

# Pharmaceutical processing

NEW TECHNOLOGY FOR THE PHARMACEUTICAL INDUSTRY

## Understanding the Pharmaceutical Manufacturing Process

### Tools and techniques to integrate PAT into your process

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The PAT initiative aims to benefit the industry by supporting innovation and efficiency in the development, manufacturing and quality assurance of pharmaceuticals.

In an effort to support innovation and efficiency in drug manufacturing, the U.S. Food and Drug Administration (FDA) introduced the Process Analytical Technology (PAT) initiative in 2003. Ever since, pharmaceutical manufacturers around the country have searched for technology to improve manufacturing performance.

The PAT initiative aims to benefit the industry by supporting innovation and efficiency in the development, manufacturing and quality assurance of pharmaceuticals. Specifically, plants hope to see results by reducing production cycle times; preventing rejects, scrap and reprocessing of materials; increasing automation to improve operator safety and reduce human errors; and enabling real-time release.

Much of the initial work with PAT has focused on the development and application of analytical devices for timely measurements; however, it is only one aspect of the initiative. To fully address PAT's goal of achieving complete understanding and control of the manufacturing process, a wider variety of tools must be applied.

To integrate PAT into the overall scheme of process

control and automation, there are various types of tools the FDA has identified, including:

- Multivariate tools for design, data acquisition and analysis
- Process analyzers
- Process control tools
- Continuous improvement and knowledge management tools

Using these tools allows manufacturers to focus on the five key elements of manufacturing: people, materials, facilities, equipment and documentation.

Additionally, by integrating these tools into the process control system, benefits such as faster development of new products, shorter manufacturing cycle times, higher yields, reduced waste materials, and fewer product recalls will be realized.

#### Successful Tools for PAT

The foundation for the use of multivariate tools for design, and analysis leading to process improvement is reliable data. Industry tools, such as the Uniformance Process History Database (PHD) from Honeywell Process Solutions, collects, stores and replays historical plant process data. This makes timely information visible at the production level and throughout the enterprise.



Access to timely data empowers plant staff to better align, plan, execute and improve business performance, which increases efficiency and translates to the overall goal of the PAT initiative.

With a foundation of reliable process data, multivariate analysis tools, such as those found in Honeywell's Profit Suite, can be applied effectively. When selecting a multivariate tool, it's important to consider two factors: its ability to continuously monitor and quickly detect impending abnormal situations, and its ability to localize and identify the root cause of the impending events to allow a measured and appropriate response.

Profit Suite can be used for root cause analysis and the development of statistical models that identify cause and affect relationships to improve process understanding. Equally important, these models can be applied as part of a PAT control strategy to improve manufacturing performance by avoiding abnormal situations and reducing human errors.

Another tool that lends to the overall goal of PAT is the process analyzer. Process analyzers provide proven measurement and control solutions to keep plant operations running smoothly, efficiently and safely. An example of a process analyzer is the Laser Induced Fluorescence (LIF) sensor, a non-invasive device used to determine the homogeneity of dry powder blends.

The benefits of using an LIF correspond directly with the basis of the PAT initiative. This specific tool reduces the cycle time by eliminating off-line analysis and by defining a real end point that can be measured online. Quality assurance is also tracked through use of the LIF as well as rapid analysis.

Process control tools are an important ele-

ment of a PAT solution. Process control tools help collect, synthesize and share process and business knowledge from multiple sources across the enterprise, and recommend appropriate actions so operators can increase their productivity. Taking advantage of tools found in control systems, such as Honeywell's Experion PKS, more consistent operation through the application of automated control strategies, helps to prevent rejects and reduce human error.

Improvements to alarm system design can also lead to improved operator efficiency and decrease the amount of possible process upsets. Alarm management solutions help ensure that alarm systems perform effectively to protect uptime and safety operations by allowing operators to detect and correct process faults at an early stage.

Other alarm management tools support PAT by offering functions that provide metrics of events and process history for root cause analysis of abnormal situations. Features that separate automatic notifications as low-priority alarms from true alarms are also valuable to alarm management. This feature permits the alarm system and operator to focus on alarms requiring immediate action.

These tools mentioned above are critical to ensuring that collected data are relevant and representative of process and product attributes, and allows the operator to be more effective. They directly address the reasons why the FDA launched PAT, to help the drug industry deliver higher quality products and improve the manufacturing process.

#### **Complete Understanding and Control**

The FDA began this initiative with several goals in mind, particularly recognizing the need

to free the industry from the hesitation toward implementing new technologies and innovative systems that could impact regulatory processes.

Manufacturing must employ innovation, cutting edge scientific and engineering knowledge, along with the best principles of quality management not just to continue as before, but to respond to the challenges of manufacturing new drugs and new ways of doing business.

The PAT initiative is needed by the pharmaceutical industry to allow them to bring more innovation and efficiency to their manufacturing processes. Technologies that incorporate greater product and process understanding provide a high assurance of quality on every batch and provide alternative, effective mechanisms to achieve greater results.

Product quality and performance are ensured through the design of effective and efficient manufacturing processes. The tools necessary to optimize pharmaceutical manufacturing processes are available today and becoming increasingly essential.

Additionally, as pharmaceutical manufacturing continues to progress with increased emphasis on science and production principles, effective use of integrated tools and systems can improve efficiencies in not only the manufacturing processes, but the regulatory process as well.

The PAT initiative is about process understanding, predictability and efficiency. PAT should be thought of as a system for designing, analyzing and controlling manufacturing with the goal of ensuring final product quality. ■

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