Data at Work

More than a decade after process analytical technology (PAT) arrived on the life sciences manufacturing scene, the industry is continuing to find new ways to use analytical software for reducing costs and risks, as well as increasing process understanding across manufacturing networks. A manufacturing intelligence platform enables valuable comparisons between sites, which can contribute to achieving these goals

Ultimately, this type of analytical software helps to avoid unacceptable manufacturing variability while implementing valuable process improvements when needed. More specifically, biopharmaceutical companies are using manufacturing intelligence software for site-to-site and batch-to-batch comparisons that lead to improvements across geographically dispersed manufacturing plants, including operations outsourced to contract manufacturing organisations (CMOs). Such technology is particularly useful when a new plant is ramping up for production and lessons can be learned from the experiences of an existing, more seasoned manufacturing facility.

Enabling Comparisons

The scenarios that follow are based on real-world examples of how manufacturers have used manufacturing intelligence software in innovative ways for better process understanding. It is important to first understand the general capabilities of the manufacturing intelligence platform used by these companies. The platform allows access to data through standard interfaces to existing disparate data systems (for example, LIMS, ERP, process historians, data warehouses and paper-based records). With the right software in place, aggregation of data in context and

accounting for batch genealogy ensures lots can be traced throughout the manufacturing process. A process hierarchy can be built by analysts to show the aspects of the process that are of interest, such as a simultaneous view of two plants to compare performance and outcomes.

Software solutions can then monitor critical process parameters (CPPs) to shed light on various aspects of the manufacturing processes. From a remote desktop screen, alerts can be seen for manufacturing sites across geographic locations. Process development, manufacturing and quality teams can collaborate to pinpoint problems through cause-and-effect investigations and process understanding resulting in:

- Better visibility into the manufacturing process and access to data
- Less time to correct deviations
- Fewer production crises due to inadequate process controls and understanding
- Faster and better preparation of records to support regulatory inspections and reporting requirements
- Easier and faster preparation of CMC and other regulatory filings
- Improved process predictability and increased supply chain efficiencies

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- More efficient production planning
- Accelerated time to market for new drugs and devices
- Better records and control of intellectual property
- Data at work across continents

In the following example, a new plant in Europe was built to manufacture a biopharmaceutical drug that had been produced in the US for more than two decades. The older plant had a manufacturing intelligence platform in place, and had tweaked its process over many years to run efficiently and have a high output. To meet high demand and maximise the use of its assets, the company needed to accelerate the learning curve at its new facility to be

as efficient as possible. It knew that a language barrier would make communication more difficult as details can be lost in translation from the US scientists who have the most process expertise.

The company needed a common hierarchy view of data at its new plant to help scientists reach the same efficiency level and ensure tech transfer from the older plant. With a manufacturing software platform in place across both plants, they could directly compare CPPs to easily identify differences and areas for improvement. Continuous monitoring of CPPs ensured ongoing consistency. Alerts helped them examine whether an issue was taking place in both locations or only at one plant, which helped focus root cause investigations.

Through knowledge sharing and collaboration, production at the new plant eventually exceeded the US plant, and the new site was able to take advantage of its newer equipment to increase efficiencies. When deviations were identified, the manufacturer could examine both plants to determine the root cause. Was it a raw material used at

both sites, or was another variable present in just one location? The new plant was so successful at quickly ramping up to capacity and meeting market demand that the company was able to close its older, US plant – eliminating the need for additional capital investments there.

Sharing knowledge and lessons learned across the two countries enabled the company to spend less time on similar problems and could focus on increasing efficiencies. The US scientists could see what was happening remotely, so they avoided travel to the new site and related costs. From around the world, they could bring a view of the new plant right to their computer screens to monitor processes and help with any issues.
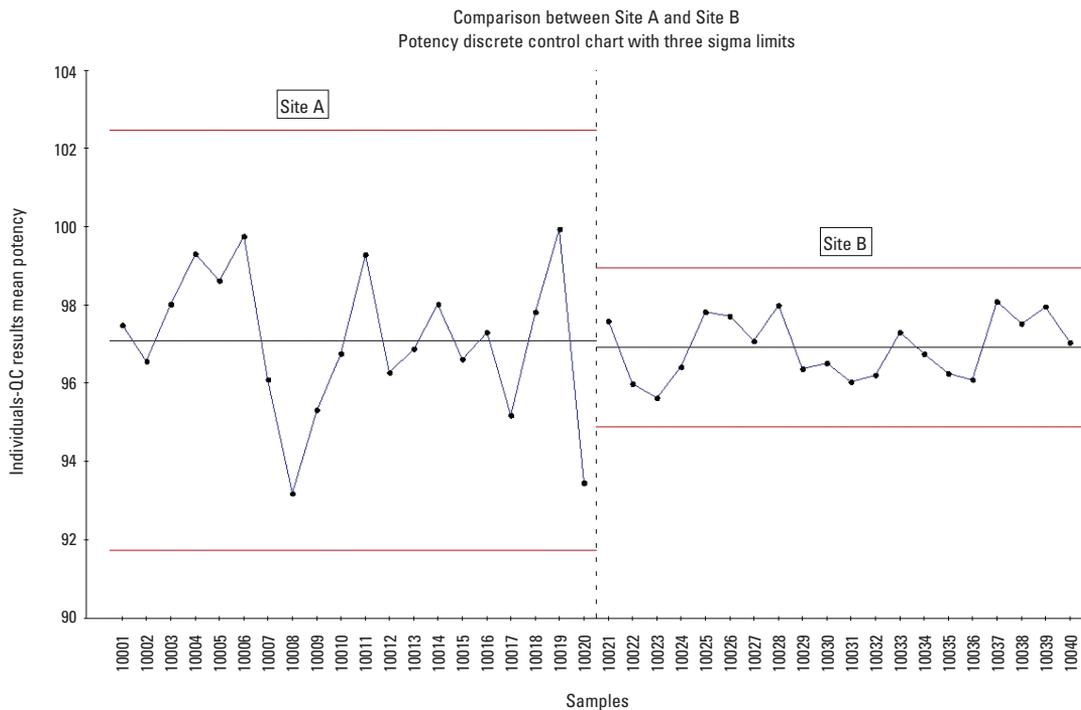
Data Across Companies

Life sciences manufacturing companies demand from CMOs the same level of purity and safety that the FDA requires of them, and the FDA wants outsourced manufacturing to be viewed as part of the sponsor's operations. A common data platform that provides a single view of process data to mitigate risks is

an effective tool for collaboration between sponsor companies and CMOs.

At another large medical device manufacturing company, a common data platform has been used to better manage CMO relationships to ensure consistency in product quality and limit variability and liability. As in the previous, cross-continent example, software can be used for technology transfer from a sponsor organisation to its contractor. Similar CPP comparisons can be made to monitor performance and identify areas for further investigation.

With access to data from the CMO – which was specified in its legal agreement – the device manufacturer could easily compare how its CMO was operating to its own site. This helped to make business decisions about quantities manufactured at its various locations and whether the CMO relationship was delivering value. In this case, the manufacturer especially wanted to view quality data to ensure it was minimising its risks and liabilities as the party ultimately responsible for device efficacy. It also wanted connectivity to monitor points

Figure 1: Chart showing two line graphs for a CPP at old and new plant

Comparison between Site A and Site B
Potency discrete control chart with three sigma limits

Calculated mean and calculated standard deviation process in use

> ## "When a company's manufacturing is completed across several locations, the ability to view the entire supply chain becomes essential"

necessary for the annual product reviews (APRs).

Another global biopharma manufacturer has installed a manufacturing intelligence software platform that provides a collaborative data access, contextualisation, analysis and reporting environment to eliminate geography as a factor in its working relationships with all of its CMOs.

Its CMOs can monitor their own operations, which takes process understanding for all parties involved even further. Using an enterprise server model for software installation allows the sponsor to view process hierarchies with information gathered from server locations around the globe. The sponsor and its CMOs can use powerful analytics and reporting to make relevant-time, on-demand comparisons that ensure consistency in product quality and limit variability.

Data Across the Supply Chain

When a company's manufacturing is completed across several locations, the ability to view the entire supply chain becomes essential. One particular European company uses a manufacturing intelligence platform to identify the root causes and locations of supply chain problems for a drug for which bulk product manufacturing is completed at two different sites and is then packaged at a plant in a nearby country.

The company looked at CPPs across the two plants making the bulk product to identify which one of the bulk products is performing better in packaging. Could they tell the difference? Was there an issue that originated at one plant or another? It found that its freeze dried product material from one

plant formed different crystals than the product from its second site. This helped conclude that packaging issues were likely to have originated with the bulk materials.

For packaging steps that can ultimately ruin a biopharmaceutical product, a company might compare two facilities to better understand processes. If the company is rejecting a high percentage of vials from one plant because of bad labels and rejects very few from its second finishing site, it can compare the two processes. This same manufacturer also could compare packaging operations on two processing lines within the same plant. Such evidence can help justify replacing equipment, because the manufacturer can clearly find the root of the specific problem and save costs due to waste or delays getting to market.

Manufacturing Intelligence Platform Criteria

Selection of the right data access, analytical and reporting platform and tools for effective collaboration between the process development, manufacturing and quality teams across manufacturing networks is a critical first step to automating trending and reviews of CPPs and enabling investigations and understanding of cause-and-effect relationships when needed. Design considerations for technology solutions that enable better process understanding – ultimately enhancing production capabilities and accelerating commercialisation – include

efficient data management and analysis, automated process genealogy calculations and enabling self-service data availability for technology transfer.

Conclusion

Across all of the real-world examples shared, manufacturers benefitted from global views of their manufacturing processes on a computer screen, reducing travel time and expenses while enabling more consistent and efficient production that lead to bottom line business benefits. The right software solution will have the ability to work with continuous online and discrete data together and enable data sharing, results analysis and reporting across disciplines, scales of operation and geographically dispersed sites. It will simplify the preparation and distribution of analysis results and automate the generation of periodic reviews and reports of batches and campaigns that can add tremendous value.

About the Author

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