DRUG GMP REPORT™

Issue No. 270
January 2015

INSIDE THIS ISSUE

Drugmakers Win Four-Month Reprieve From Product Tracing Requirement

The FDA has pledged to delay enforcement of key elements of its new track and trace regulations for drugmakers, promising that until May 1 it will take no action against companies that do not capture and transmit product information.

Drug supply chain trading partners such as manufacturers, wholesale distributors and repackagers initially had been required to start capturing and passing on details about their products on Jan. 1. However, in guidance published Dec. 24, the FDA says firms along the supply chain that don't capture and pass on product history and other information during the first four months of this year will not face any sanctions.

The decision stems from industry concerns that some parties in the supply chain aren't ready to comply with the track-and-trace

(See **Guidance**, *Page 4)*

FDA Quality Metrics Program Delayed, Extended to Biologic Products

The FDA's quality metrics collection program is facing delays as the agency expands it to include biologics manufacturers in addition to drugmakers.

The agency this fall announced it planned to select metrics by the end of the year, and start collecting data on them by fall of 2015. But now officials say they have no timeline on implementation.

In another wrinkle, agency officials said they will give manufacturers a two-year grace period to comply with the reporting requirements as opposed to the one-year period it initially planned. Once the metrics are finalized, data collected during the grace period could be used for positive actions, such as fewer inspections for a high-quality facility, but won't drive enforcement decisions.

Including biologics manufacturers poses several hurdles. While CDER will apply the quality metrics programs to all manufacturers,

(See **Delay**, *Page 8)*

New Quality Office Among Top 2015 CDER Priorities

Setting up the new pharmaceutical quality super office is among the roughly dozen top priorities for CDER in 2015.

CDER Director Janet Woodcock outlined the office's 2015 plans last month in an internal presentation given to agency staff, and many are continuations of projects started in 2014.

Starting up the Office of Pharmaceutical Quality (OPQ) on Jan. 11 is a top-tier priority, Woodcock said. Particularly important for OPQ, which will be the office in charge of all drug safety issues, will be implementing its manufacturing metrics collection program to evaluate the quality status of all drug facilities selling into the U.S.

Another key priority in the quality realm will be integrating the Office of Regulatory Affairs' pre-approval facility inspections into the OPQ team review so that drug manufacturers receive more standardized quality assessments, she said.

Additional front-burner priorities include reexamining agency policy on drug advertising and promotion, which comes in light of the 2012 *Caronia* decision in the U.S. Second Circuit that found off-label promotion was protected by free speech, participating in the 21st Century Cures Congressional roundtables to shape future drug regulation, responding to the Ebola outbreak and filling more than 600 job vacancies at the agency.

Other priorities include addressing the ANDA backlog and finalizing 2013 guidance on the development and labeling of abuse-deterrent opioids. Ongoing priorities for CDER include continuing to meet the goals of PDUFA and reducing the freedom of information request backlog.

See the presentation here: www.fdanews.com/12-19-14-CDER-2015-Priorities.pdf.
– Bryan Koenig

Drug Import Oversight to be Consolidated by FDA

The FDA plans to consolidate its 16 districts overseeing pharmaceutical imports into either four or five districts under a reorganization plan that aims to make inspection policies and procedures more uniform, regardless of port of entry.

The consolidation is part of the agency's Program Alignment Group (PAG) initiative to reorganize investigators into specialized teams that will focus on individual product types — such as pharmaceuticals, devices or food — rather than on all FDA-regulated products generally.

It remains undecided how such product specialization will be addressed within import inspections, said Domenic Veneziano, director of the FDA's Division of Import Operations. Import operations, however, will remain in the Office of Regulatory Affairs (ORA), he told a Food and Drug Law Institute conference on enforcement, litigation and compliance.

Under the reorganization, CDER and ORA also plan to create a strategy by fall 2015 to speed up the way they screen imports by creating risk-based imports entry reviews that will allow the agency to identify adulterated products more quickly (*DGR*, November).

Veneziano told *DGR* he didn't know when the reorganization of FDA import operations will be finalized under the PAG plan, but he's confident the restructuring will make the agency more efficient.

One observer remains skeptical. The import district consolidation plan will create a more centralized bureaucracy, said Ben England, founder of FDAimports.com and a former regulatory counsel to FDA's associate commissioner for regulatory affairs. It represents a further paring back of inspector discretion and power at the local level, and could make it more complicated for industry to resolve import issues, he told *DGR*. — Bryan Koenig

Compounders Face Murder Charges over Poor Quality

The Justice Department has charged two people with murder and 12 others with serious crimes over alleged manufacturing violations at the New England Compounding Center (NECC) that led to 64 deaths due to meningitis and sparked a federal law to rein in large compounders.

According to the 73-page indictment, unsealed last month, from 2008 to 2012 the pharmacy allegedly disguised expired or expiring stock solutions by mixing them with current stocks and passing off the finished solution as an up-to-date product.

In addition, NECC employees allegedly shipped purportedly sterile drugs that were never tested or for which the results were unknown. When microbial growth was later discovered in sterility tests, NECC personnel did not call for a recall or alert physicians and patients of the microbial contamination, the indictment said.

Pharmacy personnel also skipped cleaning and disinfecting clean room suites to meet production schedules, and falsified cleaning logs, the indictment reads.

NECC owner and head pharmacist Barry Cadden and supervisory pharmacist Glenn Chin have been accused of 25 counts of second-degree murder in eight states, and would receive life sentences in prison if convicted on all counts, DOJ said. The indictment alleges the two knowingly distributed lots of methylprednisolone acetate that weren't properly sterilized or tested and verified for sterility. The remaining 12 individuals, including pharmacists and executives, were indicted on multiple counts of racketeering, mail fraud, conspiracy, contempt and violations of the FD&C Act.

Chin's attorney Stephen Weymouth told *DGR* that the charges were a blatant overreach, and he was shocked prosecutors believe Chin's behavior rises to the level of a criminal violation. Cadden's attorney Bruce Singal called the outbreak the result of a terrible accident, but not a federal crime.

All 14 individuals charged in the case made an initial appearance in federal court in Boston last month.

The DOJ took two years to bring criminal charges because of the complexity of the case, said Carmen Ortiz, U.S. attorney for Massachusetts. DOJ officials told *DGR* they could not say if this was the first time murder charges have been connected to a drug quality case.

Howard Sklamberg, deputy FDA commissioner for global regulator operations and policy, said the FDA has inspected more than 175 compounding facilities since the fall 2012 outbreak, resulting in recalls of compounded products for substandard conditions and shut down facilities, he added.

The outbreak also sparked Congress to create a new voluntary regulatory category for large compounders in the 2013 Drug Quality and Security Act to bring them under GMP rules.

Attorneys for the other NECC personnel did not return requests for comment as of press time. — Robert King

Chinese API Manufacturer Warned for Data Integrity

The FDA last month warned a Chinese active pharmaceutical ingredient (API) maker for data integrity violations, marking the agency's 13th warning letter to cite the issue out of 18 overall warnings issued for quality violations as of late December.

By contrast, last year, the agency cited data integrity problems in only seven out of 26 warning letters it issued for GMP violations. The figures only represent drug and API makers that received a warning letter for violating GMPs. A vast majority of the data integrity letters issued in both 2013 and 2014 were to international manufacturers.

The latest letter, released Dec. 30, warned Novacyl Wuxi Pharmaceutical for a slew of

(See **Data***, Page 4)*

Data, *from Page 3*

GMP and data integrity violations stemming from an October 2013 inspection of its Jiangsu, China, facility.

Investigators, for example, discovered that personnel had thrown away a chromatogram result for an API that was out of specification. The API manufacturer also didn't use separate passwords for each analyst's access to the laboratory systems, according to the Dec. 19 letter.

The letter is more evidence that the FDA is making good on its promise of raising data integrity to a high priority. One violation could cast doubt on the reliability of all data generated at a facility, officials have said. The FDA also has called on drugmakers to do a better job of reviewing data integrity practices of their suppliers (*DGR*, November 2014).

The focus on data integrity problems is expected to continue in 2015, especially with the FDA planning to conduct more international inspections.

Novacyl was not available for comment. To read the warning letter, visit www.fdanews.com/12-30-14-NovacylWarning.pdf. — Robert King

Guidance, *from Page 1*

requirements, and that unforeseen complications with the tracing requirements could disrupt the supply chain and impact patient access, the FDA says.

The reprieve mirrors concerns expressed by the Healthcare Distribution Management Association. In a Nov. 25 letter to the FDA, HDMA President and CEO John Gray asked the agency to exercise discretion in enforcing the requirements, noting that while most of the supply chain is ready, some firms would not be able to fully meet the obligations by Jan. 1.

Draft guidance published in November suggested a variety of ways drugmakers can track the data in print and digital formats, but the timing of its release gave firms little time to comply by the deadline. Still, the guidance contained no surprises and many companies had already begun to preemptively implement track-and-trace procedures based on common industry practices.

While industry will get a reprieve from the product tracing requirements, other elements envisioned under the 2013 Drug Quality and Security Act are slated to take effect as planned Jan. 1. These include illegitimate product verification and response and restricting business to authorized trading partners. Also still on schedule: a July 1 deadline for drug dispensers to meet the tracking obligation.

Last month, the agency released guidance on how distributors can submit annual reports to drugmakers on their licenses and any disciplinary actions taken by state or federal officers.

Reports of significant disciplinary actions must identify the type and final date the action was taken, as well as if it resulted in a revoked or suspended license or limited the ability of the facility to conduct drug-related business, according to draft guidance released yesterday on reporting requirements for wholesale distributors and third-party logistic providers.

Initial reports are due between Jan. 1, 2015, and March 31, 2015, for wholesale distributors, and from now until March 31, 2015, for third-party logistics providers. Subsequent annual reports must be filed during the first three months of each year, while disciplinary actions should be submitted within 30 days of final action.

Comments on the new draft guidance are due Feb. 9, 2015. Read the *DSCSA Implementation: Annual Reporting by Prescription Drug Wholesale Distributors and Third-Party Logistics Providers* here: www.fdanews.com/12-14-FDA-DSCSA-Guidance.pdf.

The guidance on the product information deadline extension, *DSCSA Implementation: Product Tracing Requirements — Compliance Policy*, can be read at www.fdanews.com/12-29-14-Track-and-Trace.pdf. — Bryan Koenig, Jonathon Shacat

FORM 483 INSIDER

GSK Biologicals Gets 483 For Persistent Mold Problem

GSK Biological's Belgium plants continue to have mold issues that led to a fresh Form 483 for the facilities.

The agency first cited vaccine production plants in Rixensart and Wavre, Belgium, in 2012 for poor prevention of mold in the manufacturing area. FDA visited the facilities again in September and October and did not find much improvement.

Since the 2012 inspection, there were 190 mold deviations that caused four batches to be rejected, according to the Form 483 with 20 observations.

GSK conceded in 2012 that leaks in one of the buildings could contribute to the mold issues and would upgrade the water systems impacted by the leaks.

However, leaks in various manufacturing buildings continue. Significant leaks were documented during the filling manufacturing area that could allow for the growth of molds, the FDA said.

The agency said it found 118 manufacturing equipment and tank leaks during various vaccine manufacturing processes such as aseptic processing that could result in contamination.

GSK said it responded to the FDA and is addressing the concerns.

To read the Form 483, visit www.fdanews.com/12-30-14-GSK483.pdf.

Lax Water Testing Lands Generic Drugmaker 483

High Chemical Company's stalled investigation into color changes of its generic products and use of dirty water resulted in a Form 483.

The company's Levittown, Pa., facility was inspected by the FDA in September. The agency found that High Chemical, a division of National Generic Distributors, didn't properly test its distilled water.

Investigators found that three out of eight receipts of distilled water in the past two years failed total organic carbon testing but were released and used in production in any case.

The agency also found that an investigation into a color change and appearance failure for a finished product lot wasn't completed. The lack of investigation was first cited during a 2012 inspection, however samples of the drugs weren't provided to a laboratory for analysis until June 2014.

The investigation remains in progress so no preventive action has been taken, said the form with eight observations.

The agency also found High Chemical didn't check the reliability of a supplier's certificate of analysis for raw materials at appropriate intervals.

High Chemical did not return a request for comment as of press time.

The Form 483 can be accessed at www.fdanews.com/12-30-14-HighChemical483.pdf.

Poor Validation of APIs Result in 483 for Manufacturer

A Japanese active pharmaceutical ingredient manufacturer received a Form 483 for poor validation of its manufacturing methods and supplier controls.

During a September inspection of Ishihara Sangyo Kaisha's Yokkaichi, Japan, facility, the FDA found problems with the facility's procedures.

Ishihara didn't show that it properly validates the production process and testing methods used in the manufacturing of APIs, according to the Form 483 with three observations.

The FDA also chided the API manufacturer for lax supplier controls. The written procedure for auditing raw material suppliers doesn't explain the requirements a supplier must meet in order to be acceptable, the agency said.

Ishihara could not be reached.

To read the Form 483, visit www.fdanews.com/12-30-14-Ishihara483.pdf.

FDA Considers New Inspection Scoring System

The FDA is considering a new inspection scoring system that would for the first time recognize drugmakers that go beyond normal compliance with good manufacturing practices.

The system, which hasn't been finalized, would offer drugmakers six scores: critical failure, major failure, minor failure, acceptable, exceeds and superior. Drugmakers would receive a score for each aspect of an inspection, including whether a facility meets GMPs, has an adequate quality system and quality culture.

The proposed system is part of an inspections protocol project that is intended to revamp the inspection process so CDER gets a better idea of a facility's state of quality.

The scores would be given in addition to the traditional overall classifications: no action indicated, voluntary action indicated and official action indicated, Neil Stiber, CDER senior operations research analyst, told *DGR* after a session at the Parenteral Drug Association's quality metrics conference last month.

Scores to Provide More Information

The scores are intended to provide more information to drugmakers than the broad classifications, and won't interfere with the process for levying enforcement actions such as Form 483s, Stiber said. The scores also wouldn't directly translate into an inspection classification such as NAI, OAI or VAI.

Inspection classifications depend on many factors, including prior issues, drug availability and how well the facility responded to problems previously, he said. Those issues will still help determine the inspectional outcome.

A goal of the scoring system would be to recognize manufacturers that go beyond meeting agency regulations and GMPs. The scoring system would also provide more specific feedback on inspection results than the broad, overall classifications, Stiber said.

Any score also would be in addition to the upcoming ranking that a facility will receive based on a series of quality metrics. The rankings will be used to compare manufacturers to the rest of industry and determine inspection frequency.

Stiber declined to comment on when CDER will make a decision on the scoring system.

Agency officials have offered details on other parts of the inspection protocol project. Next year, for example, CDER will conduct an internal pilot wherein investigators will be trained to examine a facility's quality culture for the first time. — Robert King

FDA Shoots Down Drone Speculation

The FDA wants everyone to know that it doesn't have a drone program in place, nor is it exploring the technology for inspections or surveillance.

The agency sought to downplay reporting by *DGR* and other media outlets on a test of unmanned aerial drone technology that had been scheduled last month at the FDA's White Flint office. That test was postponed due to technical issues.

Word of the drone test came from an email sent to D.C.-area employees, the FDA acknowledged. The email spoke of looking into drones for research and development in manufacturing site inspections, farm inspections and land area inspection surveillance.

However, the test was meant purely for research and development purposes on emerging technologies, the FDA said. It added: "The agency is not considering the use of drone technology in connection with inspections or surveillance."

The postponed test had been planned by the FDA's Office of Informatics and Technology Innovation under Chief Health Informatics Officer Taha Kass-Hout. — Bryan Koenig

FDA Laid Foundation in 2014 For Massive Inspections Overhaul

In 2014 the FDA laid the groundwork for an unprecedented overhaul in the next few years in how the agency will measure pharmaceutical quality and conduct inspections. This is a look back at 2014 and the year ahead.

Last year, CDER laid out plans for the creation of its new quality "super office" that starts running this month. The Office of Pharmaceutical Quality (OPQ) combines all of the center's quality functions and is led by CDER Director Janet Woodcock.

OPQ takes over responsibility for preapproval and postmarket inspections from the Office of Compliance. Agency officials have said drugmakers will be able to learn of potential quality problems much earlier in the review cycle.

One of the biggest changes expected to start this year is team-based inspections of drugmakers rather than by a single investigator. The team will likely include microbiologists, chemists and other experts to thoroughly review a facility.

Currently teams are only utilized in more complex manufacturing facilities, but the agency plans to broaden team-based reviews to every drug manufacturing facility.

The agency will start a pilot program this year to evaluate the team-based approach.

The number of investigators isn't the only thing that is expected to change. FDA unveiled a broad plan last fall outlining the steps it will take in 2015 to create a more specialized inspectorate.

In the next few years, drugmakers could be inspected by experts in drug formulations and dosage forms. By contrast, under the current system, an investigator may inspect a drug manufacturing facility one day and a food production facility the next.

The shift could mean fewer frivolous or erroneous 483 observations for drugmakers since pharmaceutical experts will be inspecting facilities, experts said.

When those teams of investigators arrive at a facility, the company should be ready to allow them to take as many photographs as they want. This past fall the agency finalized guidance that explains what constitutes delaying, denying or limiting an inspection. The guidance keeps intact a controversial position that investigators have the right to photograph any area of a facility during an inspection.

Industry complained to no avail that the provision could enable trade secrets to get photographed.

Metrics Program Delay

The agency did not make progress on all of its new quality programs last year, however.

CDER had planned to release guidance by the end of 2014 outlining eight to 10 quality metrics the agency would collect from drugmakers by the end of this year.

However, no guidance was released and agency officials have not offered any timeline on when the metrics program will begin. The delay announced last December came roughly the same time the agency announced that CBER will participate in the metrics program.

The agency did say it will give manufacturers time to set up systems to collect the metrics. Manufacturers will have a two-year grace period wherein data collected during that time won't drive enforcement decisions. However, the data could be used to support fewer inspections for a high-quality facility.

Including biologics manufacturers poses several hurdles. While CDER will apply the quality metrics programs to all manufacturers, CBER will apply it selectively. Center officials are still deciding which product categories will be affected.

More details are expected to emerge this year on quality metrics and the inspectorate reorganization. — Robert King

EU Bans Ranbaxy's Injectable Antibiotic

The European Union has banned imports of Ranbaxy's injectable antibiotic cephalosporin following an inspection by German regulators who found the company's Dewas, India, facility was not in compliance with GMPs.

Germany's noncompliance report, issued late last month, stems from a June 27 visit to the plant that uncovered deficiencies with the operation of cleanrooms and the sterilization of equipment.

The ban does not require the EU to recall products already delivered to EU states from the plant. The remaining areas at the Dewas site have been found to be compliant with GMPs, the European Medicines Agency told *DGR*.

Ranbaxy said it discontinued production of injectable cephalosporin after the June inspection, but that its decision was made prior to the visit. Discontinuing the product is not expected to have a significant impact on business, Ranbaxy told *DGR*.

Since the inspection, Ranbaxy's facilities in Dewas have received EU approval for manufacturing dosage forms and active pharmaceutical ingredients, including oral cephalosporin, the company said.

The Dewas facility is one of five Ranbaxy plants that the FDA cited for GMP violations and subjected to a 2012 consent decree that prohibits the manufacture of products for the U.S. market. — Jonathon Shacat

---

Delay, *from Page 1*

CBER director of compliance Mary Malarkey said the center will apply the metrics program selectively, and it is now deciding which categories of products will be involved.

Once the CBER selection process is complete, CDER and CBER plan to create a standard set of 8 to 10 metrics that they will require manufacturers to submit to the agency, Russell Wesdyk, head of the quality metrics program told the Parenteral Drug Association's Quality Metrics conference last month.

"We don't want two sets of metrics for different organizations," he told *DGR*.

Wesdyk added that the FDA is still considering collecting nine metrics already disclosed by agency officials, such as batch failure rate, right-first-time rate, number of corrective and preventive actions conducted and number of annual product review reports conducted on time (*DGR*, November 2014). These metrics will be used by the FDA to decide which facilities to inspect.

He said that the initial metrics will be published as either a draft guidance or proposed rule, and emphasized that industry will have an opportunity to comment on the metrics.

The FDA has said it will hold a public meeting early next year to get feedback on the metrics, and plans to publish final guidance by September 2015 (*DGR*, October 2014). — Robert King

Industry Pushes Back Against FDA's Quality Culture Metrics

Manufacturers are urging the FDA to ax three proposed quality metrics related to annual product reviews that would measure a facility's quality culture, claiming they are too burdensome, unnecessary and confusing.

The three APR-related metrics, which are among a set of nine the agency is considering, center on management engagement, deadlines and corrective and preventive action (CAPA) rates.

The management engagement metric measures whether a senior manager signs off on an APR. Drugmakers contend this metric didn't measure either quality or whether an executive is engaged.

Focusing just on whether a senior manager signed an APR is too narrow, suggested Joseph Noll, director of Mylan's quality council, at the Parenteral Drug Association's quality metrics conference last month.

Differences in manufacturing capacities also would skew this metric. Some brandmakers produce only 10 products while other generic or OTC makers manufacture more than 1,000, said Deb Autor, senior vice president of global quality and regulatory policy at Mylan. A CEO could end up signing off on 1,300 APRs, she told the conference.

Participants also worried that the metric on deadlines for APRs to be finished within 30 days after its cutoff date could end up lowering the quality of APR. This metric will force some drugmakers to cut corners to meet the deadline and affect the quality of the review, Noll said.

The third quality culture metric would ask companies for the number of CAPAs initiated by an APR and divided by the total number generated. Participants believed this metric was far too difficult and confusing to interpret.

A large majority of the attendees voted to recommend elimination of the three metrics altogether.

However, attendees were more split on whether to eliminate one of the production metrics: right-first-time rate. While 44 percent voted to eliminate it, 41 percent wanted the FDA's definition of the metric to change. The agency defined right-first-time as the number of lots with at least one deviation by the facility in a year divided by number of lots attempted.

The sticking point is deviation, as different facilities have different definitions of deviation. The metric's definition needs to change so that it includes no mention of a significant or critical deviation, said Guy Villax, CEO of the manufacturer Hovione.

Russell Wesdyk, head of the FDA's quality metrics program, declined to comment on the industry reaction to metrics. However, CDER Director Janet Woodcock said that determining a facility's quality culture is very important to the agency, indicating that it will be measured in some form or another. — Robert King

U.S.: China Cutting Red Tape For Innovative Drug Imports

China has agreed to streamline its regulatory processes and cut red tape for imports of new drugs, a move that should benefit the U.S. pharmaceutical industry, the U.S. Commerce Department says.

U.S. officials made the announcement at the conclusion of discussions during last month's U.S.-China Joint Commission on Commerce and Trade (JCCT) in Chicago. Under the agreement, China will accelerate reform of its regulatory review and approval system, including eliminating its drug approval backlog within two to three years.

The U.S. and Chinese governments agreed that excessively long timelines for getting innovative drugs to market in China is problematic for companies, the U.S.-China Business Council (USCBC) told its members following the event. — Jonathon Shacat

Tenn. Compounder Pleads Guilty To Making Contaminated Products

A compounding pharmacy pled guilty recently to manufacturing contaminated products that caused skin infections, the first compounder to be convicted of criminal charges for poor quality since the FDA gained new authority in 2013.

Tennessee-based Main Street Family Pharmacy and its co-owner Christy Newbaker will pay separate $25,000 fines for one federal misdemeanor charge each for violating the FD&C Act by shipping contaminated methylprednisolone acetate (MPA). Main Street also entered into a consent decree that prohibits it from manufacturing, holding and distributing products until the pharmacy comes into FDA compliance. Newbaker received a year of probation from a federal judge in the U.S. District Court for the Western District of Tennessee.

The charges stem from a 2013 recall of all of Main Street's sterile products (*DGR*, July 2013). The recall was initiated after the agency received 26 adverse event reports, including skin abscesses, from patients in four states who were injected with MPA compounded by Main Street, the FDA said.

The FDA inspected Main Street's Newbern, Tenn., facility in May and June last year and uncovered several troubling good manufacturing practice violations.

Investigators discovered the compounder had no written pest control procedures, and observed two spiders in the facility's clean room. Main Street also didn't use any type of sporicidal cleaning agent inside or outside of its clean room, says a Form 483 issued to the company.

The agency identified other problems with the company's equipment and processes. For example, a motor used in the lyophilization unit started to leak oil. Facility personnel placed a paper towel between the motor and lyophilization unit to absorb the oil rather than fix the issue, the FDA said.

Main Street also tests the potency of a finished product on a random basis, with no scientifically justified schedule or plan, said the form with 25 observations.

The compounder is halting all operations related to manufacturing, holding or distributing drug products, according to the consent decree. To resume operations, Main Street must comply with agency quality regulations and hire an expert to inspect its facilities.

Main Street was the first compounder to face criminal charges since the New England Compounding Center and several employees were charged with compounding contaminated drugs that caused a nationwide meningitis outbreak in 2012. That investigation is still ongoing.

The meningitis outbreak sparked Congress to grant the FDA additional powers in 2013 to regulate larger compounding facilities. The agency has warned more than 25 compounders since the Drug Quality and Security Act was signed into law late last year.

Main Street could not be reached for comment.

To read Main Street's Form 483, visit www.fdanews.com/12-05-14-MainStreet483.pdf.

— Robert King

FDANEWS

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

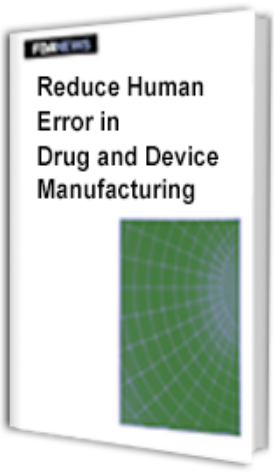
Editor: Robert King
(703) 538-7644
rking@fdanews.com

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: Meg Bryant, Elizabeth Orr, Lena Freund, Kellen Owings, Bryan Koenig, Jonathon Shacat

President: Cynthia Carter; **Content Director:** Dan Landrigan; **Editor-in-Chief:** Neal Learner



Reduce Human Error in Drug and Device Manufacturing

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.

Then you'll be introduced to root cause analysis techniques and how to apply them. The report includes the following tools that are essential to root cause analysis:

- Cognitive Load Tool
- Root Cause Determination Tool
- Predictive Load Tool
- Human Error Prediction Tool Assessment Form
- Task Criticality Assessment Tool
- And more…

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.

FOUR EASY WAYS TO ORDER

1. **PHONE:** Toll free (888) 838-5578 or +1 (703) 538-7600
2. **WEB:** www.fdanews.com/47079
3. **FAX:** +1 (703) 538-7676
4. **MAIL:** FDAnews 300 N. Washington St., Suite 200 Falls Church, VA 22046-3431

☑Yes! Please send me ____ copy(ies) of ***Reduce Human Error in Drug and Device Manufacturing*** 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

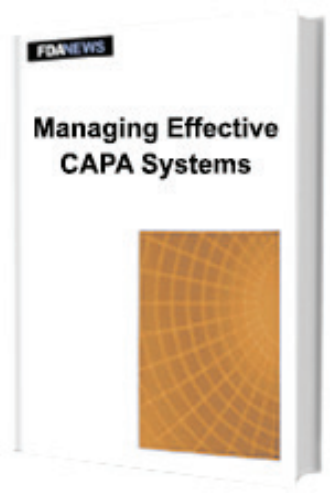
Credit card no. _____

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.

14FLYR-N



Managing Effective CAPA Systems

Recently released from FDAnews, **Managing Effective CAPA Systems** is the industry's most authoritative guide on building and implementing an effective CAPA compliance program.

Nine of the industry's top experts, who have together managed thousands of root cause investigations and successfully opened and closed more CAPAs than they can remember, will share everything from simple nuts and bolts to the most innovative best practices.

Here's a sampling of what you'll discover in its pages:

- Breaking down "silos" – how to assemble cross-functional CAPA teams
- Key quality metrics – how to measure, organize, analyze and store data …
- 7 statistical and 5 nonstatistical methods and tools to trend data …
- Using dashboards and scorecards to track data trends …
- Creating SOPs to cover every CAPA area, including nonconforming products …
- 5 tools and techniques to run failure investigations and root cause analysis …
- Root cause analysis pitfalls and how to avoid them …
- 'How critical is this problem?' Determining severity via risk assessment …
- 'Is my CAPA working?' How to be sure you've remedied every problem …
- Writing effective CAPA reports – what it takes to convince the FDA …
- And much more!

Whether your company is small and just beginning to build its CAPA system or medium to large looking to improve or fine-tune its system, these experts tell you how. 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/48441
3. **FAX:** +1 (703) 538-7676
4. **MAIL:** FDAnews 300 N. Washington St., Suite 200 Falls Church, VA 22046-3431

☑**Yes!** Please send me ____ copy(ies) of **Managing Effective CAPA Systems** 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.

14FLYR-N