Pharmaceutical MANUFACTURING

Addressing the Pharmaceutical Quality Testing Bottleneck

Eliminating efficiency drains and compliance risks through informatics

The demand on drug manufacturers to get operations right has never been more urgent. Most agree the myriad of challenges the Pharma industry faces in the market today will continue to mount in the coming years as companies work to fill product pipelines and leverage the torrents of information generated by commercial operations to win in the marketplace. As a result, life-science companies are seeking new ways to optimize product lifecycle processes from early stage development to commercial scale manufacturing. Pharma industry leaders are increasingly turning to information-based technologies and paperless, automated informatics platforms to manage complex quality and compliance regimes. This also includes laboratory operations that are often considered a bottleneck but still needed to support overall product quality and proactive compliance.

Whether it's Research and Development at a bio start-up or Quality Assurance/Quality Control programs at an OTC antihistamine plant, an integrated platform of informatics systems that automates routines and limits paper-based data gathering and storage is an industry best practice that is transforming these operations. Highly developed Laboratory Execution Systems (LES), Electronic Laboratory Notebooks (ELN) and Laboratory Information Systems (LIMS) are providing drug manufacturers and developers new opportunities to manage risk and eliminate efficiency drains as they strive to manage ever-changing business ecosystems. Quality testing programs are long recognized not only as a focal point of compliance, product quality and risk management, but a choke point as well, because the success of an organization's overall operations are so dependent on quality testing and the efficiency of its processes required to administer work and manage the information and documents effectively.

A Common Issue

Do Pharma's operational managers and leadership feel quality testing is, in fact, a bottleneck? In order to validate and quantify the discontent observed with executing quality testing operations, BIOVIA sought to gain a better understanding of the industry's own perception of the efficiency and effectiveness of quality testing programs. In collaboration with *Pharmaceutical Manufacturing* brand, BIOVIA surveyed approximately 100 industry-leading pharmaceutical, biopharmaceutical, contract and generic pharmaceutical manufacturers to gauge their perceptions of the pain points associated with quality testing regimes, as well as to better understand the current state of quality testing programs within pharmaceutical and biopharmaceutical operations.

Ultimately, over 120 QA/QC, manufacturing, operational and compliance executives completed the survey. Their responses revealed the challenges they face managing these operations effectively and how they and

their organizations are working to meet the needs of the internal constituencies that rely so heavily on quality testing programs.

Is quality testing considered a bottleneck by Pharma's operations leadership and is it a high priority to address? These two questions and responses are closely related. Of those surveyed, nearly two-thirds responded that their current quality testing process is indeed perceived as a bottleneck, and nearly three-quarters (72 percent) said addressing the bottleneck is a high priority for their organizations. It's interesting to note more respondents felt it was an issue to address as opposed to those who responded they perceived it as a bottleneck – but that result may have more to do with the order in which the questions were asked rather than the disconnect it seems to suggest. Regardless, it's clear that a majority of responders agree there is a bottleneck and that their organizations are making it a priority to unknot its constraints and free up these important resources so their QA/QC teams can effectively fulfill their multifaceted roles in support of operations.

The Usual Suspects

Pharmaceutical Manufacturing's readers were asked where bottlenecks are being observed in their organizations. The responses in Figure 1 identified some familiar suspects including time-consuming manual data entry and transfer, ponderous review cycles and similar problematic documentation handling procedures. The results reflect BIOVIA's own internal understanding of the constraints quality testing departments deal with but with one twist: transcription errors and tedious document management are actually a result of manual data entry and transfer.

Many of the responses to the "Other" category choice under this line of questioning pertained to lab resources and equipment or instrumentation availability. Fortunately, there are quality testing solutions that address all these challenges including a highly integrated offering from BIOVIA.

Time Killers

Responders were asked to choose which tasks they felt were taking more time than they should within their current quality testing approach. As shown in Figure 2, "Reviewing Tests" was chosen most (49.6 percent) followed by "Ensuring data quality/correctness" (47.1 percent).

Again, based on experience, BIOVIA anticipated that "reviewing tests" would be a popular response and reveals tasks of this nature are taking more time than they should within a quality testing process. The extended effects are easy to imagine; slow review of tests prolongs the time it takes to ensure data quality and thus its

Figure 1. What are the causes of bottlenecks within your current Quality Testing approaches?

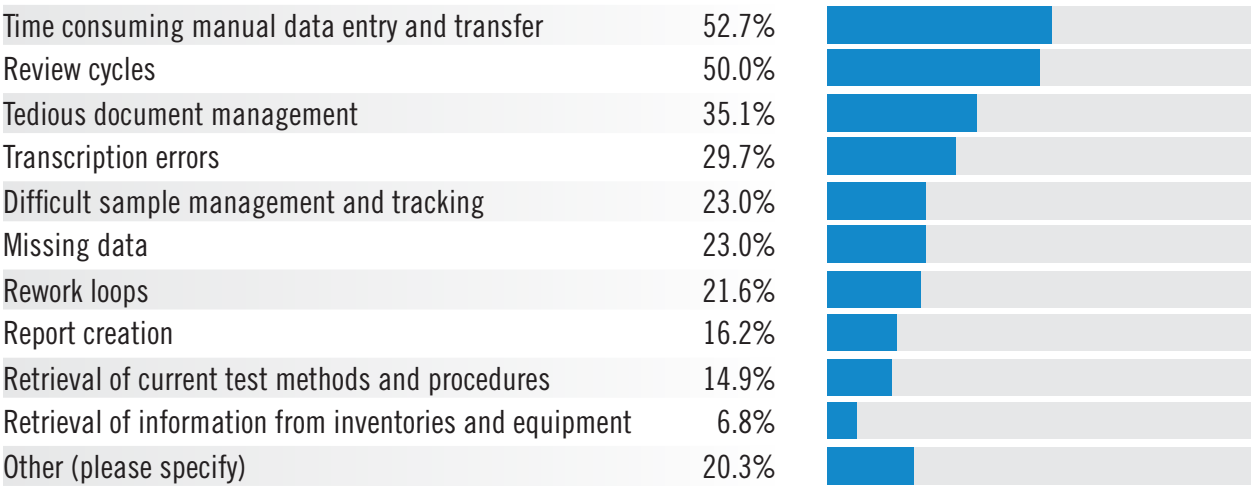
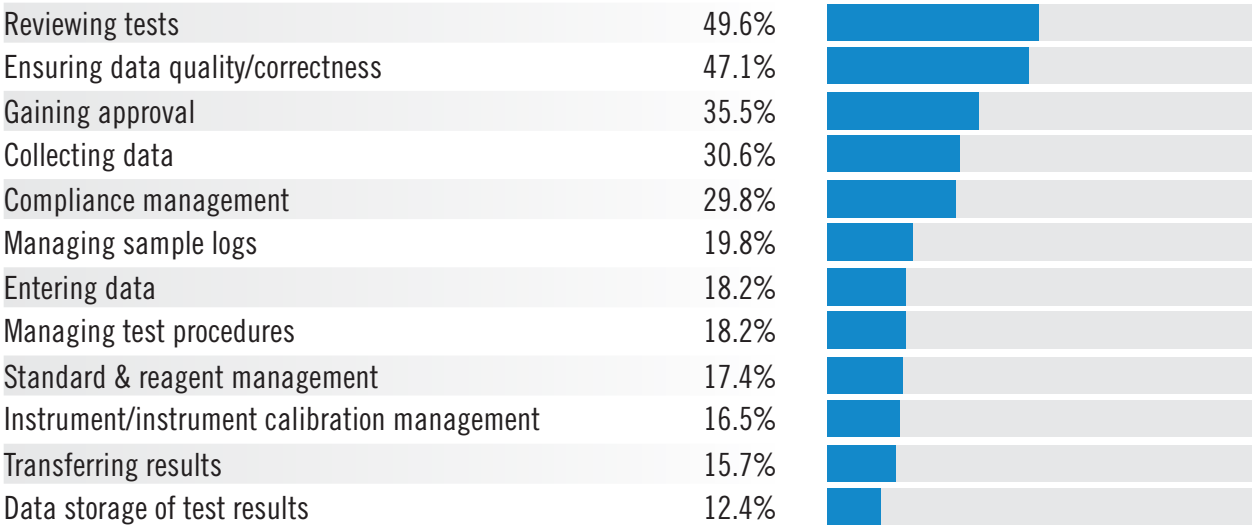


Figure 2. Which tasks are taking more time than they should within your current Quality Testing approach?



correctness and suitability for approval. It seems apparent that many of these responses are a direct result of inherently error-prone manual work flows.

The survey's results indicate that most responder's quality testing processes are likely based on manual work. However, two-thirds indicated their organizations have already introduced an electronic environment for the development and deployment of their QA/QC processes across the enterprise. Our conclusion from these responses is that for many of those surveyed, electronic systems are not implemented as widely or, are as well-integrated with other systems as they should be, or that the electronic systems they've implemented are not robust enough to handle their quality testing processes.

In Pursuit of Real Benefits

With two-thirds of responders indicating they have deployed electronic systems, and two-thirds complaining that their quality systems are a bottleneck, it is perhaps not such a leap to conclude that a large number of organizations which use an electronic system to manage quality testing regimes are not realizing the full benefits of the technology they've invested so much time, money and effort to implement or perhaps that they can do a better job of deploying the solution and institutionalizing these applications across various departments.

Paper and Its Contribution to Risk

Do paper-based quality testing systems contribute to compliance risk? *Pharmaceutical Manufacturing*'s readers were pretty well split on this one; 51.2 percent chose "No" while the remaining 48.8 percent chose "Yes." This may reveal that not all respondents work in GMP-compliant labs. For those in non-GMP regulated laboratories, poor quality testing processes may not be a compliance risk. But for those that are, managing risk and achieving compliance proactively means institutionalizing operational excellence.

Another way to look at it is to ask one's self how organizations with a manual quality testing process could *not* consider it a compliance risk? Is it that respondents in this category have elaborate processes with well-articulated and documented paper trails and superior filing procedures that minimize compliance risk? Perhaps, but even the most well designed manual process is no match for the capacity, throughput and productivity of a fully featured electronic quality testing solution integrated with other lab informatics systems and enterprise business applications.

The Importance of LIMS

Over half (55.8 percent) of those responding indicated they use a Laboratory Information Management Sys-

tem (LIMS) for quality testing. Recalling however, that two-thirds already say their quality processes are a bottleneck, how is it that this critical application is not pushing the perception the other way? From BIOVIA's perspective, this could indicate that perhaps more than a few of the organizations queried likely need more than a traditional LIMS system and should consider moving toward implementing something like an end-to-end integrated quality testing system.

We asked *Pharmaceutical Manufacturing*'s readers, "In which areas are you using an informatics solution to automate your Quality Testing efforts," instructing responders to check all that apply. As depicted in Figure 3, nearly 62 percent indicated they applied digital technologies to accomplish Data Acquisition" followed by more than 56 percent selecting "Compliance Documentation." Next comes "Review and Reporting" (47.8 percent) and finally "Method Execution" at just over 32 percent.

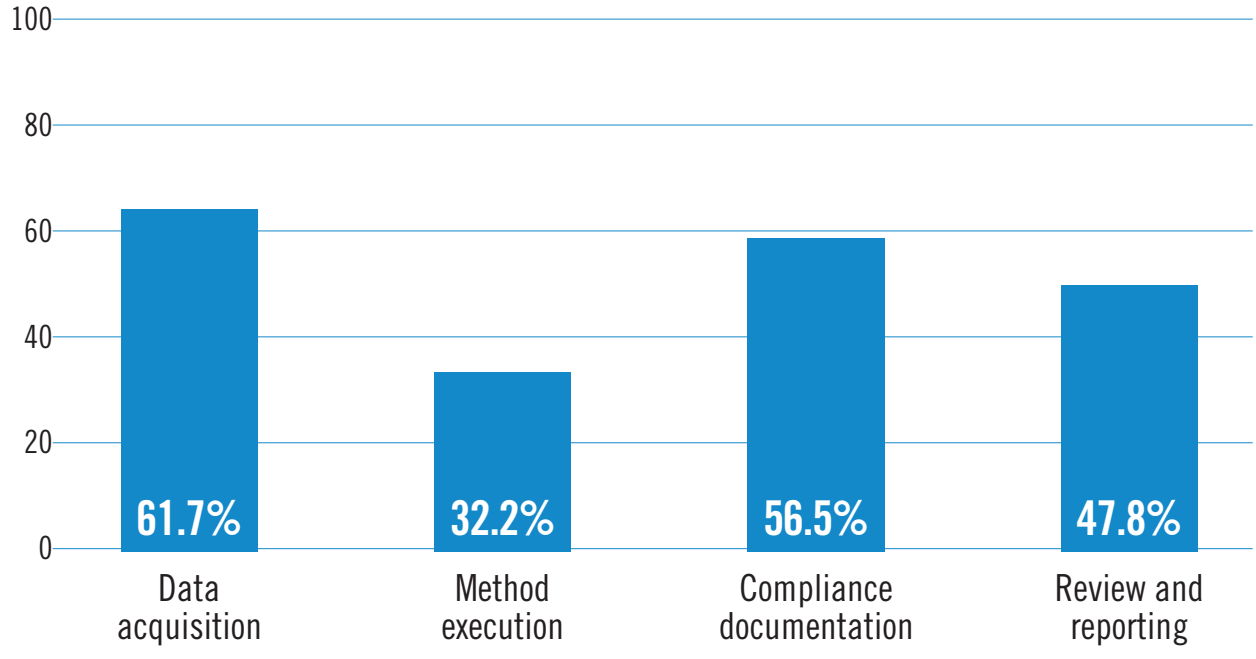
Similarly, those who indicated they have an electronic solution for their quality testing processes responded that they are still plagued by inefficiency. So, why the disconnect? Only a third of responders have an informatics solution that covers method execution, and that gap in functionality is likely the source for the perceived shortcomings of their operations capabilities.

More about Method Execution

An automated method execution solution is an important supplement to the system because it enables automated data entry and transfer within the laboratory, covering the work within the lab, right there at the bench. Most of the automation pertaining to compliance documentation and review and reporting is done outside of the lab. This helps to explain why quality testing is still a bottleneck, even with these processes managed electronically. The data acquisition is likely trending higher as this is typically handled by a direct interface to an instrument, but does not necessarily mean that the work in the lab is supported by an overall end-to-end system.

About half of the responders to the *Pharmaceutical Manufacturing* reader survey indicated that they have an efficient approach to managing Out of Limit data values. This likely means that they have a system that flags Out of Limit values such as a LIMS, which makes sense because about half of the responders indicated that they use a LIMS for their quality testing operations.

Figure 3. In which areas are you using an informatics solution to automate your Quality Testing efforts?



Managing Out of Limit Data

Are responding organizations efficient when it comes to managing Out of Limit (OOL) data values? Nearly 29 percent chose "Efficient" while the majority (41 percent) chose the less confident "Somewhat efficient," which may reflect a not-so-well-integrated system to manage this data reliably. Only 7.4 percent selected "Extremely Inefficient" which must be a tough operational reality to admit to; on the other end of the spectrum, though, 9 percent said their abilities to manage OOL data were "Extremely Efficient."

The responses indicate that about half of the managers feel that they have an efficient approach to managing OOL data values and a system (likely a LIMS) which flags Out of Limit values. This makes sense because about half of the responders indicated that they use a LIMS for their laboratory operations. It would be an interesting follow up question to ask whether or not these people manage their OOL data values within an end-to-end quality system, or if they need to manually input OOL data values into another disparate system.

Challenges from the Field

Respondents were asked to identify challenges they regularly face within the context of Quality Testing Operations. Comments reflect pharma company manager's anxieties and pain points – with several issues familiar to many (like human error and scarce resources) because many such "issues" are common among compliance-related operations like quality testing and similar data-driven compliance routines. For *Pharmaceutical Manufacturing*'s readers, the following areas frame their everyday operational challenges and outline the things that can impede a quality testing workflow:

- CAPA process and compliance performance
- Competing operational, marketing and organizational priorities
- Availability of lab resources, equipment and instrumentation
- Outsourcing testing to contract service providers
- Human error, quality culture and poor communication
- Delays caused by traditional testing methods
- Addressing gaps between validation and quality testing

The Challenges of Paper Continue

Looking at a typical quality testing workflow, (Figure 4) there are numerous points where quality, efficiency and accuracy can be lost. For example, the transcription of data from instruments is tedious and inefficient. Given the ability for IT tools to directly connect to the

Figure 4. Challenges of a Paper-based quality Testing Workflow

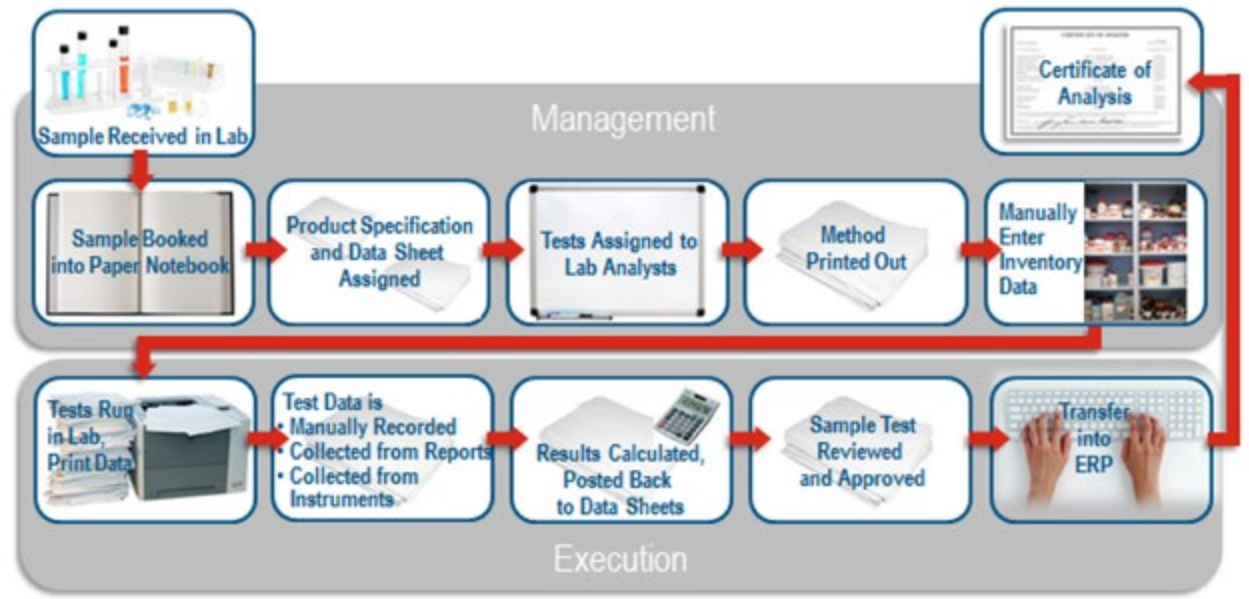
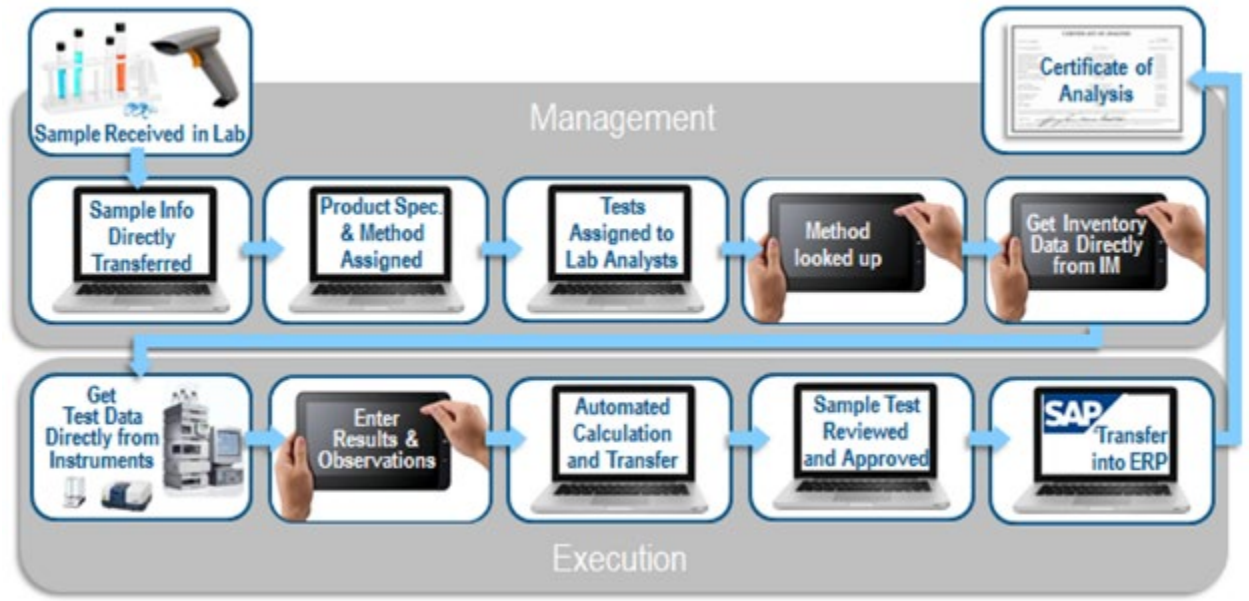


Figure 5. Increased efficiency, reduced compliance risk with an integrated quality testing solution



instruments, it allows for the required data to be parsed and displayed for that step within the analytical test method. Arguably, at the center of the quality testing bottleneck are paper-based processes that do little to enhance efficiency and introduce accuracy problems that compound data quality and similar issues. Further, reviewing of data in a paper-based system is tedious, time-consuming and provides no visual indication of an inaccurate data value that has the potential to be approved in error.

Managing the expiration dates of consumables is yet another pain point. Paper-based systems are bound by tedious routines. Vigilance and risk management in this area are not supported well by traditional oversight and QA methods. An Inventory application that constantly checks availability, location and expiration dates and flags expired consumables will automatically prevent an analyst from wasting time and effort finding required chemical materials for testing samples and to test samples with expired substances drawn by accident. With an integrated solution in place, the opportunities for error diminish throughout the Quality Testing process.

Calculations being handled manually, paper-based review and approval and transcription of results are incredibly inefficient processes and introduce many potential inaccuracies in results data. Today's IT tools can automate calculations, results data transfers and similar tasks, as well as make review and approval routines more efficient via dashboards and other, similar interfaces. Without advanced tools a typical Quality Testing workflow exposes many of the challenges listed by the respondents, but almost all of these gaps can be filled with the BIOVIA Quality Testing solution (see Figure 5).

Even if the process is partially supported by electronic systems and some of the tasks are covered by a system like a LIMS, the overall end-to-end process is still not connected or automated and therefore does not provide the benefits of a full electronic solution.

With an integrated and electronic Quality Testing Solution, the processes become more efficient, less error-prone and even less costly.

The Business Value of an integrated Quality Testing Solution is clearly associated with the system's capabilities. Ranging from comprehensive electronic review processes to faster data review, including compliance and successful relationships with regulators. The figures for associated business value are impressive and can add up to as much as $1 million in reduced costs, and a significant improvement in productivity from reduced cycle times to as much as 50 percent. The bottom line? Quality can be improved by as much as 80 percent (See Figure 6).

Figure 6. Business value of an integrated quality testing solution

Capabilities	Business Value
• Total electronic review process with automated data transfer • Enforced procedures and good documentation practices	10 x increased compliance with regulations and guidelines
• Eliminated reworks and investigations by automation • Less paper — reduced costs for printing, storage and handling	Reduced cost > $1M/year & lab
• Integration of all related functions to Quality Testing with automaed data transfer (Inventory, ERP)	Improved productivity by >25%
• Fully integrated paperless process for Quality Testing • Total electronic review process, Approve-at-a-Glance	Increased efficiency by up to 70%
• Removal of error-prone manual or missing steps • Automated calculations	Improved quality by up to 80%
• Removal of manual non-value added process steps • Faster data review, approvals in QA	Reduced cycle times by >50%

A Quality Testing Solution: BIOVIA

The integrated Quality Testing Solution that BIOVIA offers users:

- A comprehensive solution supporting all aspects of the testing workflow including planning, management, execution and review and reporting. It is integrated with the inventory system for materials and consumables as well as with the instrument inventory that includes metrology. It also provides an out-of-the-box integration with business systems like an Enterprise Resource Planning System (ERP) from SAP.
- A comprehensive package of validation templates including user requirements, a validation plan, functional specifications, a traceability matrix and automated IQ/OQ scripts.
- An end-to-end solution for Quality Testing that is part of a larger Total Quality Strategy from BIOVIA covering all aspects of a total quality approach.

BIOVIA is suitable for organizations that are looking for a reliable long-term partner:

- BIOVIA's parent company, Dassault Systèmes is a strong partner with a focus on informatics and science with BIOVIA at the core for requirements of the Life Sciences industry.
- It is a publicly traded company with a long-term strategy providing BIOVIA customers with the required stability and reliability of a large organization.
- ONE Quality Lab is an Industry Process Experience provided only by BIOVIA which helps improve your Quality Testing processes by integrating people, resources, systems and data while maintaining compliance..
- BIOVIA does have deep expertise in Quality Testing as well as compliance. BIOVIA has actually defined the now industry-accepted term "Laboratory Execution System," which is the core application of Quality Testing.

From BIOVIA's perspective, the results of the *Pharmaceutical Manufacturing* survey indicate that many companies feel their quality testing regime creates a bottleneck that needs to be addressed in their overall quality processes and, after reflecting on their quality testing process, many feel addressing this bottleneck challenge is a high operational priority.

However, quality testing processes are still plagued by inefficiencies and compliance risks that are mainly attributed to time-consuming and error-prone manual data entry and transfer. Even those using electronic solutions are still facing inefficiencies because their electronic systems are not robust enough, not implemented as widely, or not integrated with other systems as well as they should be in order to provide a reliable automated end-to-end solution for their quality testing processes.

About Dassault Systèmes

Dassault Systèmes, the 3DEXPERIENCE Company, provides business and people with virtual universes to imagine sustainable innovations. Its world-leading solutions transform the way products are designed, produced, and supported. Dassault Systèmes' collaborative solutions foster social innovation, expanding possibilities for the virtual world to improve the real world. The group brings value to over 190,000 customers of all sizes, in all industries, in more than 140 countries. BIOVIA provides a scientific collaborative environment for advanced biological, chemical and materials experiences. The sophisticated enterprise system of modeling, simulation, laboratory and quality management enables innovation for science-based industries.

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This whitepaper, as well as the previously released recorded presentation and industry survey conducted by *Pharmaceutical Manufacturing* were sponsored by BIOVIA (formerly Accelrys). To learn more about Quality Testing from BIOVIA, see the following links:

- Click here to view the full results of the Pharmaceutical Manufacturing/BIOVIA research survey
- Click here to view "Industry Analysts LNS Presents: The Importance of Implementing a Total Quality Strategy in Life Sciences"
- Click here for the Recorded Webinar: Building Compliance and Operational Excellence into your Quality Lab Operations
- Click here for the Total Quality Datasheet
- Click here for the Quality Testing Datasheet
- Click here for the Quantified Benefits of Quality Testing from BIOVIA
- Click here for the Quality Testing overview video
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