Industry: 510(k) Guidance Should Not Usher in New Data Requirements

Industry groups are warning the FDA that its draft guidance on risks versus benefits in 510(k) submissions could trigger new requirements for clinical trials that are inconsistent with the premarket notification process.

Under the proposed guidance, the FDA would assess the benefits and risks of 510(k) candidates both individually and against those of the predicate device. The guidance is aimed at 510(k) devices with different technological characteristics than the predicate.

But in comments on the draft, the Medical Device Manufacturers Association says the agency must ensure that it doesn’t lead to requests for data beyond that typically required for 510(k) devices.

Participants in Single-Audit Pilot Unlikely to See Warning Letters

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 the issues pose an immediate threat to public health. Meanwhile, Canada is adding additional pressure, announcing that as of 2016, any companies 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 (D&DL, Sept. 12).

But Kimberly Trautman, associate director of international affairs at CDRH 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 a Thursday meeting.
FDA Grants Class II Status to IVDs For Mycobacterium TB Complex

The FDA issued a final rule Wednesday placing nucleic acid-based IVDs for the detection of Mycobacterium tuberculosis complex in Class II with special controls. The rule also covers use of the tests to detect genetic mutations associated with MTB complex antibiotic resistance in respiratory specimens.

The tests help with diagnosing pulmonary tuberculosis and determining initial treatment and, as such, carry certain risks, the agency notes. These include false positives, false negatives and biosafety risks to healthcare workers who handle specimens and control materials.

According to the rule, sponsors should use an external positive-assay control and internal controls, as appropriate. External controls may include MTB complex isolates with at least one antibiotic resistance-associated target sequence detected by the device. Internal controls may include human nucleic acid co-extracted with MTB complex-containing nucleic acid sequences associated with antibiotic resistance and primers amplifying human housekeeping genes.

The intended use section of the labeling must specify the drugs or drug classes targeted by the assay, the FDA says. The performance characteristics section should discuss the specificity of the assay oligonucleotides for detecting mutations associated with antibiotic resistance of MTB complex, as well as information on the potential for nonspecific binding.

Companies that use frozen samples in performance studies or claim their product can be used with frozen samples must evaluate the effect of freezing samples prior to testing and the effect of multiple freeze/thaw cycles.

Nucleic acid extraction methods must match those used for the detection of MTB complex nucleic acid and show that detection of any genetic mutations associated with antibiotic resistance will not be affected.

Analytical studies should evaluate the limit of detection, analytical reactivity and within-laboratory precision testing.

Sponsors should determine the limit of detection in the most challenging matrix claimed for use with the device, using both antibiotic-susceptible and antibiotic-resistant strains of MTB complex.

Reproducibility Studies

For analytical reactivity, testing should evaluate the device’s ability to detect genetic mutations associated with antibiotic resistance in a variety of MTB complex strains. Within-laboratory precision studies, if appropriate, must include at least one antibiotic-resistant and one antibiotic-susceptible strain of MTB complex.

The protocol for the reproducibility study can vary slightly with assay format, but the panel must include at least one antibiotic-resistant and one antibiotic-susceptible strain of MTB complex.

Sponsors should use prospective studies of patients with active TB to establish the clinical performance of these IVDs, the FDA says. Studies must try to enroll subjects at risk for antibiotic-resistant MTB complex, but may need to include supplemental antibiotic-resistant retrospective and contrived samples, the agency adds.

Clinical studies should compare results with both phenotypic drug susceptibility testing and genotypic reference methods. The genotypic reference method must be a polymerase chain reaction-based method and use different primers than those in the experimental device.

The rule was prompted by a June 2013 request from Cepheid for de novo classification of its Xpert MTB/RIF Assay. The FDA determined the device can be safely regulated in Class II with special controls.

In addition the controls outlined in Wednesday’s rule, the FDA refers devicemakers to the Class II special controls guideline, Nucleic Acid-Based In Vitro Diagnostic Devices for the Detection of Mycobacterium tuberculosis Complex and Genetic Mutations Associated with Antibiotic Resistance in Respiratory Specimens.

— April Hollis
CMS Proposes Limited Coverage Of Prolaris Prostate Cancer Test

The Centers for Medicare & Medicaid Services is willing to pay for Myriad Genetics’ Prolaris prostate cancer test via a local coverage determination proposed by a South Carolina Medicare contractor. The LCD would let a specified subpopulation of cancer patients receive the test while CMS considers broader coverage.

Under the LCD, Medicare would cover the genomic assay for prostate cancer patients who are considered to be at low risk or very low risk and who are expected to live at least 10 years. The patient must be weighing whether to have conservative treatment or more definitive therapy, such as prostectomy, the LCD notes. Prolaris’ results can be used to determine which type of treatment is most appropriate.

The most commonly used type of prostate cancer test determines severity of disease by looking at the blood level of a tumor-related antigen, but this technique has been criticized for the number of false positive results it yields. By contrast, Prolaris analyzes 46 genes to determine prostate cancer risk.

The LCD was cleared through Palmetto GBA’s molecular diagnostics pilot program and ensures some coverage of Prolaris pending a national coverage decision by CMS, says Myriad spokesman Ron Rogers.

If the LCD is successful and ongoing clinical trial data shows good results, Medicare could expand coverage in 2015, Rogers says. Myriad is seeking an indication for use that would cover all men with localized prostate cancer, regardless of risk status.

Physicians ordering the test must be certified in a Prolaris Certification and Training Registry and monitor patients for disease progression. Myriad must update the CMS every six months on physicians enrolled in the registry and inform the agency of metastasis or prostate cancer death in patients who were deemed low risk by the assay.

About 233,000 men in the U.S. are diagnosed with prostate cancer each year, and 29,000 succumb to the disease.

Prolaris was cleared for marketing under CLIA requirements in 2012 and has been used more than 3,500 times, according to Rogers.

Comments on the LCD may be submitted to CMS from Nov. 10 until Dec. 25. View it at www.fdanews.com/10-27-14-prolaris.pdf. — Elizabeth Orr

FDA Told to ‘Fix’ Vulnerabilities In Information Technology Network

Weaknesses in the FDA’s IT network security could allow hackers to gain access to confidential trade secrets, an HHS audit finds.

While auditors working for the Office of Inspector General were unable to hack into the agency’s network during a test conducted last year, the OIG found several weaknesses that make the agency’s networks vulnerable to cyber-attacks.

One of the most glaring concerns was that the FDA only performed security testing on one out of seven external systems. OIG did not try to hack those systems, which are not named, because the agency deemed them “mission critical” and didn’t want them to go offline.

The office did, however, find vulnerabilities in one system it did review. That system also was not named, but it is one of the FDA’s web portals for receiving submissions.

One problem, according to the eight-page report, was that error messages displayed to users submitting regulatory information were far too detailed. Hackers can glean useful information from error messages, such as the software version or application code, and use that data to launch specific attacks against a network, OIG warns.

The FDA’s systems also have been lax in securing sensitive documents about some software programs. For example, software often is accompanied by demonstration programs that show how they’re used (See FDA IT, Page 4)
submissions. “It is critically important that FDA continue to implement 510(k) requirements in a manner that is consistent with the ‘as safe as’ standard,” the group says.

MDMA is concerned that the guidance could become a “back door” for reassessing device classifications of products previously cleared via the 510(k) process (D&DL, July 18). The group notes, for instance, that the guidance frequently references clinical data without clarifying that these factors are only considered when clinical data is provided in the submission.

The agency’s “misplaced focus on the total device violates Congress’ clear intent for the 510(k) review process ... and it contradicts FDA’s stated position that the Draft Guidance ‘does not change the 510(k) premarket review standard,’” the association says.

MDMA also asks the agency to clarify how surrogate endpoints will be used in benefit assessments and recommends less focus on clinical data in assessing magnitude of benefit. Use of literature and expert clinical reviews in benefit assessments should also be clarified, the group says.

In separate comments, AdvaMed takes the agency to task for not giving “sufficient prominence” to nonclinical data. “Future reviewers may reach the conclusion that clinical studies are the primary means for evaluating product risk and benefit when there are technological changes,” the group warns. AdvaMed notes four of seven 510(k) examples provided in the guidance contain clinical data.

The Minnesota Medical Device Alliance goes even further in criticizing the draft guidance, calling it an “abomination” that “results in an illegal construction of the 510(k) program.”

Writing on the alliance’s behalf, Mark DuVal, principal of DuVal & Associates, says the guidance, as drafted, would allow the FDA to request any information it wants on a 510(k), introduce new concepts that are not appropriate for the 510(k) program, such as risk/benefit, risk mitigation, consumer and physician preference, and human factors, and lead to complex, irrelevant questions during reviews, making it more difficult for devicemakers to get products cleared.

If finalized, the guidance, would also take the decision of which devices are best for patients out of the hands of healthcare providers, serving as a form of cost control, Du Val adds. — April Hollis

**510(k)s, from Page 1**

The FDA also failed to lock out a user after multiple failed login attempts, in violation of federal policy, the report says. Without this limit, a hacker could repeatedly try to enter various user names and passwords until they find the right one.

Another concern: The FDA did not check the validity of all user-supplied data entered into its systems. The validation check ensures that a hacker hasn’t installed malicious programs, OIG says.

The inspector general’s recommendations are intentionally vague, given the sensitive nature of the information. The office urges the FDA to “fix the web vulnerabilities identified, implement more effective procedures to protect its computer systems from cyber-attacks and periodically assess the security of all of its internet-facing systems.”

The FDA says it has put in place new measures to correct the problems. OIG say it will follow up with the agency in the near future to ensure its remediation activities are working.

A request to the FDA for further comment on the findings was not returned by press time.

To read the report, visit www.fdanews.com/10-20-14-OIGReport.pdf. — Robert King
Australia to Accept 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 CE mark certificates issued by European notified bodies, under a government action plan introduced this month.

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.

Creation of ‘Growth’ Centers

Also envisioned in the 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. 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 Prostèse breast implants, which passed a TGA conformity assessment despite containing industrial-grade, rather than medical grade, silicone (D&DL, Nov. 4, 2013).

Read the government’s report on innovation and competitiveness at www.fdanews.com/10-14-AustraliaReport.pdf. — Jonathon Shacat

J&J Wins Texas MoM Hip Case

A federal jury in Dallas, Texas, on Thursday ruled in favor of Johnson & Johnson’s DePuy division in the first bellwether trial concerning the Ultamet metal-on-metal hip joint replacement. The claim was one of 6,000 involved in multidistrict litigation alleging that the design of the Ultamet hip can cause bits of metal to rub off and disperse into the bloodstream. The problem can lead to bone and tissue death and repeated surgery (D&DL, Sept. 26). J&J said it will continue to fight future trials in the multidistrict lawsuit.

Dexcom CGM Device Approved

The FDA has approved the Dexcom SHARE, the first remote mobile communications device used for continuous glucose monitoring. The SHARE is an accessory to the Dexcom Monitoring system and uses a secure wireless connection to transmit a diabetic’s glucose levels to up to five designated

(See Briefs, Page 8)
MDSAP, from Page 1

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.”

To date, two MDSAP audits have been performed, with positive feedback from both companies and inspectors, according to Trautman. The device-makers 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.

Brazil’s Anvisa will take over the MDSAP chairmanship in 2015. — Elizabeth Orr
Health Canada to Require Labeling With Device Licensing Applications

Devicemakers seeking authorization to market Class II products in Canada will need 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.

Sponsors of devices that contain nanomaterials 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.

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 D&DL. “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.

Comments on both 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. — Jonathon Shacat

FDA Urges Outside Collaboration To Tackle Device Cyber Threats

Action is needed to protect medical device security, but industry — not the FDA — should be at the center of that effort.

That was the word from William Maisel, CDRH’s deputy director for science, during a public workshop on collaborative approaches for medical device and healthcare cybersecurity in Arlington, Va.

“There are more than a hundred thousand FDA-regulated devices,” Maisel said. “It’s not a viable solution for us to be the keeper and arbiter of taking in vulnerabilities and passing them on to the community.”

Maisel said a “different ecosystem” is needed where such information can be shared.

While panelists agreed on the need for a consensus on cybersecurity, there were few concrete ideas about how it might look. Carlos Kizzee, a deputy director in HHS’ Office of Cybersecurity and Communications, suggested that outside groups, such as Industry associations, build a third-party aggregator that could gather and republish valuable cybersecurity information. The service might allow for anonymous reporting, similar to one used by the avionics industry, others said.

Questions also cropped up about what types of information should be shared, how, and with whom.

(See Device Security, Page 10)
Briefs, from Page 5

recipients at remote locations. The device uses Blue-
tooth technology and an Apple iPhone/iPad app.

Steris Pays $1.9B for Synergy

Infection control company Steris announced
plans to pay $1.9 billion for outsourcing company
Synergy. The deal will allow Steris to offer more
comprehensive options to devicemakers, pharma
companies and hospitals, CEO Walt Rosebrough
said. As part of the terms of the acquisition,
Steris will relocate its headquarters to Synergy’s
UK offices, allowing its tax rate to drop from 35
percent to 25 percent. New U.S. Treasury rules
on this type of deal, known as an inversion, were
announced last month (D&DL, Sept. 26).

BSX Legal Reserves Near $1 Billion

Boston Scientific has squirreled away a total
of $945 million to pay future legal expenses,
company CFO Dan Brennan revealed during a
Wednesday investor call. The litigation reserve
grew by $139 million over the course of the third
quarter of 2014, dwarfing BSX’s cash on hand of
$236 million. The company faces multiple lawsuits
on issues including a $1.5 billion tax dispute with
the IRS, product liability lawsuits involving pelvic
mesh and a challenge by Johnson & Johnson on
Boston Scientific’s 2006 acquisition of Guidant.

AZBio Chief to Chair AdvaMed Group

Joan Koerber-Walker, president and CEO of
the Arizona Bioindustry Association, has been
named head of Advamed’s State Medical Tech-
nology Alliance. The alliance is a consortium of
state and regional medical technology trade asso-
ciations that work to support best practices, pro-
mote the industry and lobby for policies favoring
healthcare innovation. Koerber-Walker replaces

DG SANCO Retains Oversight of Devices

The incoming head of the European Commiss-
ion, Jean-Claude Juncker, has acceded to indu-
try and political pressures and will keep over-
sight of medical devices in the health directorate.
In September, Juncker proposed moving medtech
to the industry directorate. On Wednesday, the
European Parliament confirmed Lithuanian phy-
sician and Social Democrat Vytenis Andriukaitis
to lead the health directorate, replacing outgoing
commissioner Tonio Borg.

Managing Effective CAPA Systems

Recently released from FDAnews, Managing Effective CAPA Systems is the industry’s most authoritative guide on build-
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Devicemaker Warned on Averaging Supplier Quality, Delivery Ratings

Western Enterprises/Scott Fetzer Company received an FDA warning letter after averaging its suppliers’ quality ratings with its delivery ratings, resulting in a higher overall rating for some suppliers.

The practice means a supplier’s quality rating could be as low as 60 percent and still be acceptable, according to the Oct. 10 warning letter published recently online.

In August 2013, one supplier’s quality rating was 66.7 percent, but its delivery rating was 100 percent, making its overall rating for the month 83.3 percent. This is considered acceptable by the company, the letter says, adding “no further action was taken regarding the quality issues with this supplier.”

The Westlake, Ohio, company makes medical gas pressure regulators and suction regulators.

Western also failed to investigate suction regulator bodies that were received from a supplier with “dents and dings that can cause leakage when assembled.” No supplier corrective action request was issued and “the regulators were just returned to the supplier,” the letter says.

The warning letter followed a July 10 through Sept. 2 inspection by the FDA’s Cincinnati district office.

Several of Western’s suppliers lacked a self-survey or current registration certification, which the company’s procedure requires. Meanwhile, the firm did not treat test labs and consultants as suppliers, as required by the procedure. “As a result, you have not ensured the received services conform to specified requirements,” the warning letter says.

The FDA also critiqued the company’s customer complaint procedure. On April 21, Western learned of a complaint involving an “ignition” event with a medical gas pressure regulator that it contract manufactures. However, the information wasn’t entered into the complaint system until July 25, during the inspection.

The procedure also fails to address reviews and updates to product risk analyses based on postmarket data. For example, the three risk analyses for the OxyTOTE regulators weren’t updated after the complaint involving the ignition event.

The failure investigation for that complaint was deemed inadequate as well. An outside laboratory performed the investigation and recommended further chemical and/or metallurgical analysis to shed light on the origin, ignition mechanisms and propagation characteristics. But “you closed this complaint without any further testing and there was no documented rationale as to why this testing was not needed,” the letter says.

Validation, CAPA Issues

The investigator also found issues with Western’s process validation procedure. According to the procedure, established processes that have “historically provided acceptable output without significant nonconformities” don’t need to be validated.

“There is no documented rationale as to why the four product families, which were being manufactured prior to 2011, have no processes that need to be validated,” District Director Paul Teitell writes. He notes that the products involve processes — such as cleaning, lathing, milling, deburring and plating — that would require validation.

Meanwhile, Western’s corrective and preventive action procedure fell short. Among issues cited by the investigator were:

- Only the top six complaint failure codes listed in a Pareto Analysis Report are evaluated to see if a corrective action is needed;
- Only the top six failed final inspection codes for each product listed in trending analysis reports are evaluated to see if a corrective action is needed; and
- Scrap is not documented and analyzed as a data source.

The company did not respond to a request for comment by press time. The warning letter is available at www.fdanews.com/10-21-14-Western.pdf. — April Hollis
Device Security, from Page 7

Intellectual property concerns are a serious concern for devicemakers, said Jeffrey Secunda, AdvaMed’s vice president for technology and regulatory affairs. While it’s important to identify security risks that are common across multiple systems, it’s often not clear whether the vulnerability arises from the shared code or from something proprietary to the manufacturer, he explained. “It’s hard to have a meaningful collaboration in an environment where it’s unclear what other people are doing and what’s relevant.”

In other industries, outside groups have been able to ease IP worries by breaking down types of information into distinct subcategories that help companies understand what they’re sharing and with whom, said Deborah Kobza, executive director of the National Healthcare Information Sharing and Analysis Center. Subcategories of cybersecurity threats for the device industry might include device-specific vulnerabilities, cross-sector implications and protocols affected by the threat, she said.

Improve Industry Standards

But Secunda questioned whether it was fair to compare the threat of cyber-attacks on devices with those facing other industries, such as financial services. While researchers have found numerous vulnerabilities, very few are being exploited in the field, he said.

Secunda suggested improving industry standards on cybersecurity as an initial step toward ensuring manufacturers are comfortable sharing information.

Panelists also expressed concerns about the cost of securing devices from cyber-attacks. “We need to establish voluntary incentives for compliance, but we also don’t want to set a regulatory floor people can’t afford,” said Kizzee. “Whatever we design needs to be economically viable.”

Historically, that’s been a challenge for devicemakers, according to Rick Hampton, wireless communications manager for Partners HealthCare, who complained that the FDA “has everything tested until a $5 device costs $5,000.” But he doubts hospitals or health IT companies will fund cybersecurity fixes if they don’t have to.

Marty Edwards, assistant deputy director of the Department of Homeland Security’s National Cyber and Communications Integration Center, disagreed. “Every time we do an incident response, the comment across the board is that it cost an order of magnitude more to clean up than it would have [cost] to invest in the security in the first place,” he said.

Maisel encouraged devicemakers and customers who detect cybersecurity issues to alert the FDA through the MAUD database or send the information directly to Suzanne Schwartz at suzanne.schwartz@fda.hhs.gov.

The meeting was called to address a perceived growing threat to device security. The FDA finalized guidance on the topic several weeks ago (D&DL, Oct. 3). — Elizabeth Orr
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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

Visit www.CAPAworkshop.com or call (888) 838-5578
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

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.

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