Industry-wide initiatives, such as Continued Process Verification (CPV), Process Analytical Technology (PAT) and Quality by Design (QbD), are driving today’s pharmaceutical manufacturers to improve product and process quality and efficiency. By adopting a proactive approach to monitoring the according critical key parameters, life-science manufacturing companies can identify and understand variability and trends in their manufacturing processes to predict and avoid quality events, like process deviation or batch failure.

The International Society for Pharmaceutical Engineering’s (ISPE) Product Quality Lifecycle Implementation (PQLI) initiative was launched in 2007 with the goal of helping the industry find practical approaches to the global implementation of quality guidelines. The PQLI lists the “process performance and product quality monitoring system” as one of its four key product quality system elements.

From a high level, product and process understanding in manufacturing includes identifying and monitoring Critical Process Parameters (CPPs) and Key Performance Indicators (KPIs) for one site or across the extended manufacturing network comprised of geographically dispersed sites and contract manufacturing organizations. Analysis of process data helps improve understanding for better decision-making.

Product and process monitoring leads to improved process understanding, which results in significant business benefits for manufacturing operations: greater efficiencies from reducing non-value-added work, improvement of overall batch quality and fewer deviation investigations, faster tech transfer and a more predictable product supply.

AN INDUSTRY DISCONNECT

In collaboration with Pharmaceutical Manufacturing, BIOVIA surveyed approximately 115 industry-leading pharmaceutical, biopharmaceutical, contract and generic pharmaceutical companies to learn more about current product and process understanding approaches among life sciences manufacturers and to identify opportunities for industry-wide improvement.

When asked whether their “organization sees a direct correlation between process and product understanding and quality,” (see Figure 1) more than 89 percent of respondents answered “yes.” Additionally, the majority of respondents saw a direct correlation between process and product understanding with profitability, as well as noting a direct correlation between process and product understanding and “operating optimally” within the current pharmaceutical industry environment (see the full survey results at the end of this document).

Survey responders clearly voiced their assertion that process and product understanding was directly related to product quality, profitability and productivity, but when asked whether they were currently using an information technology tool to analyze their production processes in real-time, more than half said they currently do not (see Figure 2). Among the other respondents, 33 percent said “yes, for some of our production processes” and less than 16 percent use an IT tool for ALL of our production processes.”

This reveals a disconnect: If most manufacturers understand the benefits of product and process understanding and recognize that technology tools make efficient and complete process understanding possible, then why is half of industry not answering the call-to-action?

Figure 1: Does your organization see a direct correlation between process and product understanding and quality?
DATA SILOS

Data silos can be the bane of productive and profitable business and prevent anyone from ever getting the “big picture.” Data that flows easily within and between internal groups as well as external partners is essential for powering the real-time and predictive analytics that generate business value.

When survey respondents were asked how siloed is the data across their organization (specifically product development, manufacturing and quality data), only 8.9 percent said that their data was not siloed at all. Additionally, 26.6 percent said “very siloed,” 43.4 percent said “somewhat siloed,” and 21.2 percent said “mostly not siloed” (see Figure 3).

This shows there is a crucial need for an IT solution that allows the integration of data. Researchers are wasting time assembling and contextualizing data from siloed data sources rather than performing the analysis that leads to process understanding.

As a follow-up question, we asked respondents if the siloed nature of their organization’s data, again specifically pertaining to product development, manufacturing and quality data, impairs their organizations’ abilities to respond to current challenges within their companies. Almost 70 percent said yes (see survey question 4). Dealing with siloed data means an organization cannot quickly react to issues. Instead, highly educated resources are wasting time on activities that could be eliminated or minimized with an IT solution.

TECH TRANSFER WOES

Tech transfer is a critical step in the product lifecycle leading to successful commercial manufacturing. As stated in ICH Q10, “The goal of technology-transfer activities is to transfer product and process knowledge between development and manufacturing, and within or between manufacturing sites to achieve product realization. This knowledge forms the basis for the manufacturing process, control strategy, process validation approach and ongoing continual improvement.”

While 81.6 percent of survey respondents said effective and efficient tech-transfer management has become a high priority issue within their organizations, more than half (57.1 percent) said their current suite of implemented information technology tools DO NOT support tech transfer as robustly as they would like (see survey question 13).

Nice Insight reports that the global contract pharmaceutical manufacturing market is growing at an average annual rate of 7.5 percent, with 23 percent of companies spending more than $50 million annually on outsourcing – solidifying the growing importance of effective tech transfer between manufacturers and CMOs. And yet, the Pharmaceutical Manufacturing survey results indicated that only 27.7 percent of respondents are using a technology tool that allows process monitoring and collaboration within contract manufacturing relationships (see survey question 19).

This is especially surprising as the FDA has officially designated that sponsor companies are responsible for compliance pertaining to products made at their contract manufacturers. In fact, recently the FDA delayed approval of a major pharmaceutical company’s New Drug Application (NDA) based entirely on deficiencies observed at the CMO enlisted to manufacture the drug.

GETTING TO THE ROOT CAUSE

The term “root cause” is seen often in quality documentation, audit reports and 483s. Root cause analysis is a structured evaluation method that identifies the causes for an undesired outcome and the actions needed to prevent recurrence. Regulatory inspectors check not only that the manufacturer has carried out a root cause analysis, but also will verify any findings of such analysis.

Thus, one of the most important aspects of root cause analysis is data collection.

In our survey, 58.6 percent of respondents reported they are not using a technology tool for root cause analysis (see survey question 17).

Root cause analysis is a key component of product and process understanding. And it’s only possible with easy access by process and quality scientists and engineers to the right data at the right time for analysis. So it is surprising that this is still a manual process for a large part of the industry.
CONTEXTUALIZING DATA

Contextualization is the organization of related data elements that enable analysis and interpretation. A key challenge facing the pharmaceutical industry is developing the contextual link from the routine production/manufacturing data sets to the vast array of additional data obtained that are providing the required context. By correlating CPPs in the plant with the critical quality attributes (CQAs) and relating the variations to the R&D development data sets, a production facility can define a platform for real-time operational excellence.

Examples of useful contexts for data analysis:

• Data type context: enables specific types of data analyses
• Batch context: enables batch-to-batch comparisons
• Time/volume: enables comparisons in continuous manufacturing
• Process context: enables process-to-process comparisons
• Site context: enables site-to-site comparisons
• Genealogy context: enables upstream/downstream correlations

BIOVIA provides users with a role-based hierarchical view of process parameters that can be accessed in read-only mode from the original data sources. Users select the parameters and batches to be included in their analyses and then the data are gathered from the original sources. The resulting cache of retrieved data can easily be modified by the users to remove or add parameters and to refresh the values. This gives users some high flexibility in quickly adapting to changing questions.

A PROCESS PRODUCTION OPERATIONS SOLUTION

The process development, manufacturing and quality functions generate an abundance of data, which needs to be utilized in a more user-friendly, organized and contextualized form for improved process knowledge and production operations. As organizations generate more data through implementation of QbD, PAT and CPV initiatives along with new manufacturing and measurement technologies, they need better ways to access and use their data.

BIOVIA Discoverant provides process development, quality and manufacturing users with self-service, on-demand access to process and quality data from disparate databases and paper records. It automatically aggregates and contextualizes data and enables ad hoc statistical investigations and analysis with automated validation-ready workflows to provide browser-accessible outputs for users. This includes different organizations and geographies improving the working relationship with contract manufacturing organizations.

BIOVIA Discoverant also can access and aggregate data from all kinds of sources. This includes manufacturing-related applications like Electronic Batch Record systems, Manufacturing Execution Systems (MES), Data Historians, Data Warehouses, or Enterprise Resource Planning (ERP) systems from BIOVIA or other third-party systems.

BUSINESS VALUE OF THE BIOVIA DISCOVERANT SOLUTION

<table>
<thead>
<tr>
<th>Capabilities</th>
<th>Business Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Role-based dashboarding and signal monitoring</td>
<td>Increased efficiency, easier decision making</td>
</tr>
<tr>
<td>• Integrated self-service, on-demand access to all process and quality data</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(including paper data)</td>
</tr>
<tr>
<td>• Advanced visual, numeric and statistical capabilities for ad hoc data</td>
<td>Improved process understanding, reduced</td>
</tr>
<tr>
<td></td>
<td>analysis and reporting</td>
</tr>
<tr>
<td>• Graphical display of lot genealogy with drill-down</td>
<td></td>
</tr>
<tr>
<td>• Analysis of online chromatography and other multi-phase data</td>
<td></td>
</tr>
<tr>
<td>• Validation-ready solution to make GMP decisions</td>
<td>Improved compliance, reduced cost of quality</td>
</tr>
<tr>
<td>• Automated creation of APQR’s and other templated reports</td>
<td></td>
</tr>
<tr>
<td>• Scalable enterprise solution for virtual deployment across</td>
<td>Improved collaboration</td>
</tr>
<tr>
<td></td>
<td>multiple servers/organizations/geographies</td>
</tr>
</tbody>
</table>
In the lab context, data can be sourced from applications like Electronic Laboratory Notebooks (ELN), Laboratory Information Management Systems (LIMS), or Laboratory Execution Systems (LES) from BIOVIA or third parties. Even paper records can be digitized, captured and included in analyses. Data is contextualized and ready for further analysis, visualization, reporting and sharing through role-based access supporting global collaboration.

From BIOVIA’s perspective, the results of the Pharmaceutical Manufacturing survey indicate that the industry as a whole has significant room to improve when it comes to product and process understanding. The industry sees the importance of product and process understanding as well as the tools required. However, time, talent and monetary investments in product and process understanding have not been a priority for more than half the industry. While some forward-thinking companies have technology tools in place and are using them appropriately, many organizations may need to know what specific steps they need to take to help them move forward toward a technology solution.

- View the full results of the Pharmaceutical Manufacturing/BIOVIA research study.
- Click here for the Video: Biologics Made Right First Time
- Click here for the Recorded presentation: Impact of Recent Regulatory Trends on the Pharmaceutical and Biologics Manufacturing Process and Quality Enterprise
- Click here for the Datasheet: Biologics Made Right First Time
- Click here for the Datasheet: BIOVIA Discoverant
- Subscribe to our Life Sciences Solutions Blog for insights on Life Science Industry: www.BIOVIABlog.com