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Leveraging Connect™ CPV to Implement Process Analytical Tools (PAT) for Enhanced Pharmaceutical Manufacturing

Executive Summary

Connect™ CPV is a transformative platform that aligns with the principles of Process Analytical Technology (PAT) and Quality by Design (QbD) to revolutionize pharmaceutical manufacturing. By integrating analytical methods across chemical, physical, microbiological, and mathematical domains, Connect™ CPV significantly enhances the understanding and control of manufacturing processes.

PAT and Its Significance in Pharmaceutical Manufacturing

Process Analytical Technology (PAT) is a framework employed in pharmaceutical manufacturing to design, analyze, and control pharmaceutical manufacturing processes through the measurement of critical process parameters (CPP) that affect critical quality attributes (CQA) of the final product.

The concept of PAT was introduced by the U.S. Food and Drug Administration (FDA) as part of its Quality by Design (QbD) initiative. The primary goals of PAT in pharmaceutical manufacturing are to enhance understanding of processes, ensure consistent quality of products, and increase efficiency.

PAT plays a crucial role in modern pharmaceutical manufacturing, driving improvements in product quality, process efficiency, and regulatory compliance. Its emphasis on real-time monitoring and control represents a significant shift from traditional quality control methods, paving the way for more innovative, efficient, and reliable pharmaceutical production. With innovative transformational treatments like Cell and Gene therapy, the impact of PAT plays a critical role in ensuring that patients receive timely medical care.

Introduction to Connect™ CPV and Its Integration with PAT

It is important to note that the term analytical in PAT is viewed broadly to include chemical, physical, microbiological, mathematical, and risk analysis conducted in an integrated manner. The goal of PAT is to enhance understanding and control the manufacturing process, which is consistent with QbD.

Connect™ CPV Provides the Following Capabilities to Support Analytical Needs of PAT

1. Multivariate Tools for Design and Analysis

From a physical, chemical, or biological perspective, pharmaceutical products and processes are complex multi-factorial systems. There are many development strategies that are used during process/product development, analytical development, and formulation development to identify optimal options. The knowledge acquired in these development programs is the foundation for product and process design. Data Science Studio (DSS) and NCML (No Code ML) are two integrated modules of Connect™ CPV that allow for seamless data acquisition and analysis, leading to faster and better process design.

2. Process Analyzers

Process analysis has advanced significantly during the past several decades due to an increasing appreciation for the value of collecting process data. Industrial drivers of productivity, quality, and environmental impact have supported major advancements in this area. Available tools have evolved from those that predominantly take univariate process measurements, such as pH, temperature, and pressure, to those that measure biological, chemical, and physical attributes. Indeed, some process analyzers provide nondestructive measurements that contain information related to the biological, physical, and chemical attributes of the materials being processed. These measurements can be at-line, on-line, or in-line.

Process analyzers typically generate large volumes of data. Certain data are likely to be relevant for routine quality assurance and regulatory decisions.

The *Genealogy* module of Connect™ CPV, batch records keep scientific and procedural information at a unit operation and batch level. Genealogy thus becomes the unified single source for all (experimental batches, clinical batches, and commercial batches). This single source of truth allows seamless collaboration across functions and rapid analysis of data. The *SPC (Statistical Process Controls)* module of Connect™ CPV allows the creation of a series of charts depicting acceptance ranges, confidence intervals, and distribution plots (inter and intra batch) showing measurement results. Ease of secure access to these data is important for real-time manufacturing control and quality assurance.

3. Process Control Tools

It is important to emphasize that a strong link between product design and process development is essential to ensure effective control of all critical quality attributes. Process monitoring and control strategies are intended to monitor the state of a process and actively manipulate it to maintain a desired state. Strategies need to accommodate the attributes of input materials, the ability and reliability of process analyzers to measure critical attributes, and the achievement of process endpoints to ensure consistent quality of the output materials and the final product.

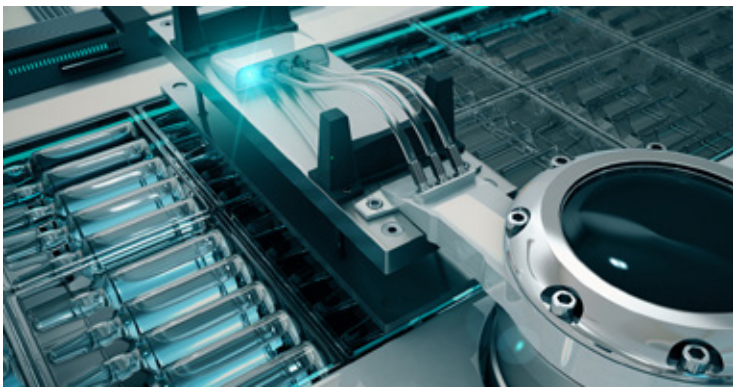
Connect™ CPV allows the optimization of process development and manufacturing processes within the PAT framework in the following ways:

- *Genealogy* captures all material, equipment, and process attributes, allowing product design and process development to flexibly analyze and measure critical material, equipment, and process attributes relating to product quality.
- *IPC (In-Process Control)* allows real-time or near real-time monitoring of all critical attributes.
- Connect™ CPV allows configurable adjustments to process control attributes to ensure control of all critical attributes.
- *DSS (Data Science Studio) and NCML (No Code ML)* allow building mathematical relationships between product quality attributes and measurements of critical material and process attributes.

4. Continuous Improvement and Knowledge Management Tools

Genealogy keeps all connected information at a unit operation and batch level. Information on clinical batches, experimental batches, and commercial batches allows flexible analysis across process development, analytical development, quality compliance, and commercial operations. Connect™ CPV serves as the integrated knowledge management platform, fostering continuous improvement, cross-functional collaboration, and knowledge management.

Challenges in Pharmaceutical Manufacturing



Complexity of Pharmaceutical Processes and the Need for Real-Time Monitoring

Pharmaceutical manufacturing involves intricate processes that require precise control of numerous variables to ensure product quality and efficacy. The complex nature of these processes, often involving sensitive chemical reactions and strict environmental conditions, necessitates sophisticated real-time monitoring. This monitoring is crucial to detect and correct deviations as they occur, ensuring that each batch meets stringent quality standards. Without real-time monitoring, there is a risk of delayed response to issues, leading to potential batch failures and reduced quality.

Data Integration Issues from Disparate Sources

In modern pharmaceutical production, data is collected from a wide array of sources, including lab equipment, process sensors, and quality control systems. Each of these may use different formats and standards, making it challenging to achieve a unified view of the entire manufacturing process. Integrating this data is essential for a holistic understanding and control of production but is often hindered by incompatibility between systems. This fragmentation can lead to siloed information, making it difficult to perform comprehensive analysis and derive actionable insights, which are vital for informed decision-making and process optimization.

Cost of Non-Compliance and Inefficiencies

The pharmaceutical industry is one of the most heavily regulated industries globally. Non-compliance with regulatory standards can result in severe consequences, including fines, recalls, or even a complete shutdown of production. Compliance is not just a legal requirement but also a critical component of ensuring patient safety and maintaining public trust.

Additionally, inefficiencies stemming from outdated methods or poor process control can lead to unnecessary waste, increased production costs, and lost revenues. There is also the cost associated with opportunity loss due to delayed product launches when processes are not optimized or when compliance issues arise. These costs can be significant and, in some cases, may even threaten the viability of a pharmaceutical company.

Addressing these challenges requires an integrated approach that Connect™ CPV aims to provide, offering real-time process monitoring, seamless data integration, and tools to ensure regulatory compliance, thereby minimizing inefficiencies and the associated costs.

Overview of Connect™ CPV Modules and Their Role in Enabling PAT in an Integrated Platform

Genealogy Module:

- Keeps scientific and procedural information at a unit operation and batch level. Genealogy thus becomes the unified single source for all (experimental batches, clinical batches, and commercial batches).
- Becomes the single source of truth, allowing seamless collaboration across functions and rapid analysis of data.
- Captures and visualizes the entire lineage of product manufacturing, from raw materials, equipment details, and test results through to the finished product.
- Supports PAT by providing traceability and detailed records of material and process attributes essential for product quality.
- Facilitates the understanding of the relationship between process variables and product outcomes, a key component of QbD.

View Module:

- Offers a customizable interface for viewing and interpreting data, tailored to the needs of different business users.
- Aids PAT by allowing users to apply specific data transformations and conduct analysis that can inform process control strategies.
- Enables governance over data, ensuring that all users work with validated and consistent information.

In-Process Controls (IPC) Charts Module:

- Allows for real-time or near real-time monitoring and visualization of critical process parameters.
- Directly supports PAT by enabling immediate detection and correction of process deviations to maintain product quality.
- Provides configurable alerts and visual aids that help maintain the process within defined control limits.

Data Science Studio (DSS):

- A Python-based environment for advanced data analysis, including multivariate analysis, crucial for PAT.
- Allows for the creation of predictive models that link material and process attributes to product quality attributes.
- Facilitates the development of deeper process understanding, as advocated by PAT principles.

Statistical Process Control (SPC) Charts Module:

- Offers tools for creating various statistical charts that help in monitoring and controlling the manufacturing process.
- Supports PAT by enabling quality control through continuous monitoring and analysis of data against control limits.
- Aids in maintaining a state of control and identifying trends that could indicate potential issues before they arise.

No-Code ML (NCML) Module:

- Allows business users and citizen data scientists to create machine learning models without coding expertise.
- Enhances PAT by enabling users to easily develop models that can predict and optimize process outcomes.
- Contributes to process optimization and control by facilitating the analysis of complex data sets.

Paper Batch Records Module:

- Digitizes and integrates data from paper batch records, reducing the risk of human error and improving data accuracy.
- Enhances PAT by providing immediate electronic access to batch records for rapid analysis and decision-making.
- Supports continuous process verification by enabling trend analysis and batch-to-batch comparisons.

Reporting Module:

- Generates customized reports that can include PAT-related insights and trends, which are vital for informed decision-making.
- Provides documentation that can be used for regulatory submissions and internal quality assurance purposes.
- Automates report generation, enhancing efficiency and enabling quick response to emerging data trends.

Data as a Service (DAAS):

- Offers API access to the integrated, contextualized data that is crucial for PAT activities.
- Ensures that data can be accessed and utilized by other systems, promoting interoperability and real-time data sharing.
- Supports a holistic approach to PAT by allowing seamless integration with external analysis tools and platforms.
- Each module of Connect™ CPV is designed to interoperate seamlessly, providing a robust foundation for implementing PAT in pharmaceutical manufacturing. By offering these targeted capabilities, Connect™ CPV enables manufacturers to ensure product quality, optimize processes, and comply with regulatory requirements efficiently.

Creating Value with PAT through Connect™ CPV

01.

Enhanced Process Understanding and Control

- Real-time data collection and analysis for informed decision-making.
- Improving product quality and consistency through in-depth process monitoring.

02.

Increased Efficiency and Reduced Waste

- Streamlining process development and scale-up.
- Reducing out-of-specification products and waste.

03.

Regulatory Compliance and Quality Assurance

- Ensuring adherence to regulatory standards.
- Utilization of data for audit trails and compliance reporting.

04.

Cost Savings and ROI

- Reduction in downtime and increased yield.
- Minimizing delays in batch release and improving time-to-market.

Case Studies

Real-Time Yield Prediction Model for a 10K Bioreactor

Using the data captured in Genealogy for 30 commercial batches and DSS (Data Science Studio), SMEs created a model that took in the characteristics of the media, feed, sensor data from the bioreactor, and cell viability data from PAT equipment to create a prediction model for cell viability.

The multivariate prediction model was made available using IPC charts to monitor the progress of the batch and create necessary alerts for operators to intervene when necessary.

As part of this exercise, users also learned the complex interplay between different parameters and the right balance of the parameters to improve the yield by up to 2%.

Real-Time Flow Adjustment for Optimal Concentration Levels

In this setup, three separate liquids from different tanks were coming together for the mixing step. The concentration of the liquids, pressure from the feeding pumps, and NIR data on concentration were available in real time.

A few experimental runs of this setup were done to gather sufficient variations in the data mix, and a model was created that used concentration, pump pressure, and concentration to adjust the pump pressure in a closed-loop manufacturing setting.

About mareana

Founded in 2015, Mareana is an AI-powered software company with the mission of accelerating digital transformation in manufacturing, supply chain, and sustainability via our connected intelligence platform.

Mareana's platform uses AI/ML to rapidly connect disparate, siloed data across the entire business process, allowing our customers to shift their time and effort from data preparation to making complex business decisions intuitively, in real time.

Our customers are market leaders in life sciences, chemicals, and general manufacturing who have realized over a billion dollars in business value by leveraging our platform.

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