Recalls Stimulate Scrutiny of Quality Assurance in Drug Packaging

By F.J. Quinn

Maintaining product quality and meeting regulatory specifications is a daily challenge for pharma manufacturers, but recent events have shown that the quality requirements do not end as pills or vials come off the production line—they must be extended through all packaging steps, and the packaging itself can be subjected to a comparable level of quality assurance. Recent product recalls show cases of the wrong dosage strength in containers (or, conversely, the wrong labels being applied) mispackaged product, or problems with the cleanliness of the packaging components. The increasing number of outsourcing arrangements between brand owners and contract packagers only add another level of complexity to the communication and coordination required. Vendors say they are taking a hard look at systems controls to ensure their products and all components are protected from contamination and other hazards.

"Companies dedicated to ensuring the quality of their products and packaging are taking steps to ensure such quality, investing in complete quality solutions that include quality planning, quality control, quality assurance and quality improvement," observes Patricia Santos-Serrao, senior product manager at Master Control (Salt Lake City), a provider of process and document management software. "Implementing a proven quality management system that enforces standards and practices for quality assurance will help improve quality and minimize risk."

Drug packaging is taking center stage as several high-profile drug recalls in 2011 were directly linked to this key component in the manufacturing process. One look no further than Johnson & Johnson (J&J; New Brunswick, NJ), which in the past two years issued more than 25 recalls and led to a high-level management reorganization. Several recalls were packaging related, drawing attention to the importance of designing quality into manufacturing processes.

In September, Qualitest Pharmaceutical had to recall multiple lots of oral contraceptives because the pills—which have a specific 28-day cycle—were rotated within their blister cards, altering the weekly regimen if followed. Last March, Pfizer's Greenstone generics subsidiary had to recall a production lot where the wrong labels were attached, switching a an antidepressant with a prostate hyperplasia treatment. A year ago, RiteDose Corp. had to recall albuterol vials that had the wrong concentration listed on their labels.

The J&J situation served as a reminder about the suitability of drug packaging materials and structures is a integral part of the drug approval process. FDA requires assurance that drugs will be protected against contamination, tampering, spoilage, and physical damage that could impact is characteristics, and makes a review of drug packaging part of the information it examines.

K.R. Karu, director of sales, Sparta Systems

"One of the biggest issues that has occurred in the last 18 months – and even earlier – is the failure of companies to report quality-related issues and customer complaints to the FDA in an efficient manner, whether they have occurred in the pre- or post-market," says K.R. Karu, industry principal, Sparta Systems (Holmdel, NJ), a provider of enterprise quality and compliance management solutions. "This has caused the agency to tighten its oversight of the industry, enforcing stricter regulations for reporting of quality issues and requiring more extensive collection of data related to these issues."

Improving Quality Assurance

Quality assurance is an important part of any complete quality management strategy. These programs can comprise hundreds of different components, including deviation management, supplier quality management, corrective and preventative actions (CAPAs), investigations, and change management. "Each of these functions is critical, and many of the most forward-thinking companies in pharma have taken to automating them within electronic quality management systems," Karu says. "In most cases, these records are related, so having them in one system instead of silos creates needed transparency."

According to industry members, drug makers are making a concerted effort to enhance quality standards for their manufacturing process, rather than simply reacting to manufacturing incidents. "This is the spirit of Quality by Design initiatives, through which companies design processes to consistently deliver better outcomes," says Randy Tatlock, customer development manager, Aegis Analytical, a provider of manufacturing and process intelligence software. "Other critical quality components include understanding a process better over time and monitoring process data to improve process understanding."

In order to verify quality, one must understand the expectation for a product, whether it is safety, durability, or performance. "One must ask, 'what is expected from this product in order for it to 'perform as expected,'" notes Master Control's Santos-Serrao. "The second component is ensuring that those responsible for assuring that the standards have been met are trained in what to look for when determining that a product meets those standards."

One of the most important steps being taken to improve quality assurance is centralizing management of an organization's quality processes, ensuring standards are enforced across global operations and geographical boundaries. The tendency in pharma companies is to have different locations working in their own unique silos, with disparate processes and ways of managing these processes. "From a quality perspective, this can be, at best, cumbersome and, at worst, devastating when a major issue arises, as they inevitably do," Sparta Systems' Karu says. "More and more companies have awoken to the fact that processes should be harmonized across the organization, and managed from a central location, so that issues can be quickly identified and resolved."

Several pharma companies outsource the packaging process, which experts say makes it even more important to work closely with contract partners' quality teams to capture and share the entire quality review information flow in a collaborative environment. "This helps quality and manufacturing teams gain access to all of the precise and timely quality review information that they need to keep current production on track, or to quickly investigate potential issues uncovered in the quality review process," explains Brian Daleiden, vice president of marketing at TraceLink (Woburn, MA), developer of the TraceLink Network, an industry-wide supply collaboration network.

As the level of outsourced production grows, pharma companies are seeking to maintain the same level of transparency and coordination in external quality review processes as they have within internal production. TraceLink offers a Quality Review service, part of the cloud-based TraceLink Network collaborative supply network platform, which helps pharma companies and their external supply partners connect the virtual quality team into a collaborative environment.

"As a result, pharma quality leaders can reduce quality review cycle times by over 20% through improved visibility and tracking from initial review submission to final review closure," Daleiden says, "reduce manual labor and data entry by over 25% throughout the process, reduce the risk of misinterpretation

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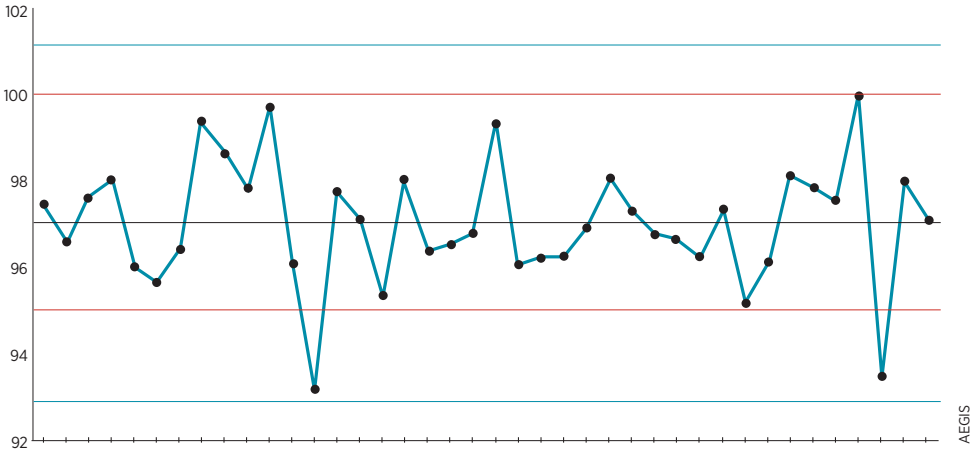
Figure 1:
Plotting batch-to-batch mean potency
Aegis' software tracks variations in product quality (in this case, potency), allowing operators to determine how to reduce variability.



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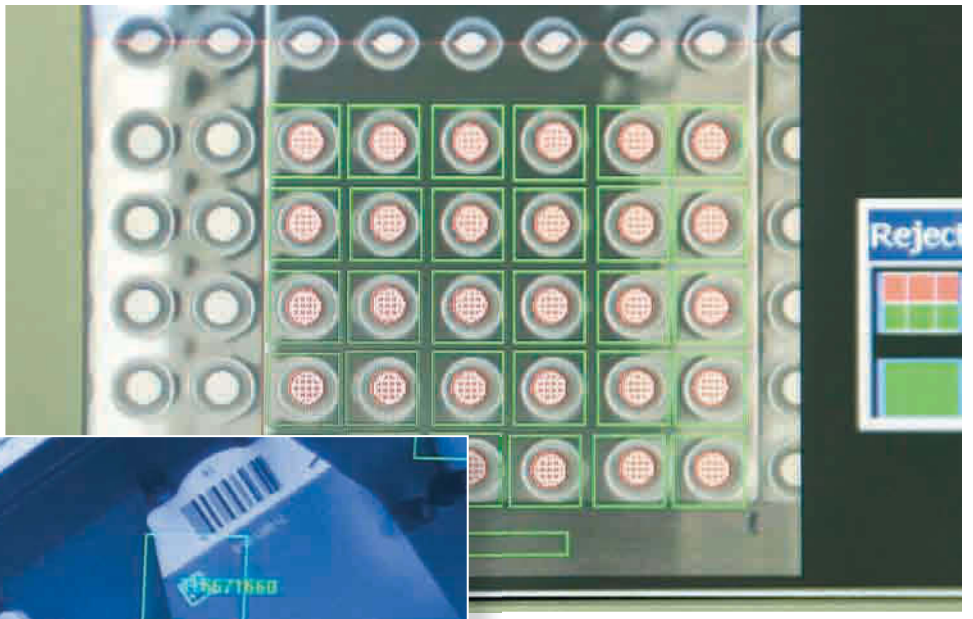
and misalignment between internal and external quality team members, and provide real-time visibility into quality review KPIs for all external supply relationships."Anderson Packaging (Rockford, IL) operates a Lean Six Sigma program which enables it to work collaboratively with customers to develop solutions to new problems, optimize systems and continuously improve its processes, according to Justin Schroeder, senior director, marketing and development services. "We also work collaboratively with industry organizations to actively stay ahead of future challenges, including participating and leading 'think tanks' and round table opportunities."

By gaining a better understanding of their processes, industry members say pharma companies can build quality into manufacturing and prevent unwanted outcomes, rather than always reacting to something that has gone wrong. This has led to an increasing number of life sciences manufacturers initiating and expanding QbD programs, Aegis Analytical's Tatlock says. "There also is increased collaboration between quality and manufacturing teams in the name of preventing and solving quality assurance problems," he adds. "While these departments often serve as a check-and-balance for one another, sharing more information and working together can have positive impacts on quality."

Howell Packaging (Elmira, NY) utilizes FMEA (Failure Mode Effects Analysis) in order to properly plan and ensure clients' contract packaging programs will be error free and conform to specifications. "We are able to produce packaging components such as folding cartons, rigid boxes, and thermoform plastics," notes Joe Lally, sales manager, pharmaceutical packaging. "In addition, we can conduct final packaging operations of product and provide storage and distribution from our Howell Marketing Services operation."

Sharp Corp. (Allentown, PA), a contract packaging services provider, deploys a comprehensive validation program coupled with failure mode analysis to develop and improve processes. "Electronic systems that perform 100% inspections are used during packaging to verify critical attributes," explains Daniel Stehn, director of biotechnology packaging. "Having a well trained staff that oversees activities on a continuous basis during production helps ensure that any errors are minimized, either during production and prior to release of any products."

Daniel Stehn, Sharp Corp. director of biotechnology packaging



Vision system checks quality at Anderson Packaging's production lines.

Quality Management Solutions

Observers concur that drug companies are realizing it's important to have a system in place for quickly identifying the root cause of incidents that arise in manufacturing. There are a number of solutions which are said to help pharma companies comply with good manufacturing practices and FDA-regulated production and packaging environments.

For example, Sparta Systems claims its TrackWise quality management software system is designed to help companies streamline quality processes within their manufacturing organizations, collect the necessary data associated with these processes, and report it to regulatory authorities in a timely and efficient manner. The software offers companies a centralized and configurable solution that speaks to their quality-related business needs. "The ROI benefits of TrackWise include, but are not limited to, significant cost savings associated with minimizing quality-related risk, transparency and accountability for the processes that govern the overall delivery of safe and effective products to market, and the assurance of brand reputation," Karu says.

MasterControl offers an integrated quality management solution that includes the management of documents, processes such as CAPAs and Deviations, training, supplier management, bill of materials, audits, and risk. "Our solutions suite is highly configurable and can be leveraged not only in quality, but in R&D as well," Santos-Serrao says.

Sharp utilizes Document Management and Corrective/Preventive Action software systems which enable concurrent routing of documents for approval (reducing cycle time), tracking and trending capabilities (which identify the most important critical items and facilitate continuous improvement), and integration of activities that allows improved efficiency from existing resources. Anderson utilizes software tools for a similar reason; it enables the firm to document and analyze complaints and defects, optimizing response time and reporting. "We employ real time Overall Equipment Effectiveness (OEE) software that is integrated into our equipment at the line level," Schroeder says. "This software provides real-time data driven analysis of our systems, including rejects and downtime."

This real-time data capture and analysis provides agility in Anderson's decision making and efficient resolution of manufacturing challenges. "In addition, we collect and monitor metrics across our business, including our ERP system," Schroeder says, "enabling us to make calculated and informed decisions, trend data, and continuously improve our business."

Howell utilizes a program called Cartons-on-Demand that integrates with its clients' planning function. "It permits us to establish re-order points, consolidate runs, reduce costs, and provide a true just-in-time program," Lally explains. Howell also uses new technology with respect to vision systems, bar-code readers, and check weighers in both its contract packaging and packaging component production operations.

AstraZeneca recently selected Aegis' Discoverant process intelligence solution for gathering, monitoring and reporting process and quality data. Discoverant is designed to help manage pharmaceutical and biopharmaceutical manufacturing processes. According to Aegis, the first deployment of the process intelligence system will be at AstraZeneca's Gärtuna facility in Södertälje, Sweden.

"Leading life sciences manufacturers want to operate robust processes within well characterized design spaces," states Mark Isaacs, vice president sales, Aegis. "To deliver this, they want a single, proven data management platform for aggregating, accessing and analyzing process and quality data."

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Manufacturing may have a quality system in place, but when the product moves to the packaging department or to a contract packager, there may not be a quality system in place, or it is disconnected from the company system. "This lack of control and visibility often causes issues that are discovered only after the product has made it through the supply chain and to the consumer," Sparta's Karu says. "Having a closed-loop system from suppliers through shipment will help minimize problems that are created outside of the traditional manufacturing process. This can be accomplished by having a single system, or having well-defined integration points between separate systems."

Pharmaceutical companies have implemented both document management systems and Enterprise Quality Management Systems (EQMS). The difference is that a document management system manages content and changes within controlled documents while an EQMS creates an electronic record that follows a predefined workflow and manages process, not content. "This means that events are recorded, and a process that includes investigations, root cause analysis, actions taken, and related CAPA and Change Control are managed and effectiveness checks are performed," Karu points out. "This facilitates events being completed without parts of the process falling between the cracks, or thrown over the wall into another silo without visibility." These are measurable problems that, when solved, ensure a safe product delivered to consumers and positively impact the company's bottom line.

Despite making strides in improving quality across the supply chain, pharma companies still face innumerable challenges in ensuring and maintaining product quality. By improving upon their quality assurance, experts say drug makers can reduce risk, improve compliance and avoid the brand liabilities that can negatively impact business growth and tarnish their reputations in the marketplace. **PC**