Elevating pharmaceutical manufacturing processes with real-time insights

(Bio)pharmaceutical manufacturing is changing considerably, with key innovations enabling companies to rethink R&D, manufacturing, quality control and quality assurance (QC/QA) operations. The spotlight is squarely on process analytical technology (PAT), which underpins the successful transition towards highly effective advanced manufacturing strategies. Martin Gadsby, Chairman of Optimal Industrial Technologies, looks at how this transformative approach is making advanced manufacturing practices more accessible thanks to the latest developments in instrumentation and data-oriented solutions.

THE (BIO)PHARMACEUTICAL industry is currently facing numerous hurdles in its path to high-efficiency production that are more complex and pressing than ever before. One of the most significant perceived challenges is the ability to implement new innovations and increase productivity while adhering to stringent regulatory demands. The race to develop new drugs and therapies demands rapid drug discovery, testing and time-to-market. To address these issues, companies should adopt more advanced production strategies such as continuous flow chemistry, as they can shorten manufacturing processes, increase productivity and throughput. Simultaneously, there is increasing need for stringent quality control and traceability throughout the supply chain to ensure patient safety.

PAT has emerged as a game-changer to drive performance, traceability and regulatory

compliance, helping the sector overcome current limitations and embrace new strategies while futureproofing it in line with Industry 4.0 principles. This is a systematic approach that harnesses the power of data and leverages real-time analysis tools to closely monitor and control critical process parameters (CPPs) and their relationship with critical quality attributes (CQAs). As a result, PAT enhances process understanding and regulatory compliance while ensuring consistent product quality. More precisely, real-time monitoring allows for meticulous scrutiny of data against predefined parameters. Should the need arise, adjustments to the process can be seamlessly made either manually or automatically, ensuring the production of high-quality goods with unmatched efficiency.

The adoption of PAT-driven processes empowers subject matter experts (SMEs) to optimise their drug discovery and development processes, which are typically time- and resource-intensive. Perhaps more crucially, PAT can bridge the gap between R&D and commercial-scale manufacturing by providing a unified framework for understanding, monitoring and controlling chemical reactions.

Historically, the knowledge sharing between – and the integration of – these two domains has posed key challenges, with the disconnect between laboratory-based insights and industrial applications creating inefficiencies. However, the knowledge generated using a PAT framework can help to seamlessly transfer these insights to pilot testing and manufacturing operations. The result is efficient, cost-effective and high-quality (bio) pharmaceutical production.

The most recent advances in PAT and associated technologies are further improving knowledge transfer and accessibility from R&D all the way to full-scale production plants. In practice, it has not typically been possible to easily leverage information from at-line analysis, obstructing the conversion of laboratory intelligence into effective factory applications, especially when it comes to advanced practices, such as flow chemistry. In such instances, the use of off-line analytics ultimately hinders QA and continuous processing.

Addressing traditional shortcomings

For example, nuclear magnetic resonance (NMR) spectroscopy generally stands as a prized non-destructive and non-invasive characterisation technique for (bio)pharmaceutical R&D, as it offers a valuable blend of qualitative and quantitative insights. In particular, NMR can provide structural information on the chemicals being tested, empowering SMEs to monitor reactions in real-time, grasp reaction kinetics and fine-tune process conditions.

These insights help to drive highly efficient manufacturing processes, ensuring competitive product delivery on time and within budget. However, historically, NMR instruments have rarely been deployed during the later stages of pilot testing and manufacturing operations, even when driven by PAT setups. In addition to being generally available as at-line options, these analysers involve substantial upfront costs as well as considerable space and facility requirements.

A fundamental innovation in NMR technology is overcoming this barrier, reshaping these instruments' roles and needs in advanced (bio) pharmaceutical production applications. Enter the era of benchtop NMR solutions. These compact, cost-effective instruments require minimal infrastructure and can support online testing. Thus, they can foster translational research from R&D to manufacturing and enhance PAT-based advanced manufacturing strategies through comprehensive product and processing insights, ultimately driving efficiencies and performance.

By implementing a state-of-the-art benchtop NMR solution within a well-designed PAT system, it is therefore possible to collect measurements, understand reaction processes and make quality predictions in real time, enhancing both laboratory and manufacturing operations. In particular, on the shop floor, this can happen while the continuous process takes place, without any interruptions for quality testing.

High-quality PAT setups incorporating benchtop NMR

An example of an effective and comprehensive PAT framework that leverages an advanced »

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Martin Gadsby
Founder of Optimal

Martin graduated from the University of Bath and after several years working for the aerospace industry, he became the European R&D Process and Process Automation Group Leader for Kraft Foods. Martin has founded two companies: Optimal Industrial Automation and Optimal Industrial Technologies. The former concentrates on innovative and highly technical process and discrete automation solutions, including smart laboratories, while the latter supplies software for PAT. In April 2022 both companies were acquired by Bruker.

benchtop NMR instrument is Bruker's Fourier PAT solution. The Fourier PAT includes a Fourier 80 compact NMR analyser equipped with a synTQ NMR dadpter that enables the integration with synTQ PAT knowledge management software.

With this setup, the NMR instruments generates data from the in-progress materials and end products under observation, that is subsequently analysed and a chemometric model can be built. This can use spectral hard modelling and peak integration to interpret the signals, especially any overlapping peaks, and consequently account for nonlinear effects, such as peak broadening and shifts. The model and results are shared with synTQ to generate intuitive visualisations, determine the most suitable operating conditions for the reaction of interest and, if necessary, support manual or automated adjustments to ensure quality targets are met.

With synTQ being vendor-agnostic and able to accommodate multiple instruments, users can equip their systems with additional analysers that may be relevant to their specific operations. Examples include infrared (IR) spectrometers or pH meters that can be used to further enhance the capabilities of the predictive model, leading to improved outcomes when it comes to product quality and efficiency.

Looking ahead

In the near future, this type of setup will likely play a key role in continuous improvement strategies, with users gathering the information and insights needed to automatically fine-tune their models on a regular basis. This can lead to refined (bio) pharmaceutical manufacturing operations that propel product quality, operational efficiency and overall productivity to new heights. Even more, companies may be able to benefit from fully scalable PAT solutions that can connect multiple manufacturing lines and plants around the world, elevating a business's ability to collaborate and standardise its processes to unprecedented levels.

Ultimately, the use of a cutting-edge PAT framework is key for (bio)pharmaceutical industry players to remain competitive in an increasingly challenging and digitalised market. It represents the route to realising successful future-oriented advanced manufacturing strategies.

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EXPERT VIEW

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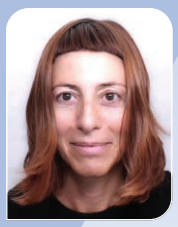

Anna Codina, PhD
Director Pharmaceutical Business Unit at Bruker Biospin

Advanced, data-driven manufacturing strategies, such as continuous processing, are key to driving (bio)pharmaceutical companies forward. They empower industry players to improve patient access to cost-effective, high-quality treatments by optimising consistency, energy and resources efficiency as well as cycle times. The transition towards more effective, future-oriented production frameworks requires enabling solutions that can usher in change. Advanced process analytical technology (PAT) implementations that leverage online, real-time analyses are a leading example of how this can be achieved.

This type of solution makes it possible for (bio)pharmaceutical companies to monitor, control and ultimately optimise processes. This, in turn, helps them deliver the best outcomes in terms of product specifications and manufacturing performance, and opens the doors to advanced practices. In line with Pharma 4.0 principles, PAT uses analysers to measure critical process parameters (CPPs) and critical quality attributes (CQAs), ideally on-the-fly, to gather insights on trends, correlations and patterns that would affect product quality or process performance. This overview supports the effective and prompt detection of deviations from the desired process conditions so that CPPs can be adjusted accordingly.

When using nuclear magnetic resonance (NMR) spectroscopy, PAT-driven operations can offer unmatched capabilities to accurately monitor reactions, chemical kinetics as well as the CQAs of products and in-process materials. Bruker's Fourier PAT solution offers a comprehensive PAT setup that leverages the power of NMR analyses. It does so by combining Bruker's compact and portable benchtop NMR spectrometer with Optimal Industrial Technologies' market-leading synTQ PAT knowledge management platform for data visualisation and automated process control.

This joint offering is paving the way for a future where data-driven, real-time control is the norm, ensuring the highest standards of performance, quality and compliance in advanced (bio)pharmaceutical manufacturing. By adopting this technology, companies can stay competitive and meet the ever-increasing demands of the global health market.

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