A comprehensive guide to PAT for OSD manufacturing

22 June 2021

Manufacturers of oral solid dose (OSD) pharmaceutical formulations need the right tools to effectively compete in a market that is continuously growing and highly regulated. The adoption of a suitable Process Analytical Technology (PAT) framework can help companies thrive in this sector by greatly reducing a product's time-to-market and increasing profitability.

Eamonn Garry, Operations Director at Optimal Industrial Automation, and Paul Gillham, Innovations Director at Optimal Industrial Technologies look at why OSD manufacturers should implement PAT.

PAT provides OSD manufacturers with a data-driven, in-depth process understanding that supports accurate and responsive in-line control across all production stages, from raw material input up to the delivery of end products. Thanks to the actionable insight gained from this, it is possible to create an intelligent as well as flexible manufacturing line that is able to address variability and meet market demands with high-quality products. PAT is therefore essential for any business seeking to implement Quality by Design (QbD), Lean and smart manufacturing applications.

What are the advantages of using PAT?

By offering a holistic approach to manufacturing, PAT offers multiple advantages to pharmaceutical producers. Firstly, this system is crucial for the transition from traditional quality control methods to more comprehensive and efficient quality assurance strategies. As a result, OSD producers can improve the consistency of end-product quality whilst considerably reducing the volume of off-spec materials, rejects and reworks. Furthermore, the advanced process understanding generated by PAT enables manufacturers to continuously increase the quality of their end products by fine-tuning operating conditions.

Moreover, the information on quality that is continuously generated, analyzed and stored offers full data traceability, which facilitates quality auditing activities to prove regulatory compliance. In practice, this provides the foundation for real-time release testing (RTRT). All these quality-oriented features also help manufacturers increase product safety, thus minimizing – if not eliminating – the risk of drug recalls.

A shared PAT infrastructure can also enhance collaboration between manufacturing facilities within an organization, improving end-product consistency and maintaining quality across the company.

In addition to increased quality, pharmaceutical companies can also benefit from more energy and resource-efficient processes. Not only do fewer off-specs and reworks result in lower waste generation and material usage, but optimum process conditions also avoid overprocessing. As a result, OSD producers can reduce their running costs, leading to substantial savings. In particular, PAT can increase operating margins by 6%[1] for mid-sized pharmaceutical companies manufacturing small-market branded, generic, and over-the-counter OSD forms.

Furthermore, the reduction of reworks and overprocessing, coupled with the elimination of downtime associated with off-line quality control, plays a key role in

shortening production times. This, in turn, increases productivity and speed to market. For new OSD formulations, it means that producers can take full advantage of a product's patent life.

Manufacturers wanting to fully optimize their operations can also leverage PAT to facilitate the transition from batch to continuous processing, which can achieve even more productivity gains. For example, leading pharmaceutical company Vertex reported how this change in production has helped the company manufacture medicines from active pharmaceutical ingredients (APIs) to commercial-ready tablets in a few days as opposed to 4-8 weeks with a traditional batch process2.

Finally, PAT-driven applications utilize the power of data, in line with Industry 4.0 or Pharma 4.0 concepts. Consequently, businesses have a key tool that enables them to continuously drive process improvements and intensification as well as to increase their flexibility in adapting to variability in market demands. OSD manufacturers can therefore address current market requirements while being ready to meet future needs.

What are the challenges for installing such systems in existing lines (retrofitting)? Is this possible/practical? Or is it best for new lines?

One of the biggest benefits of PAT is that both new and existing manufacturing lines can implement and profit from it, whether they run batch or continuous processes. Therefore, businesses adopting a PAT-driven approach do not need to build new facilities. In fact, they can leverage this framework to retrofit their plants, improving their operations.

Whether PAT is applied to grassroots or brownfield plants, it is important to seamlessly integrate the technology with the facility's control system. Therefore, it is crucial to design and validate a well interconnected setup.

When PAT is implemented on existing manufacturing lines, this requires the development of a PAT environment that can be adapted to the existing infrastructure. It may also be necessary to adapt the pre-existing control system to a quality-centric control strategy as directed and orchestrated by a PAT system.

In new facilities, it is beneficial to develop the control and PAT aspects simultaneously, so that a comprehensive solution can be created that is tailored to the application. Ultimately, the creation of a PAT-driven OSD line should follow the same principles of QbD that are applied for process and quality monitoring, where quality is built into the solution from the outset.

In both cases, companies should rely on a PAT specialist, especially if they do not have expert in-house teams. The right specialist should have extensive experience in the pharmaceutical sector and a proven track record in developing customized solutions for new and existing plants. This will ensure the creation of a suitable framework that addresses the specific needs of the OSD manufacturing plant. By collaborating with such an expert, businesses can make sure they are utilizing a high-quality system that maximizes the benefits of PAT-driven manufacturing.

When thinking about using PAT for automating/controlling an OSD manufacturing line, what are some of the things to consider?

The most important element that should be considered in automated, PAT-driven OSD manufacturing lines is certainly interoperability. PAT systems are highly likely to interface with multiple systems and devices, including instruments and analyzers,

programmable logic controllers (PLCs), supervisory control and data acquisition (SCADA) systems, historians and, potentially, distributed control systems (DCS). Therefore, it is crucial to select a PAT knowledge management platform for process orchestration and closed-loop control that can communicate bi-directionally with multiple automation, device and system vendors.

For the same reasons, it is highly beneficial to select an independent PAT platform and system integrator specialist that has experience with automation products from different manufacturers, as well as in depth understanding of PAT and how to deploy the technology effectively. By utilizing this knowledge, the specialist can select the most suitable components for an intended application as well as effectively configure devices on new or existing networks.

Another aspect that should be considered is the structure of the PAT knowledge management software used. In particular, a modular solution should be favored, as it allows specialists to conduct the installation, validation and testing of PAT setups in different stages, which can then be unified. This ability is especially important in continuous manufacturing lines, where everything should operate in sync. In these situations, having the flexibility to develop the automation and PAT strategy for each unit operation separately enables the simplified, ‘standalone’ testing of each component before each one is successfully incorporated into a larger, comprehensive automation and PAT framework for integrated testing and subsequent use.

In addition, modularity not only simplifies the creation of a suitable PAT-led manufacturing approach, but also helps manufacturers to adopt the framework in a staged PAT strategy. Such a strategy allows progressive benefits to be gained as the technology is rolled out along the processing line. In effect, OSD manufacturers adopting this manufacturing concept can begin with a simple, smaller scale project

that would enable the business to explore PAT and the possible gains while getting accustomed to the technology.

What types of maintenance must be performed when using these systems?

Another key advantage of PAT is that once a suitable system has been correctly set up, the framework can operate near continuously. A well-designed PAT system can also be adjusted to support expansions, modifications or the repurposing of existing lines and units. In addition, it can support its own optimization by utilizing increasingly accurate and representative predictive models as more process data is analyzed. For this reason, a PAT approach embraces continuous improvement.

To realize these opportunities, a modular PAT infrastructure can be highly beneficial. In particular, it facilitates a highly flexible, extensible and scalable PAT approach. As a result, its reprogramming or development, validation and subsequent addition to the complete infrastructure can be simplified and streamlined.

A key aspect that OSD manufacturers should consider when undertaking a project of this kind is the selection of a suitable partner who understands their requirements and can offer a customized PAT system. The solution provider should have a team that includes automation and IT experts, chemometricians and process specialists. An independent multidisciplinary expert, such as Optimal, has the ability to easily interact with the multitude of devices from different vendors as well as suggest new solutions that are well suited for the specific project.

References:

[1]Cogdill, R.P., Knight, T.P., Anderson, C.A. et al. The Financial Returns on Investments in Process Analytical Technology and Lean Manufacturing: Benchmarks and Case Study. Journal of Pharmaceutical Innovation 2, 38–50 (2007)

[2]Talking continuous: Q&A with Patricia Hurter from Vertex. Manufacturing Chemist (2018) Available at: https://www.manufacturingchemist.com/news/article_page/Talking_continuous_QA_with_Patricia_Hurter_from_Vertex/141888 [Accessed: 26 November 2020]

Image captions:

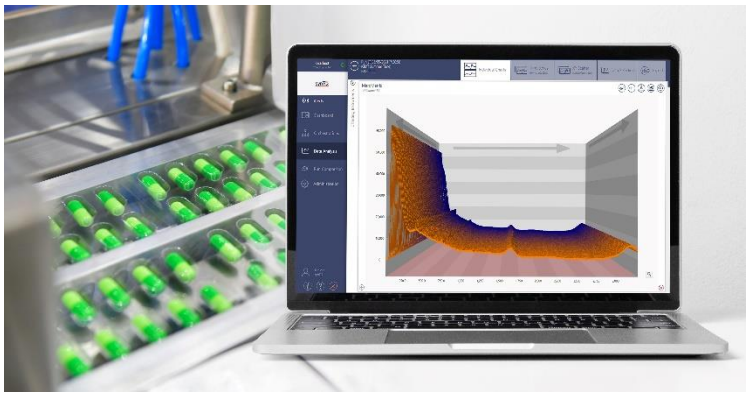

Image 1: Process Analytical Technology (PAT) can help manufacturers of oral solid dose (OSD) pharmaceutical formulations thrive by greatly reducing a product's time-to-market and increasing profitability.
(**Image Source:** Shutterstock: 1926777584)

About Optimal Industrial Automation (OIA)

Optimal Industrial Automation has more than 30 years' experience building, integrating and optimising manufacturing automation systems for challenging and highly regulated industries. Projects are typically for the pharmaceutical, life science, chemical, aerospace, green energy, food & beverage and other high-value process sectors.

The company's primary aim is to deliver measurable reductions in production costs, while finding substantial improvements in productivity, product quality and business sustainability. Part of its capability in achieving this aim is experience in the implementation of Optimal's print and inspect system product – synTI®, plus sister company Optimal Industrial Technologies' leading PAT based process management software platform synTQ.

The company employs a large technical team qualified in software, electrical, electronic, vision and control hardware disciplines. The team has built and developed individual machines and process skids to meet regulations such as FDA 21 CFR Part 210/211 – Pharmaceutical Industry GMPs, and FDA 21 CFR Part 11 – Electronic Records and Signatures. It is also ISO accredited and has years of experience working within GAMP guidelines.

Press contact:
Optimal Industrial Automation
Alan Messenger
Tel.: +44 (0) 1454 333 222
amessenger@optimal-ltd.co.uk

PR agency:
DMA Europa
Chiara Civardi
Progress House, Great Western Avenue, Worcester,
WR5 1AQ, UK
Tel.: +44 (0) 1905 917477
chiara@dmaeuropa.com
news.dmaeuropa.com