

In This Issue

Devicemakers Won't See Warning Letters Under Single-Audit Pilot.....	1
Overhaul of U.S. FDA Inspectorate Will Include Dedicated Device Inspectors	2
U.S. Investigators Issue Fewer Warning Letters, Design History Citations in 2013.....	3
EU Panel Urges Cautious Approach To New Metal-on-Metal Prostheses.....	5
IMDRF Sets Criteria for Sharing Adverse Event Information	5
Industry Demands Clarity on Fate Of Device Oversight in the EU	7
Canada to Require Labeling With Device Licensing Applications	7
Australia Opens Door to CE Mark For 'Routine' Medical Devices.....	8
India Walks Back Plan to Require Country-Specific Info Pre-Import.....	9
Only Weeks Left to Comply With Japan's New Device Regulations.....	9
Guidance Outlines Steps for Securing Device Software Against Cyber Threats.....	10
Regulators Forum Finalizes Risk-Based Framework for Software as a Device.....	11
U.S. FDA Steps Back on Reporting Requirements for Enhancements.....	12
Framework for U.S. Regulation Of Lab-Developed Tests Outlined	12
Device Review Times Improving In U.S., but Still Behind Europe	13
In Brief	14

Editor's Note: The *International Medical Device Regulatory Monitor* is available in an electronic edition, which includes web access to seven years of archived issues. For information on converting to an electronic subscription, contact us at (888) 838-5578.

Devicemakers Won't See Warning Letters Under Single-Audit Pilot

International medical device regulators are trying to entice more companies to participate in a single-audit pilot program, promising they will receive no warning letters unless there is an immediate threat to public health. Meanwhile, Canada is ramping up pressure on companies to use the program, announcing that as of 2016, marketing devices there will require shared audits.

Under the Medical Device Single Audit Program, an assessment performed by a single third-party inspector is sufficient to prove compliance in the U.S., Canada, Australia and Brazil. The pilot launched in January and is slated to run through the end of 2016 (*IMDRM*, November 2013).

But Kimberly Trautman, associate director of international affairs in the U.S. Food and Drug Administration's devices center and chair of IMDRF's MDSAP working group, says enforcement concerns could make some companies reluctant to volunteer for the pilot. She tried to allay those fears during an Oct. 23 session on the single-audit program at FDAnews' Inspections Summit in Bethesda, Md.

According to Trautman, regulators will review MDSAP audit reports only if the inspector finds multiple serious violations and even if that occurs, the FDA won't use warning letters as a primary means of alerting companies. Instead, the agency may issue untitled letters or other official communications that lack the stigma and publicity commonly attached to warning letters, she said.

That said, Trautman believes the companies volunteering for the pilot program will not be "even close to needing warning letters."

Initial Feedback Positive

To date, two MDSAP audits have been performed, with positive feedback from both companies and inspectors, according to Trautman. The devicemakers received only minor nonconformances, which they understood, she told conference-goers. The inspections also revealed a need for some minor adjustments to the program, such as greater clarity on how multiple sites should be audited.

The program still needs volunteers, including start-ups, Trautman says, adding the cost and time involved in a pilot audit

are less than that required to qualify in each market separately. In addition, companies audited before May 2015 will be surveyed on their experiences and invited to participate in a work group on program improvements.

Looking to the future, Trautman said IMDRF will hire a permanent IT director to develop a portal for sharing audit information and other records. Records entered into the portal will be protected under international confidentiality standards used by MDSAP and will not be accessible through the U.S. Freedom of Information Act.

Separately, IMDRF last month posted a final document explaining how third-party auditing organizations will be approved, including the grading of nonconformities. The final version is essentially unchanged from a proposed document released earlier this year (*IMDRM*, April).

Document Index

The following documents covered in this issue of the *International Medical Device Regulatory Monitor* are available for download at www.fdanews.com/IMDRMdocs.

IMDRF's MDSAP Assessment Process for Third-Party Auditing Organizations

U.S. FDA's Inspectorate Reorganization Plan

U.S. FDA's Device Quality Systems Data

SCENIHR's Opinion on Metal-on-Metal Joint Replacements

IMDRF's Draft Document on National Competent Authority Report Exchanges

Canada's Draft Guidance on Device Labeling

Canada's Draft Guidance on Completing a Licensing Application Form

Canada's Class II Device License Application Form

Canada's Class II Amendment License Application Form

Australia's Report on Innovation and Competitiveness

Australia's Terms of Reference for Independent Review of Device Regulations

India's Notice on Medical Device Labels

U.S. FDA's Draft Guidance on Device Cybersecurity

IMDRF's Framework for Categorizing Risk of Medical Device Software

U.S. FDA's Final Guidance on Distinguishing Device Recalls From Enhancements

U.S. FDA's Draft Guidance on a Framework for Regulatory Oversight of Laboratory-Developed Tests

U.S. FDA's Draft Guidance on Medical Device Reporting for LDTs

CHI's Report on U.S. Device Review Times

Brazil's regulatory authority, Anvisa, will take over the MDSAP chairmanship in 2015.

Read the final document at www.fdanews.com/10-14-IMDRF-MDSAP.pdf. — Elizabeth Orr

Overhaul of U.S. FDA Inspectorate Will Include Dedicated Device Inspectors

The U.S. Food and Drug Administration last month unveiled a broad plan that will change the way it inspects devicemakers, handles recalls, issues and reviews enforcement decisions and screens imports, with companies likely to start feeling the impact by the end of 2015.

Among other changes, the reorganization will create a distinct inspectorate for medical devices, eliminating the existing region-based model.

In an eight-page document released Oct. 14, the Center for Devices and Radiological Health outlined the steps it will take over the next 12 months to create a new specialized approach to inspections. The plan includes creating specialist investigators who will be extensively trained in specific types of devices.

CDRH says it will survey staff to subdivide its inspectorate into subspecialties. It has already identified one area that it intends to carve out as a subspecialty — radiological and mammography inspections.

The overhaul is designed to revise CDRH's compliance program from one that is enforcement-heavy to one that will work with manufacturers proactively to prevent compliance problems.

CDRH will work to create more metric-driven inspections, at this point planning to reach out to industry to identify specific product attributes that can be measured and used as quality indicators.

The center also will conduct a lengthy review of all compliance and policy guides and come up with a schedule for updating them. That effort is expected to take five years to complete.

Also, the agency will streamline its approach to approving and issuing 483s and warning letters to make faster decisions with respect to enforcement actions, though details of this part of the reorganization remain sketchy.

By fall 2015, CDRH and ORA will speed up the way the agency screens imports by creating a risk-based imports entry review program that will allow it to quickly identify adulterated products.

The changes coming to CDRH's recall process are also not fully fleshed out, but the agency says it will review its recall procedures to look for areas to improve efficiency. The center says it will also evaluate its current laboratory structure to look for efficiencies.

As CDRH refines its inspections approach, device-makers will still be able to opt to participate in the Medical Device Single Audit Program, which was developed by the International Medical Device Regulators Forum and recently launched as a pilot. The center will also look at ways to breathe new life into its third-party auditor program.

Steve Niedelman, lead quality systems and compliance consultant at King & Spaulding, says he is encouraged by the proactive approach.

Devicemakers should see a payoff from the increased training and specialization of investigators, Niedelman tells *IMDRM*. "All too often you hear from industry that the inspector didn't know about the product or what it does. This hopefully will dispel some of those concerns and improve the quality of the relationship during the inspection, as well as the knowledge of the investigator," he says.

One possible downside of the overhaul: Depending on how ORA realigns, devicemakers could face an investigator who is coming from far away, Niedelman says. "Firms like to have good working relationships with their districts, and that might be affected."

The action plan is available at www.fdanews.com/10-13-14-Inspections.pdf. — Robert King, Meg Bryant

U.S. Investigators Issue Fewer Warning Letters, Design History Citations in 2013

The number of devicemakers that received warning letters from the U.S. Food and Drug Administration following quality system inspections decreased 12 percent in 2013, compared with the previous year — the first decline since 2009. There were 144 warning letters with quality system regulation deficiencies in 2013, compared with 164 in 2012.

But while the number of warning letters dropped, the ones that were issued contained more citations. FDA investigators recorded 17 percent more citations in calendar year 2013 versus the previous year, according to medical device quality system data released by the Center for Devices and Radiological Health.

Of 938 warning letter citations in 2013, 30 percent were for production and process controls, 29 percent were for corrective and preventive actions, 17 percent were for design controls, 12 percent were for management controls and 12 percent were for document controls.

Inadequate device acceptance activities was the main reason for citations under the production and process controls category, appearing in 59 letters. The chief cause of CAPA citations, 117, was poor procedures, while validation led the problems with design control with 30 citations. The most common violations in the other two categories — management controls and document controls — were failure to conduct quality audits (52) and lack of device history documentation (46), respectively.

FDA investigators noted a significant drop in design history documentation violations. In 2013, the FDA issued 44 warning letters that included design history documentation violations, seven fewer than in 2012.

CDRH provides the data on inspectional observations and warning letter citations as part of the FDA's transparency initiative, which it also expanded this week with the unveiling of an inspections database dashboard that will be continuously updated.

The device center also notes a 3 percent decline in quality system surveillance inspections in 2013. CDRH says the change is due to an increase in foreign inspections, which require more investigator time per inspection and therefore reduce the total number of inspections that can be conducted.

Overall, the FDA conducted 460 foreign inspections and 1,741 domestic ones. Of those, 4 percent of domestic companies and 16 percent of foreign companies received warning letters.

In 2012, foreign devicemakers accounted for 393 of the FDA's 2,252 quality system inspections (*IMDRM*, May).

The top 10 countries for foreign inspections in 2013 were Germany (86), China (82), Canada (35), France (33), Japan (24), South Korea (24), Italy (20), Switzerland (20), Sweden (17) and Ireland (16).

View the quality system data at www.fdanews.com/09-30-14-Data.pdf. — April Hollis

Robust Simplicity.

EtQ features the most comprehensive Compliance Solution that is completely configurable to your business needs



- Automated processes such as Corrective Action, Audits, Risk Management, Complaint Handling, Document Control, and more
- Flexible to adapt to unique business processes, without programming
- Scalable solution that integrates with other business systems
- Make any application mobile and access your data from anywhere, anytime

EtQ | info@etq.com
800.354.4476
<http://www.etq.com/fda>



EU Panel Urges Cautious Approach To New Metal-on-Metal Prostheses

Given past experience with metal-on-metal joint replacements, the introduction of new prostheses should be both gradual and backed up by new and stronger pre-clinical and clinical studies, a panel of scientific experts in the EU says.

More importantly, European notified bodies should not clear new joint implants for marketing based on “minimal design changes,” according to a final opinion on metal-on-metal joint replacements.

According to the Scientific Committee on Emerging and Newly Identified Health Risks, more than a million MoM hips have been implanted worldwide, 100,000 of them in European patients. Concerns about the wearing and erosion and the release of metal alloys like cobalt and chromium into surrounding tissues helped to fuel the current push for tougher premarket and postmarket regulations of higher-risk medical devices (*IMDRM*, October 2012).

The opinion — adopted Sept. 25 and published on the committee’s website on Oct. 9 — cites major gaps in knowledge about the frequency and clinical relevance of adverse local and systemic effects of exposure to metal debris. Clinical research should focus on:

- Potential mutagenic or precancerous changes in cells at possible risk of metal exposure. These tests should be performed at sites where a cancer risk has been highlighted, such as the bladder or bone marrow;
- Long-term follow-up using modern epidemiology, breaking patients out according to degree of exposure, type and performance of implant and the presence of confounding diseases, where possible;
- Metal ion levels following implantation of any artificial prosthesis and the association of clinical symptoms; and
- Changes in corrosion at taper connections and the extent of local tissue reactions as prostheses are modified and refined.

Recommendations for preclinical research largely focus on the influence of relevant parameters on the wear of taper connections, the mechanisms that lead to erosion and the potential impact of additional metal ions, such as titanium. Devicemakers should also look at improved metal to tissue interfaces, SCENIHR says.

To improve postmarket surveillance, SCENIHR recommends creating national registries of MoM hip arthroscopy patients with follow-up for local, systemic and long-term effects. “Further research is needed, including appropriate toxicological studies using comparable routes of exposure to humans, prospective human studies with adequate exposure and outcome data and post-mortem studies,” the committee says.

View the final opinion at www.fdanews.com/10-20-14-SCHENIRhips.pdf. — Meg Bryant

IMDRF Sets Criteria for Sharing Adverse Event Information

The International Medical Device Regulators Forum is seeking feedback on a proposed plan to share adverse event reports among national regulatory authorities. The focus is on unanticipated device events that could pose a public health threat, death or serious injury.

Authorities will also share information on potential trends they are seeing in their jurisdictions that have not yet resulted in recalls or field safety corrective actions.

According to the draft document, a trend is considered reportable when the adverse event is deemed a serious public health threat and the frequency is significantly higher than that recorded in the manufacturer’s file or the frequency observed with similar devices.

Assessing whether an event is serious, from a public health standpoint, may be difficult, IMDRF notes. The draft includes the example of a contaminated eye rinsing solution that could cause serious visual impairment or blindness. The issue was detected after reports of infections and vision problems in patients who were administered the solution during eye surgery. The broader public health concern is due to the size of the batch and likelihood of its being distributed across geographical regions.

Competent authorities should also report to their counterparts if they observe an increase in the seriousness or frequency of an event compared with what previously had been reported, if there is a change in the device’s regulatory status or if the manufacturer’s postmarket surveillance or quality management system is known to be weak.

The program will allow participating authorities to compare their experiences regarding specific devices and any regulatory actions that were initiated or are being considered, the document says.

The information to be shared does not veer much from either the Global Harmonization Task Force's earlier National Competent Authority Report program or what the U.S. Food and Drug Administration shares in its government-to-government exchanges that have confidentiality agreements in place, says Kim Trautman, associate director for international affairs at the FDA and member of IMDRF's management committee.

The most notable change with IMDRF's proposal is in how reports are exchanged, Trautman says. Under the GHTF program, NCAR reports were sent to the secretariat for distribution to all NCAR participants. This, however, inhibited sharing of confidential information since not all participants in the program had confidentiality agreements with all of the other participants, she explains.

Under the revised NCAR program, instead of reports going to the secretariat for distribution, each competent authority will now be responsible for sending reports directly to other competent authorities with whom they have confidentiality agreements. Authorities will also have standard criteria and a format for sharing the information.

Trautman says the program will have little to no effect on manufacturers dealing with the U.S. FDA. The

Center for Devices and Radiological Health currently shares confidential information with counterparts where agreements are in place. Nonconfidential information, such as recalls and warning letters, is already publically available for other governments to utilize through the agency's transparency initiative, she adds.

"The change really is for other governments, including the EU member states, to have a better system of exchange with set definitions and methods of exchange," she tells *IMDRM*.

Participation in the program will be limited to members of IMDRF's management committee: the U.S. FDA, European Commission, Health Canada, China Food and Drug Administration, Australia's Therapeutic Goods Administration, Japan's Pharmaceutical and Medical Devices Agency, Brazil's Anvisa and Russia's Roszdravnadzor.

The draft updates 2009 guidance developed by the GHTF (*IMDRM*, October 2009). IMDRF made reviewing the NCAR exchange a priority when assumed the GHTF's responsibilities.

Comments on the proposed document are due Dec. 8. Read it at www.fdanews.com/10-14-IMDRF-Consultation.pdf. — Jonathon Shacat

Conducting **ADVANCED** Root Cause Analysis and CAPA Investigations *Understanding Advanced Critical Thinking Skills and Innovative Techniques to Improve the Quality of Investigations*

An **FDANEWS** Conference

Dec. 3-4, 2014 • Tampa Marriott Waterside Hotel and Marina • Tampa, FL

The FDA's enforcement plan makes it clear: Developing a successful CAPA program has never been more important. But creating an FDA-proof CAPA isn't easy. If only you could pick the brain of someone who is coping successfully with CAPA... well, you can.

FDAnews and Compliance Media, Inc. are offering an advanced version of our previous CAPA investigations class — fully updated to meet tough FDA scrutiny in 2014.

In this year's workshop, you will:

- Learn how to respond to the FDA and implement effective CAPAs
- Get an insider's view of the FDA's own training program for investigators
- Discuss lessons learned from nine years of FDA warning letter citations on CAPA investigations
- And much more!

Register online at: www.CAPAWorkshop.com
Or call toll free: (888) 838-5578 (inside the U.S.) or +1 (703) 538-7600

Industry Demands Clarity on Fate Of Device Oversight in the EU

Devicemakers are urging the incoming president of the European Commission to clarify once and for all whether medical technologies will continue to be overseen by the directorate for health or move to industry, as previously proposed.

President-elect Jean-Claude Juncker said Oct. 22 that he was dropping plans to shift medicines and pharmaceutical products to the industry directorate, after weighing concerns of lawmakers and others that health-care products should not be regulated like other commodities. However, his statement failed to make any mention of medical devices.

“The ambiguity of Mr. Juncker’s statements, and his subsequent silence on the issue, is of real concern,” said Glenis Wilmot, head of the Labour party in the EU Parliament and a rapporteur on the pending medical device regulation.

In an open letter sent to Juncker on Oct. 28, industry groups and other stakeholders urged Juncker to clarify his decision and protect patient safety by keeping medical devices in the health directorate.

“I can confirm that it is still not definite that devices go back to DG SANCO,” Erik Vollebregt, with Axon law firm in the Netherlands, told *IMDRM*, amid reports that devices would be moved to industry.

Health Action International Europe has expressed concern that the industry directorate’s role in molding EU health policy could be expanded (*IMDRM*, September). Currently, health policy is set collectively by the health, industry and internal market directorates, with health taking the lead.

In an Oct. 29 blog on the *British Medical Journal*’s website, Bernard Merkel, a retired senior health systems policy analyst in DG SANCO, said the situation regarding who takes the lead in policymaking for devices, and what the priorities should be, likely “will remain rather messy for some time.”

Separately, it remains to be seen who will lead the health directorate. Paola Testori Coggi stepped down as directorate general on Oct. 16 amid allegations that she violated tender policy in 2012 by leaking insider knowledge of a food-safety study to an NGO before it aired publicly. Ladislav Miko, a Czech politician who currently serves as deputy head of the food chain in DG SANCO, is expected to replace Coggi.

Also on Sept. 22, Parliament confirmed Lithuanian physician and Social Democrat Vytenis Andriukaitis as commissioner with responsibility for health and food safety, replacing the outgoing Tonio Borg. — Meg Bryant

Canada to Require Labeling With Device Licensing Applications

Devicemakers seeking authorization to market Class II products in Canada will have to submit labeling with their licensing applications, under draft guidance released Oct. 20. Sources say the requirement will speed up premarket reviews.

For devices that are not sold to the general public, the directions for use may be provided as an electronic label that is downloadable via electronic data storage devices or the internet. The e-label must accompany the product at the time of sale or delivery, guidance says.

A paper copy of the labeling information should be provided promptly to the user upon request, at no additional cost, the guidance adds.

Manufacturers should ensure that the e-label is identical in content and format to the paper version with the device license application. The application form must state that the labeling material is included as an attachment.

Health Canada developed the guidance to help companies comply with proposed amendments to the country’s medical device regulations. It does not apply to in vitro diagnostic devices.

The guidance also lays out new requirements for nanotechnology, radiation emission and electronic labeling. For instance, manufacturers applying for a new device license must declare whether the product is capable of producing electromagnetic or acoustic radiation.

For devices that contain nanomaterials, applicants should identify the specific type of nanoscale material that is present, such as nano titanium dioxide, nano silver, quantum dots, nano polymers, nano glasses, nano ceramics, carbon nanotubes, and nanofibers, the guidance says. Health Canada requires notification for particle sizes between 1 and 1,000 nanometers for device licensing, even though the working definition of a nanomaterial is 1 to 100 nanometers.

Tips on Applying for a New License

Klaus Stitz, vice president of regulatory affairs at MEDEC, says industry supports the proposed amendments, as they enhance patient safety.

“The labeling for Class II devices had in the past already been requested by Health Canada using existing powers in the Medical Devices Regulations,” Stitz tells *IMDRM*. “Adding it now to the requirements of a submission streamlines the process.”

The labeling guidance was accompanied by draft guidance on how to complete an application for a new device license and proposed application forms for new and amended devices. That guidance applies to Class II, III and IV medical devices, non-IVD devices containing drugs and radiation-emitting devices.

Comments on both guidance documents are due Jan. 3. Read the draft on labeling at www.fdanews.com/10-01-14-HC-Guidance.pdf. The draft on completing an application form is at www.fdanews.com/10-02-14-HC-Guidance.pdf.

The proposed forms for new Class II device licenses and amendment applications are available at www.fdanews.com/10-03-14-HC-Guidance.pdf and www.fdanews.com/10-04-14-HC-Guidance.pdf, respectively. — Jonathon Shacat

Australia Opens Door to CE Mark For ‘Routine’ Medical Devices

Manufacturers of low- and moderate-risk devices will soon be able to register their products in Australia based on conformity certificates issued by European notified bodies, under a government action plan unveiled Oct. 14.

The change — which takes effect once regulatory amendments are in place, expected by the end of the year — will allow Aussie devicemakers to compete on a level playing field with their global competitors, government and industry sources say.

Higher-risk medical technologies and implantable devices will still be subject to a TGA conformity assessment review.

The relaxation of conformity assessment requirements is one in a series of moves outlined by the government to increase innovation and competition across all industry sectors, and suggests a new willingness to rely on third-parties. In September, the TGA said it would obtain its own evidence on the quality of certificates and reports issued by select EU notified bodies whose reviews were deemed to be lax by the *British Medical Journal* (*IMDRM*, September).

Meanwhile, the Department of Health and Ageing on Oct. 24 announced plans for an independent review of the country’s device approval process with the aim of ridding it of unnecessary regulations.

Recommendations are expected to include the introduction of fast-track approvals, collaboration with trusted foreign regulators on product assessments and improved processes for navigating the regulatory system, DHA says.

The three-person review panel must submit a report to the health minister by March 31 on the regulatory frameworks for devices and diagnostics.

According to AusBiotech, the panel will first develop a discussion paper summarizing past reviews of device regulations and options put forward to address these concerns. Industry and other stakeholders will have an opportunity to weigh in on the review and raise additional concerns.

Creation of ‘Growth’ Centers

Also envisioned in the broader action plan is a medical technologies center to identify growth opportunities in biomedical devices and platform technologies. The center will bring together devicemakers, materials researchers and other scientists, with the overall aim of improving health outcomes and business profitability. The plan commits roughly US \$166 million over the next four years to this and growth centers in three other industry sectors.

The government also will create a Medical Research Future Fund, effective Jan. 1, reinvesting savings from health reforms announced in the 2014-2015 budget until the balance reaches approximately US \$17.6 billion.

Medical Technology Association of Australia spokesman Chris Szeleczky says industry should feel the effects of the new conformity assessment policy soon, as the only required change is the regulatory amendment.

In May, MTAA released a white paper on how Australia could improve its regulatory system for devices (*IMDRM*, June). One of the points the paper made was that the TGA’s reviews generally don’t identify any problems (e.g., quality, safety, performance) that weren’t already picked up during EU notified body assessments — subjecting devicemakers to extra cost and work with little improvement in public health.

As evidence, the group cited the failure of French-made Poly Implant Prosthèse breast implants, which

passed a TGA conformity assessment despite containing industrial-grade, rather than medical grade, silicone (*IMDRM*, November 2013).

Read the review's Terms of Reference here: www.fdanews.com/10-14-Australia-Review.pdf. Read the government's report on innovation and competitiveness at www.fdanews.com/10-14-AustraliaReport.pdf.

— Jonathon Shacat, Meg Bryant

India Walks Back Plan to Require Country-Specific Info Pre-Import

Devicemakers are breathing a collective sigh of relief following the Indian government's decision to let companies affix labels with India-specific information on their products after they enter the country.

The notice, issued earlier this fall, reverses a March 4 announcement by the Drugs Controller General of India that companies must immediately ensure that all India-specific labeling is added before a device is imported, in compliance with the Drugs and Cosmetics Act of 1940.

"This was a huge concern because it meant, in a very small amount of time, our companies might have had to completely reorganize their practices around manufacturing and packaging," says Abby Pratt, vice president for global strategy and analysis at AdvaMed.

The March announcement ignored a number of earlier notifications saying it was acceptable to add labels to devices at the port of entry or a warehouse upon arrival in the country, according to Pratt.

Concerned that supply of devices in India might be disrupted, industry requested a transition period and permission to label products in bonded warehouses inside the country. The government acquiesced on March 28, giving companies a six-month extension to comply with the March 4 notice.

The Sept. 25 notice basically maintains the status quo of what companies have been doing all along, Pratt says.

While industry applauds the about turn, a number of issues still need to be clarified, Pratt tells *IMDRM*. For example, the September notice says India-specific labeling will be allowed post-import, subject to approval by the DCGI, devicemakers don't know if that means they will require a one-time permission or need to obtain permission for each shipment.

The notice also says products intended for hospital or institutional sale must include a label on the outer packaging stating that fact, but it doesn't clarify if the declaration is mandatory when the facility doesn't demand the information, Pratt adds.

Read the notice at www.fdanews.com/10-14-India-Notification.pdf. — Jonathon Shacat

Only Weeks Left to Comply With Japan's New Device Regulations

With a comprehensive regulatory framework for devices set to take effect on Nov. 25, Japan's Pharmaceutical and Medical Devices Agency still hasn't published many of the implementing regulations, raising concerns that companies won't be prepared to market their products in the country.

"Given the volume of regulations and the fact that they are in Japanese, it is difficult to understand exactly what the new requirements will look like," says Philip Agress, senior vice president for global strategy and analysis at U.S. trade group AdvaMed.

Japanese lawmakers adopted legislation in November 2013 creating a separate regulatory pathway for medtech products (*IMDRM*, January). Currently, devices are regulated under the country's medicines regulations. Among the changes: Manufacturers must register their devices, but will no longer need to obtain a license; and quality management systems inspections will be performed for product groups, not for an individual product.

Industry has largely welcomed the reforms.

The law also creates a new category for cellular and tissue therapy products and calls for a provisional approval pathway to speed early access to promising therapies, Hideyuki Kondo, deputy director of the PMDA's Office of Medical Device Evaluation, told conference-goers at the recent RAPS Regulatory Convergence conference in Austin, Texas.

AdvaMed has been pressing for the reforms since the drug laws were last updated around 2005, says Agress.

"They have been regulating devices under the pharmaceutical framework, making it difficult to improve their regulatory structure in a number of areas, such as quality systems," he tells *IMDRM*. Creating a separate chapter for medtech allows the PMDA flexibility to regulate devices based on their own characteristics, he says. — Jonathon Shacat

Guidance Outlines Steps for Securing Device Software Against Cyber Threats

The U.S. Food and Drug Administration last month issued final guidance outlining the steps manufacturers of medical device software must take to spurn cybersecurity threats.

Companies are instructed to design software so that access is limited to trusted users and content is secure, while incorporating features that will detect, recognize, log, time and act upon security breaches during normal use. Features should also be built in that protect the critical functionality of the device the software supports, the agency says.

Manufacturers should have documentation attesting to the fact that their software will be sold free of malware and instructions for antivirus or firewall use appropriate to the device, the FDA adds.

The final guidance, published Oct. 1, is largely unchanged from a June 2013 draft, though the FDA did add a section on specific IT security standards the agency recognizes in response to comments by an industry association.

Premarket submissions for device software should include the following cybersecurity information:

- Hazard analysis, mitigations and design considerations relating to cybersecurity attacks against the device. Sponsors should include a list of potential risks that were considered in designing the device and a list of specific controls established to manage those risks;
- A traceability matrix linking the cyber controls to the perceived risks;
- A summary of the plan for providing validated software updates and patches throughout the device's lifecycle, to ensure continued safety and effectiveness. Software changes "made solely to strengthen cybersecurity" typically won't require FDA approval, the guidance says;
- A summary of controls to assure the software's integrity from point of origin to point of distribution; and
- Instructions for use and product specifications related to the recommended cybersecurity controls for the setting where the device will be used.

Aim to 'Contain'

The guidance comes amid concerns about the Shellshock bug, which affects a common component of computer systems and poses a threat to

Reduce Human Error in Drug and Device Manufacturing

An **FDANEWS** Publication

Minimizing human error continues to be a challenge for both device and drug makers, even those that have successful quality programs. More frequent training doesn't seem to be the answer. In fact, studies show that lack of training is responsible for only about 10 percent of the human errors that occur. So what other options do you have to reduce human error in your organization? Take a step in the right direction by ordering **Reduce Human Error in Drug and Device Manufacturing**.

With this report, you'll learn to think about human error in a significantly different way:

- The human behavior that led to an error has to be analyzed to get to the problem's root cause.
- 80 percent of human error can be controlled by managing the aspects of a job that make it more likely for a worker to make mistakes.
- The other 20 percent of human errors can be controlled by managing some employee habits.

Why not take a step that could make you a leader in your organization ... by taking on the difficult subject of human error? Order *your* copy today.



Price: \$397

Order online at: www.fdanews.com/47079A

Or call toll free: (888) 838-5578 (inside the U.S.) or +1 (703) 538-7600

internet-connected medical devices. Kevin Fu, associate computer science professor at the University of Michigan, says the bug “will likely affect a significant fraction” of devices.

But for manufacturers, it’s less important to focus on one bug than on why the vulnerability exists in the first place,” Fu tells *IMDRM*. He recommends designing devices to better tolerate this kind of flaw, which “is bound to happen from time to time.” Just as human bodies are designed to survive the occasional cold, medical devices “need to be able to tolerate this kind of stress,” Fu says.

One approach to security is to design systems that will isolate a medical device that has been hacked into, ensuring the malware doesn’t spread. Such solutions must be worked out in the early concept phase of device development, before actual design begins, says Fu. Devicemakers may also want to explore using software that monitors an embedded device’s power consumption to detect anomalies, he adds.

David Rothkopf, president of MEDicept in Ashland, Mass., says a common mistake devicemakers make is relying on a hospital’s firewall to ensure the product will be safe.

Hospital-affiliated information management systems, such as those used in radiology departments, are typically managed by the hospital itself, which create firewalls around them. But devicemakers shouldn’t rely on these, warns Rothkopf, who believes all devices should be designed with firewalls of their own to detect bugs and malware. He suggests manufacturers equip their products with a mini-firewall that protects them even if someone hacks into the hospital system.

Rothkopf notes that hospitals often don’t like these mini-firewalls because they create additional passwords that personnel must remember, but that shouldn’t deter companies from placing cybersecurity software on their systems.

Suzanne Schwartz, director of emergency preparedness/operations and medical countermeasures at CDRH, agrees. There is no such thing as a “threat-proof” device, she says. Devicemakers need to “remain vigilant about cybersecurity ... to appropriately protect patients.”

View the guidance at www.fdanews.com/10-02-14-Cybersecurity.pdf. — April Hollis

Regulators Forum Finalizes Risk-Based Framework for Software as a Device

Risk concerns are paramount in regulating software as a medical device, a harmonized document by the International Medical Device Regulators Forum maintains.

The framework establishes four risk categories for SaMDs: very high impact, high impact, medium impact and low impact. A diagnostic that helps to inform treatment decisions in patients with acute stroke would be considered highest risk, while an app that sends a heart patient’s EKG rates and walking speed to a server for monitoring would be low impact, according to the final document.

The plan also includes four functional categories: software that supplies information used to make a treatment decision; software that provides information used to diagnose; software that drives clinical management; and software that informs clinical management.

Companies should develop appropriate risk-mitigation controls for each device’s risk and functional categories, including a postmarket surveillance system that considers the possibility of unauthorized duplication, the document says. The risk-mitigation system should include a method for ensuring that end users implement software updates in a timely manner.

Risk assessments should be conducted during software updates to determine whether the change will affect the risk classification, IMDRF says. The group recommends independent oversight of any software change that affects core functionality or is needed to maintain the safety profile of a high-impact SaMD.

According to Kim Trautman, associate director for international health at the U.S. Food and Drug Administration’s device center, the final framework is not fundamentally changed from that described in a March 26 draft document.

The final version clarifies the context of the framework with respect to global regulatory systems and illustrates the thinking and rationale that led to the framework, in response to stakeholder comments on the draft, she tells *IMDRM*.

Formal adoption of the SaMD framework is projected for October 2015, and will be supported by guidance on quality management systems, IMDRF previously said. (*IMDRM*, October).

Read the final document at www.fdanews.com/10-14-IMDRF-SaMD.pdf. — Jonathon Shacat

U.S. FDA Steps Back on Reporting Requirements for Enhancements

The U.S. Food and Drug Administration has reversed a controversial position and won't require devicemakers to submit formal reports when they make safety enhancements to their products.

The decision, laid out in an Oct. 14 final guidance, walks back an earlier plan that would have required Form 806 Corrections and Removals Reports any time a recall or enhancement improved product safety. The January 2013 draft guidance was widely criticized by industry, which claimed it was confusing, overreached FDA authority and would trigger numerous additional recall reports (*IMDRM*, July 2013).

Under the final guidance, 806 reports must be filed only for corrections and removals that are meant to limit a health risk or remedy a violation of the 1938 FD&C Act. The guidance defines "risk to health" as a reasonable probability that the device could cause adverse health consequences, including death.

An enhancement, which will not require an 806 report, is defined as "a change to improve the performance or quality of a device" that was not initiated to bring the device into compliance with the FD&C Act or related regulations. The guidance cites, as an example, an *in vitro* diagnostic device that was modified to raise the sensitivity of the antigen from 95 percent to 98 percent.

Other points to consider when deciding if an 806 report is needed:

Is the product a marketed device? Changes made to products not meeting the definition of a medical device, or not yet on the market, are not considered recalls.

Is the device being changed? This may include changes to the device itself, as well as to labeling or marketing materials.

Are the changes being made to fix a failure of the device to meet specifications or perform as represented? For example, an implanted device may be labeled as having a battery life of five years. If the manufacturer swaps the batteries for ones that last 5.5 years, that's typically considered an enhancement. But if it makes the change because the original batteries were failing before the five-year point, that would put the incident in the realm of a recall, the guidance explains.

Is the labeling false, misleading or otherwise inadequate? If so, changing the labeling would likely

constitute a recall, the FDA says. Adding a new warning to the labeling to meet foreign regulatory requirements typically would be considered an enhancement.

Early reaction to the final guidance was positive.

"We are pleased that the agency explicitly states in the guidance that enhancements will not require submission to FDA of 806 reports," Jeff Secunda, AdvaMed's vice president of technology and regulatory affairs, tells *IMDRM*. The group was still reviewing the final document at press time.

Mark DuVal, principal with DuVal & Associates in Minneapolis, Minn., says the guidance is "needed and helpful" and that the FDA's examples may prove especially useful to manufacturers. But there are still gray areas regarding when a device modification may require a recall notice but not a 510(k) or premarket approval supplement. It will likely take decisions on real-life cases to fully clarify the issue, he adds.

View the guidance at www.fdanews.com/10-20-14-recalls.pdf. — Elizabeth Orr

Framework for U.S. Regulation Of Lab-Developed Tests Outlined

The U.S. Food and Drug Administration took another step toward regulating laboratory-developed tests, with the Oct. 3 publication of draft guidance on a proposed regulatory framework and another guidance on adverse event reporting.

Under the proposed scheme, LDTs would be classified as low, moderate or high risk within 18 months of final guidance. Registration, listing and adverse event reporting requirements for Class II and III LDTs would go into effect six months after the framework is finalized, and premarket requirements for Class III LDTs would commence six months later, the guidance says.

Marketing authorization of all other LDTs would be phased in over the next four years once the Class III submission process has ended, beginning with Class II LDTs and working down to the lower-risk tests.

Class I devices, meanwhile, would be largely unregulated. The FDA does not intend to regulate LDTs used solely for forensic purposes by law enforcement or LDTs that are used only for transplants. Other Class I LDTs, such as those for rare diseases and tests that have no FDA-cleared equivalent, would be regulated in a limited fashion, the agency says. Manufacturers of these tests would need to register and

list their facilities with the FDA and submit adverse event reports, but would not require premarket authorization.

Resources Could Be Issue

That said, there's plenty of room for things to change before the new regulatory scheme would come into play, says Nathan Beaver, a partner with Foley & Lardner. "I think we have a long way to go in terms of seeing both a final guidance and then the implementation, and it would not strike me as surprising if the regulatory structure is revised," he tells *IMDRM*.

One uncertainty is FDA resources. The agency has said it will fund LDT review out of its existing in vitro diagnostics office, but that may not be feasible given the size of the field. Beaver expects the agency will wind up asking Congress for increased funding to support LDT regulation, allowing lawmakers to have "significant impact" on how the framework ultimately shakes out.

If implemented as proposed, the framework could create significant barriers to market entry for LDTs, Beaver says. "This will impose a significant additional cost on LDT makers that in the past did not need to absorb the cost," he notes.

Medical Device Reporting

Under the MDR guidance, LDT makers, including foreign laboratories, would be subject to the same adverse event reporting requirements as other devicemakers. Reports of individual incidents would need to be reported within 30 days of the lab becoming aware of information "from any source" that the test may have harmed an individual or malfunctioned. Incidents that require remedial action to prevent an "unreasonable risk" to public health, and reportable events about which the FDA has requested information, would have to be reported in five days.

LDTs have been regulated by the Centers for Medicare & Medicaid Services under the CLIA amendments since the 1970s, but the FDA believes the increasing complexity of such tests requires stricter controls. Among other concerns is that CLIA doesn't require reporting of LDT-related adverse events.

The FDA also insists that laboratories that produce and market LDTs have a competitive advantage over companies that must compile premarket information and submit it for review.

The agency took its first official step toward regulating LDTs with a July report to Congress. The regulatory

model laid out in the Oct. 3 drafts hews closely to that proposed in July, with only minor technical modifications. The agency is offering a 120-day comment period, until March 2, 2015 — about twice the standard time.

The proposed framework is at www.fdanews.com/10-06-14-framework.pdf. The MDR guidance is at www.fdanews.com/10-06-14-notification.pdf. — Elizabeth Orr

Device Review Times Improving In U.S., but Still Behind Europe

The Center for Devices and Radiological Health is steadily chipping away at premarket approval and 510(k) review times, but not fast enough to compete with EU approval times, according to a new report. The slower pace threatens to drive more devicemakers overseas for clinical trials and quicker market access.

"Europe's regulatory environment continues to attract U.S. medical technology business, and all that goes with it — investment, R&D, engineering, subsequent design improvements and iterations, clinical trial infrastructure and other expertise," the report says. "Only time will tell if recent improvements at the FDA ultimately have any impact on this gap."

The gap peaked at 70 months in 2005 and has slowly narrowed since then, dropping to 59 months in 2011 and to 36 months in 2012, the report by the California Healthcare Institute and Boston Consulting Group shows.

The report looks at FDA review trends since the FDA Safety & Innovation Act came into effect in 2012 and finds improvements in both PMA review times and the PMA backlog. Review times have plunged from a peak of 464 days in 2009 to 252 days in 2013. At the same time, the backlog of PMAs dropped from a high of 100 in mid-2011 to 52 in September 2013.

More Devices Getting Approved

CBI and BCG also found more submissions were being approved or ruled approvable. In 2013, 67 submissions were approved, 17 were ruled approvable and 17 were declined. That compares with 2010 when just 33 submissions were approved and 23 deemed approvable, while 37 were ruled not approvable and seven withdrawn.

510(k) review times have not turned the corner to the same extent, the report shows. The average review time for a 510(k) in 2013 — 123 days — was down from 170 in 2010 but was still significantly above historic review times. The 510(k) backlog has begun to

clear, however, declining from 1,917 submissions pending review in 2010 to 1,402 last year.

And FDASIA, which streamlined the de novo approval process, has sparked an increase in that category of submissions. In 2013, the FDA granted 19 de novo petitions, compared with just five in 2010, according to the report.

“The evidence is overwhelming that leaders at the agency and, in particular, [CDRH], have worked to get processes, internally and with industry, back on track,” CHI and CBG say. That said, the progress is at “a pace still far slower than historic standards,” the groups add.

View the report, “Taking the Pulse of Medical Device Regulation & Innovation,” at www.chi.org/fdareport/. — Elizabeth Orr

IN BRIEF

Swiss Ramp Up NB Scrutiny

Switzerland’s drug and device authority, Swissmedic, has informed local conformity assessment bodies, known as Swiss KBS, that they must meet the same stringent requirements as EU notified bodies. The European Commission issued an action plan for improving the quality of notified bodies following the 2010 Poly Implant Prosthèse breast implant scandal (*IMDRM*, October 2013). The Swiss agency says it has discovered irregularities and improvement needs in the area of monitoring by KBSs and has initiated investigations.

EU Firms Seek New Trial Standards

MedTech Europe and the European Forum for Good Clinical Practice have formed a joint Medical Technology Working Party within EFGCP to explore ethical and quality issues surrounding the setting of standards for device clinical trials. “There’s a growing understanding in the healthcare policy arena that we can’t just copy and paste the pharmaceutical approach to clinical standards into EU legislation on medical devices and in vitro diagnostics,”

says MedTech Europe CEO Serge Bernasconi. The working group’s initial meeting will be Dec. 4 in Brussels to discuss ways of mitigating risks in a product’s lifecycle.

IP 101 for Devicemakers

The European Commission has released a fact sheet on intellectual property considerations for medical device-makers. The document covers IP clearance and protection from the concept stage of device development through manufacturing and commercial use and offers helpful tips on how to avoid copying someone else’s design and trademark and copyright considerations. There is also a section on anticounterfeiting concerns. Access the fact sheet at www.fdanews.com/10-14-EU-IPR.pdf.

Australia Puts IP Data Online

The Australian government is putting more than a hundred years of intellectual property rights data online to facilitate collaborative partnerships and increase innovation. The data, which is patents administered by IP Australia, “includes information about IP rights applications that can be matched to individual firms along with information about their size, their technology and their geographic location,” says Bob Baldwin, parliamentary secretary to the industry minister. Available at www.data.gov.au, the data is current through Dec. 31, 2013, and will be updated annually.

India State FDA Seeks Price Controls

The Maharashtra Food and Drug Administration is asking the National Pharmaceutical Pricing Authority and the Drugs Controller General of India to bring five categories of medical devices under price control. The devices are neuro coils, cochlear implants, orthopedic implants, cardiac stents and bone cement. Advamed’s Abby Pratt, vice president for global strategy and analysis, says foreign devicemakers take these kinds of calls for action seriously. “We try to work with the government around their concerns, looking at strategies and mechanisms to make sure devices are affordable, but we do caution against major across-the-board price controls that could hamper the industry in India and affect patient access,” she tells *IMDRM*.

FDANEWS

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

Editorial: Jonathon Shacat
(703) 538-7663
jshacat@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.medicaldevicemonitor.com

Reporters: Elizabeth Orr, Lena Freund, Robert King, Neal Learner, Kellen Owings, Bryan Koenig

President: Cynthia Carter; **Content Director:** Dan Landrigan; **Executive Editor:** Meg Bryant

Copyright © 2014 by Washington Business Information Inc. All rights reserved. *International Medical Device Regulatory Monitor* (ISSN 1079-6940) is published monthly, 12 issues, for \$799. Photocopying or reproducing in any form, including electronic or facsimile transmission, scanning or electronic storage is a violation of federal copyright law and is strictly prohibited without the publisher’s express written permission. Subscribers registered with the Copyright Clearance Center (CCC) may reproduce articles for internal use only. For more information, contact CCC at www.copyright.com or call (978) 750-8400.

Dec. 3-4, 2014 • Tampa Marriott Waterside Hotel and Marina
Tampa, FL

Conducting **ADVANCED** Root Cause Analysis and **CAPA** Investigations

*Understanding Advanced Critical Thinking
Skills and Innovative Techniques to Improve
the Quality of Investigations*

In the Conducting **ADVANCED Root Cause Analysis and **CAPA** Investigations workshop, you will:**

- Get an insider view of the FDA's own training program for investigators — portions of the Reid Technique DVD will be reviewed during the course
- Review lessons learned from more than 15 years of FDA warning letter citations on investigations and CAPA
- Learn key problem-solving techniques to break down a problem into its component parts
- Interact with colleagues to participate in 8 advanced, interactive exercises
- Leave this workshop better able to conduct CAPA investigations



Gregory Meyer RAC, CQA
President and Principal Consultant and Trainer
Compliance Media, Inc.

Conducting ADVANCED Root Cause

Understanding Advanced Critical Thinking Skills and Innovation

Dec. 3-4, 2014 • Tampa Marriott Waterside

"I loved this course. [I] learned so much and the take home materials are great and can be used to train employees. I will highly recommend this course to others."

— Kate Garrido, Millennium Pharmaceuticals

"Very good examples to help me understand CAPA."

— David Flemming, QA Manager, Bionique Testing Laboratories

WORKSHOP AGENDA

DAY ONE

8:00 A.M. – 8:30 A.M. REGISTRATION/ CONTINENTAL BREAKFAST

8:30 a.m. – 10:00 a.m. FDA Regulatory Requirements and Enforcement

- Patient safety is our number-one concern
- Review of FDA requirements
- Corrective and preventive action terms
- Recent FDA inspection and enforcement trends
- Required FDA notifications
- **Interactive Exercise!** What's Driving Us Crazy?

10:00 A.M. – 10:15 A.M. BREAK

10:15 a.m. – 12:00 p.m. Problem Solving and Investigations

- Identifying and reporting problems quickly
- Initial risk assessment
- Determining need for an investigation
- Problem statements and key steps
- Six solution criteria
- Creative-problem solving techniques
- **Interactive Exercise!** Analyze cases and

determine risks and need for an investigation;
draft investigation plan if needed

12:00 P.M. – 1:00 P.M. LUNCH

1:00 p.m. – 2:30 p.m. Root Cause Analysis Tools and Techniques

- Brief review of common tools: Ishikawa diagram, flow charts, 5 whys, Is/Is not, cause and effect charts
- Root cause analysis process
- Tips on determining root causes and probable root causes
- Data visualization techniques
- Collaborative analysis
- **Interactive Exercise!** Brainstorm root causes for real cases with peers

2:30 P.M. – 2:45 P.M. BREAK

2:45 p.m. – 4:45 p.m. Interviewing and Writing

- Interviewing techniques
- Writing truths and tips
- Critical thinking in a nutshell
- Review portions of audiovisual program FDA uses to train its investigators on interviewing employees and management

- **Interactive Exercise!** Practice identifying problem statement
- **Interactive Exercise!** Practice interviewing a peer

4:45 p.m. – 5:00 p.m. Lightning Round Evening Work Compliance Program Guidance Manual and Warning Letter

DAY TWO

8:00 A.M. – 8:30 A.M. REGISTRATION/ CONTINENTAL BREAKFAST

8:30 a.m. – 10:00 a.m. Best Practices

- Discussion of insights from evening assignment
- Brief review of investigation tips and techniques used by other industries
- Discussion on data sources, root cause determination, effectiveness checks, timeliness, computerized systems and other critical issues
- **Interactive Exercise!** Best practices exercise in small groups

Root Cause Analysis and CAPA Investigations

Proven Techniques to Improve the Quality of Investigations

Hyatt Regency Hotel and Marina • Tampa, FL

YOUR EXPERT INSTRUCTOR



Gregory Meyer RAC, CQA is President and Principal Consultant and Trainer at Compliance Media, Inc. Mr. Meyer has been providing quality assurance, quality systems, and clinical regulatory guidance for biopharma and medical device companies for more than 20 years. He has conducted training for industry, regulators and academia and regularly presents at meetings of the Parenteral Drug Association, the American Society for Quality, and the

Regulatory Affairs Professionals Society. He has held director level positions in biopharma, small molecule and medical device companies in quality, regulatory affairs, and compliance. His training production company, Compliance Media produced the video documentary FDA: A History for the U.S. Food and Drug Administration's Centennial in 2006 and he is a recognized expert in the history and operations of FDA, as well as ICH Guidance, ISO compliance, and GHTF standards for medical devices.

YOUR COURSE 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 the presentations
- How to respond to FDA Form 483s and warning letters
- Comprehensive CAPA bibliography and recommended reading list
- Current FDA regulations
- Pertinent guidance documents
- Three articles on problem investigations
- FDA inspection manuals
- FDA's out-of-specification guidance
- ICH E6 good clinical practice guidance
- Recent FDA Form 483s or EIRs
- Pertinent FDA warning letters
- 16 great interviewing tips
- Two articles on CAPA
- FDA recall guidance
- Writing an executive summary
- Fishbone cause and effect diagrams
- Risk matrix chart
- Tips on documenting/presenting root causes
- Preventive action flowchart
- Author's questionnaire
- CAPA checklist
- Mock failure investigation reports
- Sample investigation plan
- Sample case review form
- Tips on conducting out-of-specification investigations
- Compliance tips/best practices
- Problem-solving worksheet
- Corrective action process checklist
- And much more...

10:00 A.M. – 10:15 A.M. BREAK

10:15 a.m. – 12:00 p.m. Critical-Thinking and Decision-Making

- Key elements of critical thinking
- Avoiding analytical traps
- Logic, argument and risk assessment
- Considerations in making good decisions
- Preparing to defend your thinking and recommendations
- **Interactive Exercise!** Practice using critical-thinking skills with peers on a case

12:00 P.M. – 1:00 P.M. LUNCH

1:00 p.m. – 2:30 p.m. Advanced Writing and Corrective and Preventive Action

- Detailed suggestions for crafting and writing reports and summaries. Writing is "thinking on paper," as revered writer and teacher William Zinsser says
- Correcting detected problems
- Preventing problems from occurring, including at other sites
- Bullet-proofing your work
- Communication to all affected sites or suppliers

- **Interactive Exercise!** Review cases and develop possible corrective and preventive actions

2:30 P.M. – 2:45 P.M. BREAK

2:45 p.m. – 4:45 p.m. Major Case Development

- Determining risk and urgency of problem
- Determining if an investigation is needed
- Using flow chart to understand the manufacturing, clinical, QA/QC, or other process involved
- Identifying possible root causes and documenting them
- Developing possible corrective and preventive actions, and effectiveness checks for each
- **Interactive Exercise!** Discuss selected case and present findings and recommendations to class

4:45 p.m. – 5:00 p.m. Review and Key Insights

Conducting ADVANCED Root Cause Analysis and CAPA Investigations

Understanding Advanced Critical Thinking Skills and Innovative Techniques to Improve the Quality of Investigations

Dec. 3-4, 2014 • Tampa Marriott Waterside Hotel and Marina • Tampa, FL

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:

Dec. 3-4, 2014

Tampa Marriott Waterside Hotel and Marina
700 South Florida Ave.
Tampa, FL 33602
Toll Free: (888) 268-1616
+1 (813) 221-4900
www.TampaMarriottWaterside.com
Room rate: \$169.00 plus 12 percent tax
Reservation cut-off date: Nov. 11, 2014

TUITION

Tuition rate is \$1,897 per person and includes all workshop sessions, workshop materials, two breakfasts, two luncheons and daily refreshments.

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 of 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.

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 (888) 838-5578 for details.

FOUR EASY WAYS TO REGISTER

Online: www.CAPAworkshop.com

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



YES!

I want to attend **Conducting ADVANCED Root Cause Analysis and CAPA Investigations**

I understand the fee of \$1,897 includes all workshop sessions, workshop materials, two breakfasts, two luncheons and daily refreshments.

FDANEWS

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

Date/Location Dec. 3-4, 2014 • Tampa Marriott Waterside Hotel and Marina • Tampa, FL

(Please see "Team Discounts" above for tuition discounts when you send a team of three or more.)

Attendee 1: Name _____ Title _____ Email _____

Attendee 2: Name _____ Title _____ Email _____

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 _____

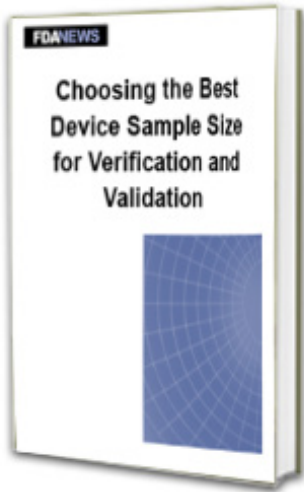
(Signature required on credit card and bill-me orders.)

Print name _____

Bill me/my company \$ _____

Purchase order # _____

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



Choosing the Best Device Sample Size for Verification and Validation

If you're like many manufacturers, you understand the essence of the *21 CFR 820.30* requirement: you must run enough test samples of a product so its test results can be successfully applied to full-scale production runs. And, like many manufacturers, you've probably had trouble for years determining exactly how many units of a product you should test to satisfy the FDA.

Choosing the Best Device Sample Size for Verification and Validation will help you select the right statistical methods to make this determination. With it, you'll learn how to get the right sample size to ensure that user requirements are met in the product design. This management report will also help you understand how to:

- Examine the discrete or continuous statistical data you collect.
- Look at variability, including variation from unit to unit or from batch to batch, as well as variation in their measurement systems.
- Design verification and validation tests, particularly regarding choice of sample size.
- Fully understand the requirements for statistical techniques, including how different techniques can affect the design control process.
- And much, much more.

Finally, you can gain a clearer understanding of how to put together a statistical methods program for design verification and validation that will satisfy FDA auditors.

Order your copy today!

FOUR EASY WAYS TO ORDER

1. **PHONE:** Toll free (888) 838-5578 or +1 (703) 538-7600
2. **WEB:** www.fdanews.com/46876
3. **FAX:** +1 (703) 538-7676
4. **MAIL:** FDAnews
300 N. Washington St., Suite 200
Falls Church, VA 22046-3431



Please send me _____ copy(ies) of **Choosing the Best Device Sample Size for Verification and Validation** 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.