Why you need PAT to move from batch to continuous processing

The future of many processes within complex manufacturing industries lies in continuous production, as opposed to batch manufacturing. For many pharmaceutical, biotech, food and chemical producers continuous operations can lead to greatly increased productivity and enhanced product quality. Other benefits include simultaneously adding flexibility, robustness and consistency to the process.

Martin Gadsby, Director at Optimal Industrial Technologies, looks at why Process Analytical Technology (PAT) provides the cornerstone to continuous manufacturing.

As opposed to batch production, where goods are produced in multiple, separated unit operations - interspersed with downtime for quality controls; continuous manufacturing is characterized by connected operations, where each unit immediately feeds the following one without any interruption.

Paradigm shift in quality management

The first step in implementing a continuous manufacturing strategy requires the adoption of an appropriate product quality management system. The traditional Quality by Testing (QbT) approach involves testing the material being processed after every manufacturing stage to ensure that the critical quality attributes (CQAs) are in line with specifications. Therefore, production needs to stop to collect samples and conduct testing in off-line analytical laboratories. As such, lengthy pauses are inherent to QbT and, as a consequence, it is impossible to implement a continuous manufacturing process.

Only by adopting a holistic, quality centric approach to product development and process design is it possible to transition from batch to continuous processing. This is known as Quality by Design (QbD) and it relies on the principle that product quality should be designed into the process, rather than tested in stages and corrected afterwards. Indeed, increased testing in a QbT paradigm does not improve product quality per se, it can just as easily introduce quality issues[1].

Conversely, a responsive system, featuring real-time monitoring of product CQAs and adjustment of critical process parameters (CPPs), allows plant operators to obtain consistent and quality compliant products while reducing the likelihood of re-work or rejects. In practice, QbD requires a scientific yet pragmatic approach that takes into account both the process and product to enable the design of effective, real-time quality control strategies. In this way, it is possible to achieve a predefined quality objective, i.e. delivering products that consistently meet or exceed the required quality standards. A key enabler for QbD is PAT, as it provides a systematic structure for measuring product quality in real time, facilitating process understanding and ultimately controlling the process to ensure product quality.

More precisely, PAT typically uses a range of spectral (multivariate) and univariate data sources together with prediction engines to make real time product quality predictions. These are at multiple points within a continuous process in order to achieve a holistic, QbD quality system. In the short term, the quality predictions available can be used by plant operators to make changes to the CPPs so as to maintain product quality at all times. In the medium to long term, quality-based control can be achieved by means of closed loop automated control systems. In this way, analytics are performed on-line and in real-time, as the process takes place, so there is no need to stop production to perform quality testing.

A seamless transition to continuous production

While QbD and PAT are normally necessary for continuous processing, they can also be applied to batch manufacturing, where they can still deliver substantial benefits. Consequentially, the adoption of these quality management tools doesn't force or rush batch manufacturers into a new realm; but allows them to consider a continuous production plant after they have experienced the gains that PAT can deliver in a batch production process.

Therefore, manufacturers can select a small and not too complex first process to start learning and applying QbD and PAT, in order to gain experience before shifting progressively to more complex processes and ultimately from batch to continuous process development and manufacturing. We have found that the most successful QbD and PAT deployments start in a modest way. After the benefits have been proved in a timely manner, the adoption of QbD and PAT within the organization grows over time to provide a firm basis for wider adoption.

Continuous manufacturing means Big Data

The key aspect of QbD and PAT lies in their ability to unlock the power of Big Data. As a prerequisite for success, the large volumes of data being generated need to be processed, presented, stored and turned into knowledge in a regulatory compliant way. A comprehensive tool to address this challenge is provided by PAT data and knowledge management software products.

These are centralized or distributed software platforms used to continuously make quality predictions in both batch and continuous processes and enable the development of science-based knowledge by presenting the data in a digestible manner to the different subject matter experts (SMEs). By doing so, knowledge management solutions ultimately enable the running of closed loop control algorithms that are based on process understanding and product quality.

One of the most advanced PAT knowledge management platforms on the market is Optimal's synTQ. This software is currently used by over half of the top ten global pharmaceutical manufacturing companies. This comes as no surprise when production cycle times on some critical drugs are being reduced from weeks to hours - with a corresponding leap in productivity and a decrease in the production footprint.

The latest version of synTQ contains features that improve both the user experience and the platform capability with regards to optimizing quality. For example, a real-time Multivariate Statistical Process Control (MSPC) viewer and user-configurable Control Charts can be used to detect when a process is moving out of its optimum operating window and act to correct the situation.

Every implementation path towards continuous processing is different. However, flexible platforms like synTQ are suitable across different industries, production lines and transition strategies; as they unify the necessary information to enable real-time control of batch and continuous processes like never before.

[1]Repeat testing procedures mean that you increase the likelihood of false positives and false negatives. As there is no clear process understanding, it is more difficult to rule out anomalies. The act of traditional sampling can actually cause process issues.

Photo Caption: For many pharmaceutical, biotech, food and chemical producers continuous operations can lead to greatly increased productivity and enhanced product quality.

About Optimal Industrial Technologies Ltd

Optimal Industrial Technologies has more than 30 years' experience in the automation and optimisation of control and data management systems for the pharmaceutical, biotech and life science industries.

The demands being placed on manufacturers in relation to production costs, product quality and business sustainability are ever increasing; hence, the company's primary aim is to deliver measurable improvements in all these target areas.

In addition to practical automation and system integration expertise Optimal Industrial Technologies has also developed a world leading PAT based data management software package – synTQ® which is used by over half of the world's largest pharma companies to increase productivity and reduce time to market for OSD and biotech based drugs and therapies.

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