PharmTech.com
ADVANCING DEVELOPMENT AND MANUFACTURING

One Step Back, Two Steps Forward To Improved Quality Processes

By Jennifer Goldsmith, Vice President, Veeva Systems

The Federal Drug Administration (FDA) has been encouraging drug manufacturers to tackle their batch-to-batch quality requirements for years but is now getting serious about it. Historically reactive in its enforcement actions, the FDA is now looking to proactively improve quality in the life sciences industry. For example, rather than just punish companies for quality missteps, the FDA is making plans to incentivize high-quality manufacturing in hopes that this will ensure better overall drug quality and a reduction in drug shortages. While the FDA is still unclear on how this can be done, it knows which sort of initiatives it wants to reward."[We are] looking at ways the FDA, using our existing authorities, can recognize manufacturers that do a particularly valuable job," said FDA deputy director of regulatory programs Dr. Douglas Throckmorton.

One major step has already been taken. The Center for Drug Evaluation and Research has created a new Office of Pharmaceutical Quality that will support these efforts by collecting performance metrics and conducting trend analysis. Ostensibly, the Office will focus on metrics such as manufacturing defects, cycle times, and overall batch quality. Makes sense, but for one point: these are all *lagging* indicators that measure the outcomes of what has already happened. Leading indicators, in contrast, provide information that may directly aid in predicting future outcomes so companies can potentially prevent errors or identify bottlenecks before the damage is done. While they can be more difficult to capture, leading indicators can be spotted early on – before molecules are processed, capsules are formed, batch reports are run. So, months before the quality management system starts processing data, life sciences companies can get a sneak-peak into potential quality problems by looking at the leading indicators hiding in the document management process further upstream. In other words, by taking one step back, organizations can jump two important steps forward.

Today, especially with the high volume of QA-related documents (SOPs, training manuals, etc.), life sciences companies can uncover trouble spots and bottlenecks just by looking at their documents – from the authoring process to related training impact. Document lifecycle metrics – such as how

much time it takes to review a change in training SOPs – can pinpoint various key leading indicators of quality discrepancies and compliance risk.

Here's one example: If there is a spike in the number of CAPA initiation documents submitted in a particular month (say 25% percent increase compared to the typical run rate), then it would be expected that there might be an increase in the number of days to complete the investigation due to time needed to update related SOPs or work instructions. Any changes to these documents require a change control process, and delays here prolong completion of the investigations. An organization that has an internal goal to speed investigation completion, could find their metric has trended adversely. However, if the company had been monitoring the status of documents in process and rebalanced document control resources to accommodate the influx of CAPA initiation documents, it might have been possible to avoid a performance decline and close investigations faster.

There are many leading quality-indicating metrics that can be derived by looking proactively at the life cycle of documents, such as how long does it take a document to be routed from draft to review to approval and distributed to staff; or how long it takes staff to be trained on a new or changed SOP. If a document gets snagged somewhere along the way, this could cause a production delay downstream – and if this is a common bottleneck…this could suggest a much bigger problem. If an equipment calibration SOP must be amended to meet new standards but approval is delayed then staff training is likewise delayed, which directly impacts manufacturing, even shutting down drug production. But, if a company sees this bottleneck in the document management system, it can take corrective action immediately. Further, if the QA Manager determines that a calibration SOP needs revision in order to improve the manufacturing process but knows that SOPs traditionally 'get stuck' for two weeks longer, he can monitor the process and work to remedy the problem in advance, or otherwise expedite the process. Long-term, the company can address the root cause to improve overall processes.

Horizon Pharma, a specialty pharmaceutical company that has developed and is commercializing products to primary care, orthopedic surgeons and rheumatologists, adopted a cloud-based electronic quality document management system enterprise-wide in late 2012. Horizon had been using paper-based processes but needed a new, more efficient solution that was also scalable and accessible globally as it began to rapidly expand. Since implementing its cloud system, the company has leveraged it to track and monitor product deviations as a means to identify areas that need process improvements. "We route all quality data and documents through our document management system for review and approval and then house all of this content in the same system so everyone has visibility and access. With everything in one place, we can spot key performance

indicators in order to improve the overall manufacturing process," said Cara Weyker, Horizon's Vice President of CmC Regulatory and Quality.

Weyker continued, "For annual product reviews, as an example, we look at how many investigations we've had, the types of investigations, and any recurring deviations by category and by location. By running a simple report, we have immediate insight into a potential glitch and can remedy the situation before it turns into a real problem. Fortunately, we haven't had any major quality problems since implementing the new system."

With an electronic quality document management system, the manager can simply run a quick risk assessment on documents in process, monitoring various metrics across the enterprise. Similar assessments can trigger a red flag so that QA managers can help ensure effective documents are produced rapidly, and people are trained thoroughly and quickly, both leading to a production line that runs efficiently and effectively for a quality output. The system can also be programmed to automatically generate 'read-and-understood' reports broken down by user, department, and facility assessments to demonstrate that proper training has been completed to meet compliance audits and to provide valuable metrics by role and by function. In addition to improving the efficiency of compliance reporting, this creates transparence for all parties across all levels – empowering staff with performance data they need to identify areas that still need improvement.

By focusing on document life cycle states and identifying areas where it takes too long to get to approve, or where other process anomalies occur, companies can also cross reference against other documents and processes to determine reasonable internal benchmarks for use across the enterprise. For example, if one particular manufacturing plant is noted for having the lowest risk of non-compliance, and their standard for reviewing critical SOPs is four days, then 'four days' can become your organization's benchmark. When leveraging a cloud-based electronic quality document system, specifically, the scope of these quality performance reports is compounded because it is easily accessible worldwide by the entire enterprise. At this level, drug manufacturers can compare SOP performance from one location to another around the globe and gain meaningful insight.

Additionally, because the cloud is so ubiquitous, cloud-based systems enable life sciences companies to establish corporate-wide quality and measurement standards, even when it comes to taxonomy, for continuity across the organization. Process data can, therefore, be compared side by side. If two or three other locations are taking six days to accomplish the same quality assurance review, the centralized quality group can examine the circumstances more closely and potentially remedy a problem or open up a bottleneck. "Since implementing a cloud-based quality document management system at Horizon, we've been able to harmonize across the organization globally,"

added Weyker. "What used to be a manual process is all handled in a single, centralized system so that processes and document templates can be standardized. This reduces the risk of errors being made or duplicating efforts and helps to ensure that the right people are reviewing the right documents at the right time."

GenomeDx, a genomic information company based in Vancouver and San Diego, recently migrated to a cloud-based electronic document solution to help improve manufacturing efficiency and quality. "Our document management system makes it easy for us to understand where a document is in its lifecycle, who's touched it, who has yet to do something about it, and where the bottleneck resides. It does it in a way that is intuitive and easy to follow," said Andy Katz, PhD, chief operating officer of GenomeDx.

Cloud-based electronic document management systems are also designed with a modern framework and consumer-like user interfaces (think Amazon) rather than legacy architectures that are notoriously clunky and difficult to use. An easy to use system encourages more people to use it and therefore more data is captured resulting in improved accuracy and increasingly reliable leading indicators. It also aligns with the business world's move away from the desktop for greater flexibility and mobility – managers can review and approve documents from wherever they are, whenever they want, from any device to improve efficiency. And, external partners such as contract manufacturers and subject matter experts who write SOPs can access and work with documents conveniently in a centralized repository, which further encourages system use, and greater data capture. With more data, companies gain visibility into leading indicators to thwart problems before they cause noncompliance…or worse.

"We run reports on a wide range of document life cycle metrics across the enterprise, and are now able to anticipate potential bottlenecks or compliance risk well in advance," concluded Horizon's Weyker.