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Process Analytical Technology: A Framework for Innovative Pharmaceutical Manufacturing

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Key Words

- FDA
- Manufacturing
- Pharmaceutical
- Process Analytical Technology
- Research & Development

Process Analytical Technology (PAT) promises to be the most radical change in pharmaceutical manufacturing in 30 years. It is part of the US Government FDA's 21st Century Initiative, built into its strategic plan and supported by Presidential Executive Order 13329 – Encouraging Innovation in Manufacturing.

Background

Inventing, developing, and bringing new medicines to market is often seen as the focal point of the pharmaceutical business, especially with patient, stockholder, government, and regulator pressure rising on pharmaceutical companies. However, the time is ripe for pharmaceutical companies to look deeply at the fundamentals of its business. It is the much less talked about but no less important area of pharmaceutical manufacturing that is receiving attention.

Traditional Pharmaceutical Manufacturing

Traditional approaches to making pharmaceutical products lag behind those of other manufacturing industries in both the practices employed and the production metrics achieved. It is not unusual for a pharmaceutical manufacturing plant to have low product yields and variable product quality.

Although rigorous and regulated Quality Assurance systems stop poor quality products from ever reaching the market, the manufacturer is left with high product costs, high inventory levels, and poor inventory turns as a result of often fragile processes.

A deep understanding of their manufacturing processes and the use of innovative manufacturing technologies necessary to mitigate these problems has often eluded traditional pharmaceutical manufacturing.

How Pharmaceutical Manufacturing Will Change

Other industries facing similar issues have swiftly made changes to operating practices and processes. The highly regulated pharmaceutical industry, however, with its licensed and validated products and Good Manufacturing Practice (GMP) governed processes has, until recently, struggled to do this effectively.

Things are changing. The industry regulator, the Food and Drug Administration (FDA), has been working with the pharmaceutical industry in an unprecedented manner to evolve a framework for changing the way the industry develops, implements, monitors, and controls its manufacturing processes.

Most of today's pharmaceutical manufacturing is predicated on the use of GMP controls to regulate the general operating systems of a firm and the use of validated and licensed manufacturing processes for each medicinal product. Once a product process has been validated and licensed, it is effectively 'locked'. The pharmaceutical company is then reluctant to make changes, even when things do not go well.

This validated process approach has meant that the process analytics and process control – readily adopted by the likes of the petrochemical, chemical, and food industries – have not been embraced by the pharmaceutical industry.

Learning from other Manufacturing Industries

These other industries have long had an understanding that if a process can be monitored at critical points and the information used to actively control the process, then a constant quality final product can be produced. They have used process analytics and process control to ensure that each batch of product is produced from an optimized and controlled process.

This has given them a high degree of understanding about how their processes operate and better, more reliable quality in their finished products. Ultimately this drives down to a better bottom line as the benefits produce cost savings along the whole manufacturing value chain.

The PAT Vision for Pharmaceutical Companies: From R&D to Manufacturing

The Process Analytical Technology vision for pharmaceutical companies is radical. It foresees an industry that moves away from a rigid validation-based manufacturing paradigm, often bordering on an art form, to a science and engineering-based approach to understanding processes, understanding and mitigating risks to poor product and leading to increased process quality.

As a regulatory framework, PAT will encourage the rapid development and implementation of innovative pharmaceutical manufacturing and quality assurance practices.

In R&D and product development, PAT tools will be used to gain greater understanding of the chemistry and physics of the manufacturing process, enabling tomorrow's new products to move into the market faster and easier with more effective and efficient processes.

In routine manufacturing, PAT will enable continuous and real-time quality assurance to ensure consistently high product quality and performance, batch after batch.

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Main Pharmaceutical Business Benefits from PAT

In Pharmaceutical R&D:

- A deeper scientific and engineering understanding of manufacturing processes
- Reduced product development times, more robust licensing packages, faster scale up, and faster time-to-market for new products
- Implementation of innovative manufacturing and quality strategies

In Pharmaceutical Manufacturing:

- Reduced waste, right-first-time manufacturing, higher production asset utilization
- Real-time quality assurance and validation
- Movement toward real-time release of products
- Lean manufacturing practices for reduced raw material, work-in-progress, and finished goods inventories
- More robust product supply to the public

Strategies for PAT Implementation

Pharmaceutical firms will develop different approaches to exploit PAT. These will range from using the initiative in a tactical manner to 'fix' poorly performing processes and move to a 'right-first-time' manufacturing regime through to those with a developed business strategy for PAT that will imbed it deeply into their business process.

This comprehensive PAT strategy will require the integration of measurement technologies, application development, and process interfacing to measure the process. It will also require the use of informatics tools to gain process knowledge and ultimately control the process through feed-forward or feed-back protocols. Measurement technologies will be required to be robust and designed for operating in the process environment in what could be a 24/7/365 mission critical application.

The Role of the Vendor

Implementing PAT will require a wide set of scientific, measurement, informatics/knowledge management, and process integration capabilities. Access to these toolsets will vary depending on the capabilities of the pharmaceutical firm. Large firms may wish to establish an in-house capability, choosing to partner with vendors to gain access to measurement technologies or co-develop future technologies.

Other pharmaceutical firms will look to their vendor to provide access to measurement technology and as a source of application development, process integration, and business integration services. Often they will look for one-stop-shopping and develop a strong partnership with their chosen vendor. These vendors will need to have very wide ranging technologies and capabilities stretching from analytical science through process integration and control through informatics. The vendors will also need the ability to combine these effectively to create and execute PAT projects for customers.

Thermo Fisher Scientific and PAT

We have been closely involved in pharmaceutical process monitoring quality control/quality assurance processes for a long time, in many cases pre-dating the PAT initiative. Our large, experienced team of experts can provide the knowledge and guidance needed through every step of the PAT process. We have seen examples of its FT-NIR, FT-IR, Raman, and Mass Spectrometry measurement and control technologies used to radically change the way customers gain understanding and control of their manufacturing plants. From manufacturing the bulk drug substances to producing the finished medicines, our involvement in PAT is well established.

Summary – A Bold and Exciting Future for Pharma

PAT offers the pharmaceutical industry a framework for revolutionizing its R&D and manufacturing businesses, producing value for both themselves and patients. Implementing PAT will be a scientific, business, and cultural challenge to both the pharmaceutical firms and their suppliers of technology and services. PAT will ensure that if you are in a pharmaceutical firm or part of its supplier community, the next five years will be exciting and challenging.

With its unique mixture of measurement technologies, application knowledge, and process control capabilities linked to a worldwide service and support structure, Thermo Fisher Scientific is ready to meet this challenge with our customers.

The Thermo Scientific Antaris Target blend analyzer provides blend end-point determination and confirmation of blend uniformity for tablet manufacturing.

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