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2014 Brought Inspection Changes, Global Plans for Enforcement

2014 proved a key year for inspection changes affecting devicemakers, with the biggest news being an overhaul of the FDA's handling of inspections, recalls and other enforcement issues. Last year also brought the final version of the FDA's recall versus enhancements guidance, and a variety of global plans for FDA device enforcement. These include efforts to boost coordination of inspections and enforcement activities with international counterparts.

In the fall, the agency 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 next year (*GMP*, November 2014). The reorganization creates a distinct inspectorate for medical devices, eliminating the region-based model.

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Multiple UDI Issuers Could Delay Adoption, Experts Say

An FDA decision to allow multiple entities to issue unique device identifiers could backfire and actually impede the uptake of UDIs, warn medical device and healthcare industry experts.

Speaking at a workshop hosted by the FDA, HHS' Office of the National Coordinator for Health IT and Pew Charitable Trusts, panelists said having three different standards for UDI design is proving a significant barrier to the program's launch.

"There's no good case for the lack of a mandate" on a single UDI standard, said Leslie Kelly Hall, senior vice president at Healthwise and a member of the federal advisory committee on health IT. Other panelists agreed that UDI will only have value if it is widely adopted in a universal format.

Currently, devicemakers can obtain UDIs from one of three standards-issuing organizations: GS1, the Health Industry Business

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The FDA also promised a streamlined review process for approving enforcement actions (*GMP*, March 2014). Earlier in the year, CDRH Office of Compliance Director Steve Silverman said the center would focus its limited resources on encouraging quality rather than on compliance enforcements.

Devicemakers were promised 13 new product-specific guides by the end of the year to tell them what quality-related metrics FDA investigators will focus on during site inspections (*GMP*, October 2014). And the FDA launched a new data dashboard, providing a more user-friendly way for manufacturers to obtain inspection and recall data (*GMP*, November 2014).

On the recall side, the FDA reversed itself and said it won't require devicemakers to submit formal reports when they make safety enhancements to their products. The decision, laid out in 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 (*GMP*, November 2014).

Recalls Continue to Drop

The number of all medical device-related recalls in the second quarter of the year — 275 — was the lowest it has been since the second quarter of 2012 and 17 percent below the tally for the 2014 first quarter, the Stericycle ExpertSOLUTIONS Quarterly Recall Index found. The recalls involved 148 companies, 28 percent of which had two or more recalls. Seven percent of companies had five or more recalls.

Another report from 2014 shows a near doubling of medical device recalls from fiscal year 2003 to 2013. But a greater focus on safety — not shoddier products — appears to be behind the uptick. The FDA attributed the rise in overall recalls to increased reporting by industry and a better collaboration between CDRH and industry to improve the quality and safety of devices.

Meanwhile, the number of devicemakers receiving FDA warning letters following quality system inspections dropped 12 percent from 2012 to 2013 — the first decline since 2009. There were 144 warning letters with quality system regulation deficiencies in 2013, compared with 164 a year earlier (*GMP*, November 2014).

But while the number of warning letters dropped, those that were issued contained more citations. FDA investigators recorded 17 percent more citations in calendar year 2013 versus a year earlier, according to medical device quality system data released by CDRH.

UDI Advice

The year saw a plethora of advice and requirements for UDI compliance. HHS' health IT coordinator called for all electronic health records to incorporate the unique device identifiers of implantable devices by 2015. Meanwhile, the FDA advised manufacturers to update their medical device tracking procedures to account for UDIs and to bake in extra time to set UDI codes with the FDA (*GMP*, June 2014).

FDA staff charged with implementing the rule suggested not publishing codes through the UDI system until the device's manufacturing date is solid. That allows extra time for trouble- shooting and making last-minute modifications.

CDRH also promised to help devicemakers on UDI transitioning with flexible, gradual enforcement as it is implemented over several years.

"Our main focus is getting the UDI system implemented correctly and actively helping companies comply with system requirements — not on enforcement," FDA spokeswoman Jennifer Rodriguez told *GMP*.

The Future Is Global

Going forward, devicemakers can expect more global enforcement initiatives. Over the

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CAPA, Complaint Procedures Top 2014 Inspectional Observations

Inadequate CAPA procedures led all other causes for Form 483s issued to devicemakers in fiscal 2014, while purchasing control issues jumped from sixth place to third in the FDA's annual ranking of inspection observations.

The data are from the agency's annual statistical report of 3,467 domestic and foreign device inspections that were scheduled from Oct. 1, 2013, through Sept. 30, 2014. During this period, the FDA issued 972 Form 483s to devicemakers, down from 1,099 in the prior fiscal year and 1,090 in 2012.

The top 10 observations in device 483s were:

- Lack of or inadequate procedures (cited in 360 forms, down from 378 in 2013);
- Lack of or inadequate complaint procedures (251, up from 245);
- Lack of or inadequate procedures for purchasing controls (129, up from 110);
- Lack of or inadequate process validation (122, down from 127);
- Lack of written MDR procedures (117, down from 124);
- Failure to adequately document corrective and preventive action activities and/or results (101, down from 133);
- Lack of or inadequate procedures for nonconforming product (100, up from 98);
- Lack of or inadequate procedures for design changes (95, up from 93);
- Lack of or inadequate procedures for quality audits (90, up from 73); and
- Investigation of device failures (68, down from 69).

The top 10 observations largely reflect those on the 2013 list, with some key differences—among them, the rise in purchasing control observations and the fact that observations on documentation of CAPA activities and/or results dropped from number three to number six.

Many of the observations reflect small companies struggling to follow overly complex SOPs, says John Avellanet, managing director and principal at the consulting firm Cerulean Associates. These companies would fare better if they identified the end goal of the FDA regulation and got there the best way that they could, he says. They can make SOPs very simple and straightforward using process maps and workflow diagrams.

Instead, some devicemakers purchase a 20- or 30-page SOP online and put a company logo on it, without having the manpower to follow the procedure, Avellanet tells *GMP*. "I have heard this from numerous FDA investigators: It is better for you to flowchart out a process that you actually do and will follow on a cocktail napkin and use that as your procedure than to write some 30-page SOP that looks great on paper but nobody follows. I think that's ultimately what happens a lot of the time."

SOP Should Generate Record

Avellanet also tells clients that each SOP should generate some form of documentation, whether that be a record, form, checklist, template, draft letter, batch record or other document.

According to Avellanet, the increase in purchasing control issues this year was likely due to devicemakers relying solely on a purchase order instead of negotiating a quality agreement with certain suppliers. This can be challenging, he acknowledges, as many suppliers won't take the time to negotiate these agreements with smaller clients.

Meanwhile, a common mistake smaller companies make with complaint procedures is having the office manager review complaints with a customer service focus and not follow a decision tree for reporting decisions to the FDA. For process validation, many devicemakers follow the recent FDA guidance for pharmaceutical companies, but have not adequately documented the justification for that decision, he says.

To view the FDA's 483 statistics report, visit www.fda.gov/ICECI/Inspections/ucm424098.htm. — April Hollis

Brazilian Devicemaker Warned On Informal Design Change Docs

Greiner Bio One Brasil Produtos ran afoul of the FDA after documenting design changes in informal meetings with informal notes, a recent warning letter shows.

During a Jan. 13-16 inspection of its Americana, Brazil, facility, the investigator reviewed a labeling change and found Greiner did not have a formal procedure specifying change activities. The company, which makes Vacuette blood collection tubes, also lacked a formal procedure for verification and documentation of the change activities' completion, according to the Aug. 8 letter posted recently online.

"Available procedures including the change control procedure, change control form, and change log form do not address timing of change implementation or effect on existing stock," the letter says. Applicable design changes were being managed and documented using "informal meetings and … uncontrolled meeting notes," the letter adds.

Greiner's quality manager indicated that the local procedure for design change control activities does not specify local methods to track or document required change implementation activities, according to the letter.

The investigator also found that Greiner did not adequately document inspection requirements for rubber stoppers, and its incoming acceptance documentation lacked data or certificates of conformance showing the prescribed acceptance testing protocol was performed.

Greiner also came under FDA scrutiny for failing to measure its quality audits against agency requirements. The company's internal audit criteria did not identify any requirements from applicable FDA regulations, the warning letter says.

Manfred Abel, quality system and regulatory affairs manager, said Greiner takes the warning letter seriously and is working with the FDA to resolve and correct the deviations.

The warning letter is available at www.fdanews.com/12-04-14-Greiner.pdf. — April Hollis

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next four years, the FDA plans to increasingly coordinate its inspections and enforcement activities with its international counterparts (*GMP*, August 2014).

The ambitious plan, laid out in the agency's Strategic Priorities 2014-2018, envisions an international operating model based on information-sharing, data-driven risk analytics, enhanced intelligence-gathering capabilities and smart allocation of resources through multinational partnerships. The goal is to enable different regulators to share real-time information and better allocate resources based on risk.

Over the summer, the FDA and U.S. Customs and Border Protection began accepting applications for an 18-month "trusted trader" pilot program. The initiative aims to reduce inspections and oversight of products imported from manufacturers that establish tough internal import control programs of their own (*GMP*, July 2014).

Meanwhile, the International Medical Device Regulators Forum is trying to entice more companies to participate in its single-audit pilot program, promising they will receive no warning letters unless the issues pose an immediate threat to public health. Canada is putting additional pressure on firms to sign on, announcing that, as of 2016, any devicemakers selling products there will require the 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. — April Hollis

FORM 483 INSIDER

Incoming Inspections, Procedure Issues Draw Form 483 for Surgical Design

Surgical Design came out of an FDA inspection with seven Form 483 observations, including for its incoming inspection procedure.

The company's procedure required it to pull 2 percent of incoming circumcision clamps for lot sampling. However, five of 13 incoming inspection documents reviewed from 2013 to 2014 found inspections at less than 2 percent.

Surgical Design was also rapped for lack of design control procedures, nonconforming product procedures, management review procedures, document control procedures for SOPs, and training records for the inventory management worker and quality control manager. The form also notes inadequate CAPA procedures at the Lorton, Va., facility.

Surgical Design did not return a request for comment by press time. The Form 483 is available at www.fdanews.com/12-22-14-Surgicaldesign.pdf.

Vasomedical 483 Details Complaint, CAPA Issues

Vasomedical received a four-observation Form 483 due to shortcomings in complaint reviews and other GMP slips.

The Westbury, N.Y., company did not automatically consider service repairs and product returns as complaints and process them according to requirements, the forms says. Vasomedical also did not consistently issue corrective action requests to evaluate complaints for possible device, labeling or packaging failures.

Further, Vasomedical's complaint handling procedure did not specify that, when there is no investigation, the company must keep a record explaining the decision and include the name of the employee responsible for the decision.

The form detailed CAPA problems as well. Vasomedical's CAPA procedure did not require it to implement and record changes to methods and procedures that are made to correct and prevent quality problems.

Meanwhile, the company opened a corrective action report after a customer complaint about the noise level of the TS4 system during treatment. The firm initiated a corrective action, but did not document any verification or validation.

Vasomedical did not provide a comment on the form. The Form 483 is available at www.fdanews.com/12-22-14-Vasomedical.pdf.

Biomet Spine 483 Relates to Validation Records, Complaints

FDA investigators handed Biomet Spine a four-observation Form 483 for deficiencies with validation records and complaint-handling problems.

A protocol at the Broomfield, Colo., facility set certain acceptance criteria for microbial contamination of water produced by a system. But reports documented in the lab exceeded the acceptance criteria and Biomet Spine did not investigate the elevated microbial counts. Instead, the devicemaker changed the acceptance criteria in the report, according to the form.

Another observation relates to Biomet Spine's handling of a complaint that documented a patient death during a procedure using a Timberline retractor to remove an artificial disc. According to the complaint record, the sales representative indicated the retractor did not contribute to the death. But there was no documentation of information supporting this statement from a person qualified to make a medical judgment, the form says. And Biomet Spine did not report the death to the FDA as an MDR.

The company also failed to report a recall of 120 Durango Anchored Anterior Lumbar Interbody Fusion Plate Sets following two complaints of set screws dislodging from the plates.

Biomet Spine did not return a request for comment by press time. The Form 483 is available at www.fdanews.com/12-22-14-Biometspine.pdf.

Expiration Dates Challenging With Combo Product GMPs

Devicemakers whose products include a drug component could find GMP compliance especially tricky, due to a 2013 regulation that requires expiration dates like those used for drugs, an industry expert says.

The 2013 cGMP final rule on combination products mirrors the drug GMP focus on expiry dates, but these can be difficult to establish for devices, which typically don't change over time, according to Linda Mummah-Schendel, senior medical research manager at the NAMSA.

"There's no easy way to hit all the required testing on both the drug and the device attributes of a combination product," Mummah-Schendel said on a recent webinar sponsored by the Regulatory Affairs Professionals Society.

Reserve Sample Rules

Under the final rule, labeling for combo products must show the expiration date, and the product must continue to meet the manufacturer's specs regarding quality of the product. Manufacturers must also establish an in-house definition for "batch" and perform stability, identity and strength testing on at least three sample devices of each size per batch.

Reserve samples of all components of a combination product must be kept for at least a year for future strength testing, says Mummah-Schendel. The FDA requires manufacturers to hold onto at least twice as much of each product as is needed for testing.

Combo product makers also need to ensure the security of container closures and see that any pharma ingredients are properly handled, she says. Drug regulations require a calculation of actual and theoretical yield of the drug component at each stage of manufacturing, processing and packaging, Mummah-Schendel explains.

Mummah-Schendel cautions devicemakers not to overcomplicate their combo product GMPs. For example, a CAPA regulation that requires too many steps may result in actions going undocumented. "If it's not documented, it's not done" in the eyes of inspectors, she says.

Mummah-Schendel also stresses that devicemakers must designate one person to be responsible for compliance with combo product GMPs. This information should be included in the company's organizational chart so that it's easily available to auditors, she says.

The FDA's initial attempts to adapt drug GMPs to devices did not work well due to the wide range and complexity of medical technologies, says Mummah-Schendel. The result was tweaked to allow for a more risk-based approach, à la the quality system regulations.

Ultimately, though, the 2013 final rule removed much of that flexibility by making some requirements legal mandates, Mummah-Schendel adds. — Elizabeth Orr

Trucare Biomedix Warned Over Supplier Audits

The FDA has warned Miami-based Trucare Biomedix-USA over slips on supplier audits, purchasing controls and other good manufacturing practices.

According to the Nov. 24 warning letter, the company stated on its website that suppliers are audited each quarter. However, during the inspection, Trucare's president said that information was not accurate.

Trucare is a specification developer, distributor and importer of IV administration sets and an importer/own label distributor of IV poles and syringes. But its purchasing control procedures don't ensure that suppliers have adequate quality control programs, including personnel qualification for bonding, process validation of special and automated processes and equipment maintenance, the warning letter says.

While the company has documentation from its current IV administration set contractor on sterilization validation, package integrity validation and certificates of analysis and sterilization, its purchasing control procedures don't require these documents for potential future suppliers, the FDA investigator found. The letter follows a Sept. 11-17 inspection of Trucare's South Miami facility.

The investigator further noted that Trucare's internal audit SOP requires it to generate an audit schedule and cover all major systems and areas at least once a year. However, the company has no documented schedule and no documented internal audit criteria and had not completed any official internal audits, the letter notes.

The company's CAPA procedures also came under fire for lacking requirements to verify or validate CAPAs and for not including definitions

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Contract Manufacturer Warned On String of GMP, MDR Failures

San Antonio, Texas, contract manufacturer Voss Plastics received a 10-citation warning letter for serious lapses in good manufacturing practices and lack of written procedures for adverse event reporting.

According to the Nov. 5 warning letter, Voss had no established procedures for developing, conducting, controlling and monitoring production processes to ensure that they conform to manufacturing specifications. The plant's manager told the FDA investigator that he visually inspects each unit during the run to verify that products are manufactured properly, but there are no written procedures on how this inspection is done or when and how often samples are to be pulled, the letter adds.

The warning letter follows a Sept. 8-12 inspection of Voss' Helotes, Texas, facility where the company makes disposable coronary bypass cannulas.

The investigator goes on to rap Voss for lacking receiving, in-process and finished product acceptance activities for its cannulas, and for not having procedures for documenting how these activities are performed and how the results are recorded and approved.

Voss also failed to establish procedures for nonconforming product, corrective and preventive actions, reviewing and evaluating complaints, maintaining device history files and managing reviews. And the FDA found Voss' products were misbranded because the company had no written MDR procedures.

Voss responded to the FDA's concerns in September, but the agency deemed the response inadequate. "Although you indicate you will correct the deviations through the generation of new procedures, you did not provide copies of the procedures or sufficient detail of the content of the procedures for our review," the warning letter says.

The company did not respond to a request for comment by press time. View the warning letter at www.fdanews.com/12-22-14-Voss.pdf.
— Meg Bryant

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of preventive actions or instructions regarding how preventive actions will be controlled.

A 2012 CAPA addressing three complaints about leaky IV administration sets, which had the potential to harm patients, was deemed inadequate by the FDA. The CAPA said that the contractor responsible for the manual bonding defect was removed from the accepted supplier list; however, it failed to assure that purchasing control procedures were changed to prevent a similar incident in the future.

The company now requires its contractor to conduct 100 percent leak testing for IV administration sets, but this requirement has not been documented as part of written purchasing control procedures, the warning letter says.

Other citations state that:

- The company could not provide the FDA investigator with an English translation of a risk analysis that was documented in Spanish;
- Document control procedures don't specify how the company will control draft or obsolete documents; and
- Trucare lacked written MDR procedures and failed to report three complaints related to a 2012 recall as MDR malfunction reports.

As part of the recall, the company had trucks pick up leaking IV administration sets from various sites — an action the FDA determined is a Class II recall, which should have been reported within 10 days. However, the company didn't notify the agency within that time frame, the letter says.

The FDA notes that a follow-up inspection may be needed to assess the company's corrective actions.

The company did not provide a comment by press time. View the warning letter at www.fdanews.com/12-09-14-USInfusion.pdf. — April Hollis

FDA Warns AngioDynamics Unit Over Hair in Sterile Product

AngioDynamics subsidiary Navilyst Medical received an FDA warning letter for quality issues at two manufacturing facilities, including the sale of sterile product that contained foreign matter such as hair.

The contamination problem, noted at the company's Marlborough, Mass., plant, is "unacceptable regardless of your complaint rate," the letter says. Navilyst also failed to open a corrective and preventive action to address complaints of hair found by end users.

According to the Nov. 4 letter posted recently online, Navilyst provided the investigator with a list of 55 complaints about hair in product packaging that it had received between May 2012 and May 2014. However, the company only conducted accelerated age testing on packaging for its Vaxcel peripherally inserted central catheter with pressure-activated safety valve, and not on the Xcela Power Injectable PICC, Xcela PICC with PASV and BioFlo (valved and nonvalved) PICCs.

The company's rationale for using the data to support other PICCs failed to account for packaging changes and worse-case kit configurations in terms of density, the warning letter says. All of Navilyst's products are long-term intravascular implantable catheters.

Additionally, the Xcela Power Injectable PICC with PASV was released for distribution before completion of a real-time aging study, although 20 catheters had fractures on their oversleeves after exposure to the temperature and humidity of accelerated aging conditions, the letter notes.

Validation Issues

The warning letter also details violations at Navilyst's Glen Falls, N.Y., manufacturing plant.

The investigator notes that the process for curing silicone sheets used to make catheter valves appeared not to be fully validated and didn't allow for all of the valves to be tested. The silicone curing process using one oven was considered not fully validated because the bake time for silicone sheets varied from batch to batch and scaled-down samples of baked silicone sheets used to calculate the average modules and final bake time had different load configurations. The production yield and rework activities also showed batch-to-batch variation.

The letter goes on to note that the Vaxcel, Bio-Flo and Xcela catheters are designed with a PASV, and the design verification activities include a test for performance characteristics under accelerated age and real-time conditions. However, Navilyst's design verification processes didn't test the catheters "with PASV at real-time conditions showing the catheter's ability to draw blood samples without damaging blood cells."

Working to Resolve Issues

Following an uptick in complaints of hemolysis with the PICCs in 2012, Navilyst tightened a manufacturing specification but didn't include a test in the design history file to verify real-time conditions to show the valves are capable of aspirating human blood samples without damaging blood draws, the warning letter says.

Navilyst said it has responded to the FDA and will continue to work with the agency to address its concerns.

"We have never knowingly shipped product containing foreign matter and have submitted detailed responses to the FDA with regard to this issue," AngioDynamics President and CEO Joe DeVivo tells *GMP*. He says the issues are fairly narrow in scope and should not have a serious impact on the company's business.

The warning letter followed an April 9 through May 28 inspection by the FDA's New York district office. View the letter at www.fdanews.com/12-2-14-Navilyst.pdf.
— April Hollis

UDI, *from Page 1*

Communications Council or the International Council for Commonality in Blood Banking Automation. The idea, explained former FDA staffer and UDI architect Jay Crowley, was to minimize disruption of devicemaker operations. Many companies already work with GS1 and HIBCC, while ICCBA standards have wide currency in the blood and tissue markets, said Crowley, who is now a vice president at west coast consultancy USDM Life Sciences.

Russell Branzell, president and CEO of the College of Healthcare Information Management Executives, cautioned that allowing each hospital or healthcare system to implement UDI on its own could lead to "a big mess" where trading partners aren't able to integrate their UDI systems. A clear, common UDI standard, along the lines of the drug code, is what is needed, he said.

Create Trust and Collaboration

Leigh Anderson, COO of informatics and technology services at Premier healthcare alliance in Charlotte, N.C., said integrating UDI into EHRs will require greater trust and collaboration throughout the industry. But, he added, the technology for sharing UDI data from a manufacturer's system to a hospital's system and then to a patient registry exists if stakeholders are willing to pool data. The problem is an abundance of proprietary technology that is blocking the way.

Some panelists suggested that the government could speed integration by insisting that EHRs accept UDI information to gain government certification. "We need to educate software vendors on UDI," said Joseph Drozda, director of outcomes research at Sisters of Mercy Health System in St. Louis, Mo. "It doesn't seem like it should be a big deal for any one vendor; they have to know how much customers want this."

Another sticky wicket is that hospitals still need to find some efficient way to get UDIs into EHRs, as time is at a premium. "For patient safety, the last thing we want is manual UDI entry into the clinical record," said Chantal Worzala, director of policy at the American Hospital Association. She pointed out that each UDI involves up to 75 characters, and many medical procedures use multiple device components.

With regard to scanning UDIs, Denise Downing, with the Association of Perioperative Registered Nurses, said nurses would need to ensure that the tags are safe for use in the operating room and don't get lost during the procedure, then input the information, often while the physician waits.

According to Karen Conway, executive director of industry relations at the Global Healthcare Exchange, manual entry is still the default in many hospital systems, with only about 10 percent of operating room supplies being tracked via scanning.

Branzell said healthcare organizations will need to see a significant gain from UDI before tackling the job of collecting and distributing the data to patients or registries. "UDI will need to have some kind of financial or caregiving gain … Otherwise, there are already hundreds of recommendations hospitals aren't following up on, and UDI might be one more." — Elizabeth Orr

Karl Storz Warned on CAPA, Issues With Disinfection

Karl Storz Endovision was handed an FDA warning letter for cleaning slips and other GMP issues related to its endoscopes.

During an Oct. 14-29 inspection of the company's Charlton, Mass., facility, an operator failed to use the specified brush for cleaning the intubation scope in returned endoscopes. The brush being used "did not fit through the working channel," according to the Dec. 8 letter. The device was then processed through the plant's decontamination station, and the associated paperwork was stamped "decontaminated," the letter says.

An investigator with the FDA's New England district office noted that a reference document used in the cleaning/high-level disinfection area did not reference the appropriate brush models for cleaning endoscopes.

Validation Problems

The company also lacked design validation data showing that the cleaning brush specified in its instruction manual is appropriate for a particular model of the Flex-X2 flexible ureteroscope.

The FDA found Karl Storz's CAPAs were also deficient. For example a CAPA was opened in August 2013 to verify process control parameters in the shaft composite assembly procedure. The company's corrective action was an operational qualification to determine the appropriate oven settings, but data in the operational qualification noted that certain replicates fell short of the peel force acceptance criteria, the warning letter says.

Moreover, the report determined that an external factor may have caused the failures but did not provide an additional explanation.

Complaints were also a problem, the letter shows. A complaint received in September referred to "a small white foreign body" in a kidney during a stone removal procedure and noted the endoscope was missing a small white piece from the tip. "As of October 29, 2014, your investigation of this complaint did not include a review of the device history record for the device, as required by your complaint procedure," the letter says.

Karl Storz did not respond to a request for comment by press time. The warning letter is available at www.fdanews.com/12-16-14-Karl Storz.pdf. — April Hollis

New Zealand Updates Recall Process, Clarifies Roles of Recalling Parties

New Zealand's regulatory authority is updating its uniform recall procedure for devices, following a recent decision not to pursue a joint regulatory authority with Australia.

Manufacturers, suppliers and importers of devices in New Zealand must have written procedures in place that describe how recalls are initiated and carried out, according to Dec. 16 draft guidance from the New Zealand Medicines and Medical Devices Safety Authority. The document clarifies the responsibilities of the various parties and describes ways to improve communications during a recall.

Prior to initiating a recall in New Zealand, companies must discuss the issue with Medsafe. The agency retains the authority to require a different action than that proposed by the recalling firm. In general, the recall level will reflect the safety risk and distribution pattern of the product, Medsafe says.

Once a recall is deemed necessary, companies must prepare correspondence for wholesalers, retailers, hospitals and pharmacists, as well as media releases and consumer advertisements. Progress reports are required, normally at two and six weeks. A final report, including a certificate of product destruction, confirmation of product correction and an investigation of the root cause and remedial actions, must also be submitted to Medsafe.

Comments are due by Feb. 27. Read the draft Uniform Recall Procedure for Medicines and Medical Devices at www.fdanews.com/12-14-Medsafe-RecallCode.pdf. — Jonathon Shacat

India Proposes GMP Rules; Self-Certification in Works

Indian regulators are establishing quality manufacturing standards for medical devices and diagnostics to align the country's requirements with international standards and move away from a system of regulating these products under rules designed for drugs.

In a draft guideline, the Central Drug Standards Control Organization would mandate that devicemakers adhere to the comprehensive quality management system requirements of ISO 13485.

The guideline imposes specific requirements for aseptic processing areas and separate work areas for plastics processing, shaping of metal implants, cleaning, components storage, assembly, final packaging, sterilization and aeration, if applicable, and storage of finished products.

Push for Best Practices

Manufacturing operations would have to be supervised by staff that meet the standards of the state or central government licensing agency. And the new guideline would introduce product labeling requirements so that labels would have to identify the stage of production for a product, batch number and quantity so that all products could be traced throughout the manufacturing process.

For combination products, CDSCO would require that manufacturers designate separate drug and biologics sampling areas within their warehouse and have appropriate ventilation controls for hormones used in combination products.

The proposed guideline comes as India's device industry is taking its own steps to improve quality via a program that would let companies self-certify adherence with international GMPs.

The industry initiative was launched Oct. 30 with a memorandum of understanding between the Association of Indian Medical Device Industry and the Quality Council of India, a public-private enterprise that strives to bring Indian companies up to international standards.

Under the program, accredited third party auditors would be used to certify that medium- and high-risk devices are made in accordance with ISO 13485. The system for approving the third party auditors would likely be similar to the European Union's notified bodies system, says Vince Suneja, CEO of the Pittsburgh-based TwoFour Insight Group.

Anil Jauhri, CEO of India's National Accreditation Board for Certification Bodies, says the voluntary system will let local devicemakers demonstrate compliance with best standards, but would not replace government inspections unless government regulators agree to accept the audits in lieu of inspections.

Jauhri notes that Indian devicemakers historically have had to rely on foreign bodies like Intertek, TUV and BSI to certify their plants if they wanted to export to Europe or elsewhere.

View the draft guideline at www.fdanews.com/12-14-indiaGMP.pdf. An organizational chart for the Medical Device & Diagnostics Division is at www.fdanews.com/12-14-IndiaOrgano.pdf. — Elizabeth Orr, Jonathon Shacat

FDANEWS

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

Editor: April Hollis
(703) 538-7634
ahollis@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: Elizabeth Orr, Robert King, Lena Freund, Kellen Owings, Bryan Koenig, Jonathon Shacat

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

Device Supplier Controls: *Avoiding an FDA Form 483*

You're probably not surprised that in 2013, violations of 21 CFR 820.50 (the purchasing controls requirement) ranked among the top 10 FDA citations involving quality systems regulations. Despite many fewer FDA inspections of devicemakers over the last three years … the number of 483s issued to companies like yours rose 12% … and warning letters skyrocketed 24%.

That's why the timing couldn't be better for you to take advantage of the FDAnews management report **Device Supplier Controls: *Avoiding an FDA Form 483***. It's designed to help you to manage your suppliers by:

- Understanding recent FDA supplier control inspection and enforcement trends.
- Creating an assessment tool to choose the right subcontractors and suppliers.
- Writing stronger quality agreements that address legal and regulatory issues.

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MEDICAL DEVICE COMPLAINT MANAGEMENT | Building a Robust System to Meet Global Requirements

PRESENTED BY OMBU ENTERPRISES AND FDANEWS

FEB. 25-26, 2015 | WYNDHAM BEACON HILL, BOSTON, MA

YOUR INSTRUCTOR

Dan O'Leary
President
Ombu Enterprises, LLC

"Very informative and on point. This lecture was amazing and spot on. We covered a lot in two days. Dan's approach was great and he is good at helping employees at all levels."

—Shivani Persad, Associate Complaint Coordinator, Fresenius Medical Care

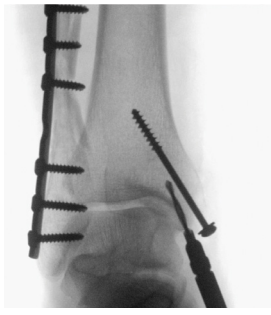
You start with hypothetical complaints, and then trace them through the regulatory system. First comes the presentation explaining the issues and illustrating them with regulations, guidance documents, Warning Letters, etc. These are followed by interactive exercises liberally spread over two days.

You find yourself out of your chair and engaging with devicemakers like yourself — from the EU, Canada and all across the US — confronting and solving shared problems.

At the conclusion of each small-group exercise, you take a test. But not to worry —you can't fail. Answers are provided, plus proven solutions to take home and apply in your operation. We know of no other workshop providing such fine-grained level of interactivity, not to mention solutions you can put into effect — at once.

Attendees to this all-new workshop will learn:

- The role of Unique Device Identification (UDI) in complaints and adverse event reporting
- Regulatory reporting requirements in three major markets: US, EU, and Canada
- Understanding why the source of a complaint (Facebook, Twitter, email, phone call) is not your chief concern — it's how to handle the communication
- The proper use of corrective action in complaint management, including statistical analysis
- Developing a complaint classification system that links to the risk management file
- Analysis methods to help determine the impact of design changes on regulatory requirements
- How to distinguish between enhancements and recalls, following the FDA guidance.
- Recall requirements in the US, EU, and Canada.



Day 1

WEDNESDAY, FEB. 25, 2014

8:00 a.m. – 9:00 a.m. | **REGISTRATION AND CONTINENTAL BREAKFAST**

9:00 a.m. – 10:15 a.m.

Part A – The Intersection of Complaints and the Regulatory Structure

- Understanding the Quality Management System (QMS) in the US, EU, and Canada
- Distinguishing records and reports to regulatory agencies (content, trigger, and timing)
- How and why the FDA conducts inspections and the guiding documents they use
  - Quality System Inspection Technique
  - Compliance Program 7382.845 Inspection of Medical Device Manufacturers
- Using sampling plans as part of the Medical Device Directive (MDD) audit

Exercise – FDA Inspection Levels
Exercise – QSIT sampling plans for records

10:15 a.m. – 10:30 a.m. | **BREAK**

10:30 a.m. – 12:00 p.m.

Part B – How Newly Enacted Unique Device Identification Will Impact Complaints

- Overview of the US regulations regarding UDI
- What are Device Identifiers and Production Identifiers — and how do they differ
- Understanding the GUDID and the information you need to supply

Exercise – Creating a new Device Identifier

Part C – Servicing: The Front Line for Complaints?

- Definition of servicing — is your definition and regulators' the same?
- How servicing relates to other QMS elements?
- Producing service records and linking them to complaints
- Tips, tools, and techniques for analyzing service records; what should you be looking for?

Exercise – Analyze a small set of service records using quality tools

12:00 p.m. – 1:00 pm | **LUNCH BREAK**

1:00 p.m. – 2:30 p.m.

Part D – Complaints

- Definition of a complaint —distinguishing regulatory complaints from customer service complaints
- Comparing and contrasting QSR vs. ISO 13485 definitions
- Successfully developing and managing complaint classification systems
- Fully understanding complaint system interrelationships, it's harder than it appears

Complaints and corrective action
- Complaints and MDRs
- Complaints and EU Vigilance
- Complaints and risk management (ISO 14971:2007)

- Complaint system flowchart
- Determining the required content for complaint records

Exercise – Analyze customer reports to determine if they are a complaint and potentially reportable

2:30 p.m. – 2:45 p.m. | **BREAK**

2:45 p.m. – 4:30 p.m.

Part E – Medical Device Reports (US)

- Understanding the criteria for reporting
- Establishing the MDR event files that serve their purpose and stand up to FDA scrutiny
- Identifying Designated Individuals
- MDR system interrelationships
- Examining the nexus between MDRs and complaints
- Getting to know the types of MDRs (30 day and 5 day)
- Reporting MDRs — paper or electronic
- Records required for the MDR system — what you must have

Exercise – Initiate a Medical Device Report

Part F – Medical Device Reports in the EU and Canada

- Understanding the criteria for reporting
- The regulatory structure in the EU (MDD and MedDev)
- The regulatory structure in Canada
- Role of the Notified Body in the

Vigilance System

- Role of the MDD Authorized Representative in the Vigilance System

Exercise – Analyze an adverse event to determine when to report

4:30 p.m. | SESSION WRAP-UP, END OF DAY ONE

Day 2

THURSDAY, FEB. 26, 2014

8:30 a.m. – 9:00 a.m. | CONTINENTAL BREAKFAST

9:00 a.m. – 10:15 a.m.

Part G – Corrective Action and Preventive Action (CA&PA)

- The difference between corrective action (CA) and preventive action (PA)
- Understanding CA&PA interrelationships in the QMS
- The CA&PA flowchart —implementing it in your QMS
  - CA&PA verification and validation
  - CA&PA effectiveness review
  - CA&PA records — opening, closing and managing the records effectively
- Tips, tools and techniques for complaint analysis; what should you be looking for?

Exercise – Analyze complaints as quality data to identify quality problems

10:15 a.m. – 10:30 a.m. | BREAK

10:30 a.m. – 12:00 p.m.

Part H – Design Changes

- Understand the role of change in the design control system
- Design change interrelationships —the five important considerations
  - When a production change is a design change
  - Does the design change create a new Device Identifier?
  - Does the design change require an updated 510(k)?
  - Does the design change impact the Risk Management File?
  - Is the design change an enhancement or a recall?
- The design change flow chart shows the picture
- Design change records —tips for maintaining the Design History File (DHF)

Exercise – Classify changes as a design change or a production process change

12:00 p.m. – 1:00 pm | LUNCH BREAK

1:00 p.m. – 2:30 p.m.

Part I – 510(k) Changes

- When a design change requires a pre-market notification change
- 510(k) change process interrelationships
- 510(k) change records and reports
- FDA's 1997 guidance document — 17 years old, but still applicable today
- The 2012 law and FDA's plan — what's the latest and what's on the horizon

Exercise – Analyze design changes to determine if they require a revised 510(k)

2:30 p.m. – 2:45 p.m. | BREAK

2:45 p.m. – 4:30 p.m.

Part J – Corrections and Removals (C&R)

- Defining the terms — a source of constant confusion
- Understanding how the C&R regulations relate to the QMS
- Distinguishing enhancements from recalls – the FDA guidance and its theory
- C&R records and reports — distinguishing between the requirements
- Overview of the integrated system and how to make it work for you
- Bringing all the pieces together — best practices for building C&R procedures that work
- The link between C&R reports and recalls
- Recalls caused by suppliers

Exercise – Evaluate proposed field actions to determine if they are a correction or a removal

4:30 p.m. | ADJOURN WORKSHOP

It was a very methodical approach, enjoyed the examples."

—Randall Lenz, CQT Consultant / QE, Stryker Instruments

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1. **FDA Inspection Level —** FDA investigators plan the extent of their inspections based on the levels in the Program Compliance Guide. This exercise provides participants an opportunity to apply these ideas and understand the factors that determine the depth of the inspection.

2. **QSIT Sampling Plans for Records —** When an FDA investigator asks for records, the number reviewed is determined by a sampling plan in QSIT. This exercise explains how the investigator classifies the records and estimates the error rate. It is not Z1.4 acceptance sampling.

3. **Creating a New Device Identifier —** The UDI regulations require manufacturers to create Device Identifiers (DI) for each version or model as well as Device Identifiers for each packing level. They must be included in the complaint records, Medical Device Reports, and Correction & Removal files. This exercise helps participants understand when a change creates a new Device Identifier (DI).

4. **Analyze a Small Set of Service Records Using Quality Tools —** 820.200 requires manufacturers to analyze service records using statistical techniques applicable for data analysis in 820.100. In some cases, servicing, complaints and MDRs are tightly coupled. This exercise introduces a small data set and gives participants an opportunity to apply techniques.

5. **Analyze Customer Reports to Determine If They Are a Complaint and Potentially Reportable —** The definition of complaint in medical device regulations is technical, and requires analysis to determine when a report alleges a "regulatory complaint". In addition, complaints must be evaluated to determine which ones could lead to a Medical Device Report. This exercise provides examples that help participants distinguish among the various cases.

6. **Initiate a Medical Device Report —** In the US, some complaints are reported to the FDA as a Medical Device Report. This exercise uses an example problem and offers participants an opportunity to see how the information relates to the fields in the MDR form.

7. **Analyze an Adverse Event to Determine When to Report —** In the EU, some are reported using the Manufacturer's Incident Report form from MEDDEV 12.2-1 on the Vigilance System. This exercise uses an example problem and offers participants an opportunity to see how the information relates to the fields in the MDR form.

8. **Analyze Complaints as Quality Data to Identify Quality Problems —** Medical device manufacturers expect to receive complaints at some rate. The manufacturer must track the rate for different kinds of complaints, for risk management post-market surveillance and for EU vigilance reporting. This exercise provides an opportunity for participants to determine a baseline rate, a trigger point, and determine if the rate is still acceptable.

9. **Classify Changes as a Design Change or a Production Process Change —** QSIT informs the FDA investigator that Production and Process Changes could be Design Changes. This exercise provides participants an opportunity to classify changes and provides insight into the decisions to make in the QMS.

10. **Analyze Design Changes to Determine If They Require a 510(K) —** Every design change for a 510(k) device must be evaluated to determine if it is significant enough to update the 510(k). This exercise provides some situations for participants to analyze.

11. **Evaluate Proposed Field Actions to Determine If They Are a Correction or a Removal —** Whenever a manufacturer changes a product in the field, there must be an evaluation to determine if the change is a correction or a removal. In addition, there must be an evaluation of reportablility. This exercise provides practice in making those evaluations.

ABOUT YOUR INSTRUCTOR

Dan O'Leary

Dan O'Leary is President of Ombu Enterprises, LLC, an education, training and consulting company focusing on Operational Excellence using analytical skills and a systems approach to operations management. Dan has more than 30 year's experience in quality, operations and program management in regulated industries, including aviation, defense, medical devices, and clinical labs. He holds a Masters Degree in Mathematics; is an ASQ certified Biomedical Auditor, Quality Auditor, Quality Engineer, Reliability Engineer and Six Sigma Black Belt; and is certified by APICS in Resource Management.

Ombu Enterprises, LLC

Ombu works with manufacturing companies, offering training and execution in operational excellence. Focusing on the analytic skills and systems approach of operations management, Ombu helps companies achieve efficient, effective process and regulatory compliance.

"Very informative and could pull documentation in support of information provided. I have high confidence in the information he provided. Great up to date information. I liked asking specific questions and getting his opinions."

—Linda Todd, Sr. Post Market Surveillance Analyst, Spectranetics

"Dan is a wealth of knowledge in regards to all aspects of medical device regulations."

— Kanan Bhavsar, PV Clinical Trial and Drug Safety Specialist, Merck

COURSE BINDER MATERIALS

- Full slides from the PowerPoint presentations
- A copy of each interactive exercise worksheet as well as answer keys
- An annotated version of MDR sections regulation based on recent Warning Letters
- An Excel worksheet that helps analyze the FDA regulations. It has a series of questions that start with a complaint and follow the reporting and record keeping decisions to help understand the integrated requirements spread across different parts of the regulations.
- Reference documents:
  - FDA guidance on Medical Device Reporting
  - FDA draft guidance on Medical Device Reporting
  - Comparison of MDR Rule Changes
  - FDA guidance on Enhancements and Recalls
  - Comparison Part 7 and Part 806 definitions
  - FDA guidance document on 510(k) changes
  - MEDDEV document on the Vigilance System
  - Health Canada document on Medical Device Problem Reporting

WHO SHOULD ATTEND

- Quality Managers
- Regulatory Affairs Managers
- Engineering Managers
- Quality Engineers
- Design Engineers
- Project Managers involved in design and development
- Specialists assigned to complaints, corrective actions or medical device reporting
- Recall coordinators
- Medical staff evaluating risk, safety or effectiveness
- General/corporate counsel

The materials are excellent and a great handout to be used in any organization. Dan really put a lot of work into the materials and workshop."

— Cheryl Landrum, Quality Analyst, Kimberly Clark

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