)
f. NIST Framework for Improving Critical Infrastructure Cybersecurity (January 2014)
g. Radio Frequency Wireless Technology in Medical Devices (Aug 2013)
h. General Principles of Software Validation
i. Content of Premarket Submissions for Software Contained in Medical Devices
j. Cybersecurity for Networked Medical Devices Containing Off-the-Shelf (OTS) Software

11:00 p.m. – 12:15 p.m.

### IV. Overview of Software & Cybersecurity Related Standards

a. ISO 14971:2007, EN ISO 14971:2012,
b. IEC TR 80002-1 Application of ISO 14971 for Software
c. IEC 62304 Medical Device Software Life Cycle Process, IEC 82304 Healthcare Software
d. NIST Framework for Improving Critical Infrastructure Cybersecurity, 2014
e. ISO/IEC 27001:20013 – Information Security Management
f. AAMI/ISO I4971 TIR in Process – AAMI Device Security Group
g. Medical IT Networks Safety, Security and Interoperability
h. IEC 80001-1 Managing Medical IT Networks and Relevant Technical Reports
i. TIR 80001-2-2:2012 – Application of Risk Management for IT Networks Incorporating Medical Devices

12:15 p.m. – 1:15 p.m. | **LUNCH**

1:15 p.m. – 2:15 p.m.

### V. Risk Analysis for Medical Device Software

a. Preliminary hazard analysis
b. Top down analysis, Fault Tree Analysis
c. Bottom up analysis – design FMEA, function FMEA, process FMEA, use FMEA, common causes of software failures
d. Connectivity analysis between top down and bottom up

2:15 p.m. – 3:15 p.m.

### VI. Group Exercise and Review With Instructors – Risk Analysis for Medical Device Mobile Apps

3:15 p.m. – 3:30 p.m. | **REFRESHMENT BREAK**

3:30 p.m. – 4:30 p.m.

### VII. Risk Assessments and Risk Controls for Medical Device Software

a. Software related risk assessment
b. Risk control basics
c. Software lifecycle process control measures
d. Risk control identification
e. Control measures implementation and effectiveness

4:30 p.m. – 5:30 p.m.

### VIII. Group Exercise and Review With Instructors – Risk Controls for Software Hazards

## DAY TWO

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

8:30 a.m. – 9:00 a.m.

### IX. Latest Updates from FDA on Cybersecurity

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. – 10:00 a.m.

### X. Cybersecurity Risk Analysis (Assets, Threats, Vulnerabilities)

a. Medical device cybersecurity basics
b. Asset profiling
c. Threat identification
d. Vulnerability identification
e. Software vulnerabilities
f. Attack Tree – top down and bottom up cybersecurity analysis
g. Connectivity between cybersecurity risk and safety risk

10:00 a.m. – 10:15 a.m. | **REFRESHMENT BREAK**

10:15 a.m. – 11:15 a.m.

### XI. Group Exercise and Discussion With Instructors – Cybersecurity Risk Analysis

11:15 a.m. – 12:15 p.m.

### XII. Cybersecurity Risk Assessments and Risk Controls

a. Cybersecurity risk assessment
b. Cybersecurity risk control basics
c. Software lifecycle process control measures
d. Cybersecurity capability and requirements identification
e. Special considerations for cybersecurity risk controls
f. Control measures implementation and effectiveness

12:15 p.m. – 1:15 p.m. | **LUNCH**

1:15 p.m. – 2:15 p.m.

### XIII. Group Exercise and Discussion With Instructors – Cybersecurity Risk Assessments and Risk Controls

# RITY RISK MANAGEMENT FOR MEDICAL DEVICES
## ON AND BEST PRACTICES FOR COMPLIANCE

**2:15 p.m. – 2:45 p.m.**

### XIV. Safety and Cybersecurity Risk Analysis Documentation for Stakeholders (FDA Reviewers, Hospitals, etc.)

a. Documentation for pre-market submission
b. Documentation for FDA inspection
c. Documentation for healthcare provider (e.g. hospitals )

**2:45 p.m. – 3:15 p.m.**

### XV. Risk Management Completeness and Effectiveness – Introduction of Assurance Case Method

a. Limitations of current risk analysis methods
b. Assurance case concept
c. How assurance case method can help

**3:15 a.m. – 3:30 a.m.** | **REFRESHMENT BREAK**

**3:30 p.m. – 4:00 p.m.**

### XVI. Safety and Cybersecurity Assurance Case Examples

a. Safety assurance case example for medical device
b. Security assurance case example

**4:00 p.m. – 5:00 p.m.**

### XVII. Post-Market Safety and Cybersecurity Risk Management

a. Post market risk assessment and evaluation
b. MDR assessment
c. FDA recall classification — HHE
d. Legacy device cybersecurity risk management

**5:00 p.m.**

### Workshop Adjournment

*"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**

## 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 INSTRUCTORS

**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.

**Lisa Simone, PH. D.,** works for the FDA as Software Engineering Team Lead and Policy Advisor in the Office of Blood and Research and Review in the Center for Biologics Evaluation and Research (CBER). In this role she leads the software group in review of devices including blood donor screening tests, retroviral diagnostic tests, and software used to test, collect, process, or store donated blood. Dr. Simone also leads the development and review of policy for software in regulated devices.

## 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
- Preliminary hazard analysis example
- Fault Tree Analysis example, FMEA examples
- Example of connectivity between FMEAs and hazard analysis
- Risk Summary Traceability matrix example
- Cybersecurity risk analysis example – assets, threats, vulnerabilities analysis
- Safety assurance case example
- Cybersecurity assurance case example
- ISO 14971:2007 and EN ISO 14971:2012, IEC TR 80002-1 Application of ISO 14971 for Software
- IEC 62304 Medical Device Software Life Cycle Process - Risk Management Section
- Cybersecurity in Medical Devices (FDA Guidance, Oct 2014)
- 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)
- Best Practices in Applying Risk Management Terminology (by Fubin Wu and Alan Kusinitz, AAMI Horizons Spring 2015 Issue)
- Documenting Medical Device Risk Management through the Risk Traceability Summary (by Edwin Bills, Stan Mastrangelo, and Fubin Wu, AAMI Horizons Spring 2015 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 Guidance, Dec 2014)
- IEC 80001-1 Managing Medical IT-Networks and relevant Technical Reports
- 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)

FDANEWS PRESENTS THE

# SOFTWARE AND CYBERSECURITY RISK MANAGEMENT FOR MEDICAL DEVICES

## UNDERSTANDING THE FDA'S POSITION AND BEST PRACTICES FOR COMPLIANCE

### LOCATIONS AND HOTEL ACCOMODATIONS

To reserve your room, call the hotel at the number below. Be sure to tell the hotel you're with the FDAnews workshop to qualify for the reduced rate. Only reservations made by the reservation cutoff date are offered the special rates, and space is limited. Hotels may run out of discounted rates before the reservation cutoff date. The discounted rate is also available two nights before and after the event based on availability. The hotel may require the first night's room deposit with tax. Room cancellations within 72 hours of the date of arrival or "no-shows" will be charged for the first night's room with tax.

### LODGING AND CONFERENCE VENUE

Oct. 14-15, 2015

**Hilton Washington DC/Rockville Hotel and Executive Meeting Center**
1750 Rockville Pike, Rockville, MD 20852
Tel: +1 (301) 468-1100 • Toll free: (800) HILTONS
www.RockvilleHotel.com
Room rate: $215 plus 13% tax
Reservation cut-off date: Sept. 22, 2015

### TUITION

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

### TEAM DISCOUNTS

Significant tuition discounts are available for teams of two or more from the same company. You must register at the same time and provide a single payment to take advantage of the discount. Call +1 (703) 538-7600 for details.

### CANCELLATIONS AND SUBSTITUTIONS

Written cancellations received at least 21 calendar days prior to the start date of the event will receive a refund -- less a $200 administration fee. No cancellations will be accepted -- nor refunds issued -- within 21 calendar days from the start date of the event. A credit for the amount paid may be transferred to any future FDAnews event. Substitutions may be made at any time. No-shows will be charged the full amount. In the event that FDAnews cancels the event, FDAnews is not responsible for any airfare, hotel, other costs or losses incurred by registrants. Some topics and speakers may be subject to change without notice.

### FOUR EASY WAYS TO REGISTER

Online: www.fdanews.com/cybersecuritymd
Fax: +1 (703) 538-7676
Phone: Toll free (888) 838-5578 (inside the U.S.)
or +1 (703) 538-7600
Mail: FDAnews, 300 N. Washington St., Suite 200
Falls Church, VA 22046-3431 USA

**Register Early — *Space Is Limited***

Hurry — register early because space is limited! Your tuition of $1,797 includes the two-day workshop, all workshop materials, continental breakfast each day and lunch on both days.

Payment is required by the date of the conference. We accept American Express, Visa and MasterCard. Make checks payable to FDAnews.

---

☑ **YES!** I want to attend **Software and Cybersecurity Risk Management for Medical Devices.** I understand the fee of $1,797 includes all workshop sessions, workshop materials, two breakfasts, two luncheons and daily refreshments. Please call (888) 838-5578 or fax to (703) 538-7676.

FDANEWS
300 N. Washington St., Suite 200
Falls Church, VA 22046-3431

Attendee 1: Name _____ Title _____ Email _____

Attendee 2: Name _____ Title _____ Email _____
(Please see "Team Discounts" above for tuition discounts when you send a team of two or more.) Email address (so you can receive order acknowledgements, updated news, product information and special offers)

**Company Information**

Organization _____

Address _____

City _____ State _____ Zip _____

Country _____

Phone _____ Fax _____

**Payment Options**

☐ Check enclosed, payable in U.S. funds to FDAnews

☐ Charge to: ☐ Visa ☐ MasterCard ☐ American Express

Credit card no. _____

Expiration date _____

Total amount $ _____

Signature _____
(Signature required on credit card and bill-me orders.)

Print name _____

☐ Bill me/my company $ _____

Purchase order # _____

(Payment is required by the date of the conference.)