TIBCO®

Continued Process Verification with Statistica and PI System

Understanding and acting on multivariate data in a continuous process

TIBCO STATISTICA AND OSISOFT PI SYSTEM

TIBCO Statistica™ and OSIsoft PI System allow you to connect to all data sources that contribute to the lifetime development of a product, aggregate the data, analyze the resulting information, automate reporting for both internal and external stakeholders, and monitor critical quality attributes for on-demand alerting. These capabilities, along with real-time access and data visualization, let you move from reactive to proactive decision-making.

Meeting and maintaining product quality is difficult, complex, and costly. However, not meeting and maintaining product quality is dangerous, even more costly, and potentially deadly. Production processes are inherently complex—with ingredients, containers, machinery, materials, and people being just a few of the variables that constantly change—making it difficult to maintain established quality specifications. Moreover, each of these variables is described by data in different formats and locations. What's needed is a secure, regulatory-compliant system that:

- Organizes the chaos
- Collects and analyzes the data
- Sends warnings using real-time alarms and alerts
- Automates standard and ad-hoc reporting

This paper describes the challenges associated with a Continued Process Verification (CPV) program and the TIBCO Statistica™/OSIsoft PI System solution for CPV.

CHALLENGES

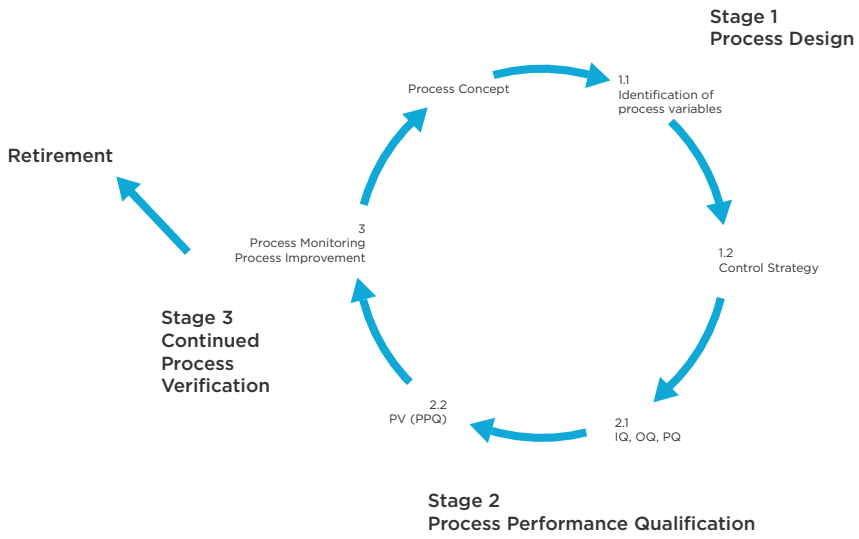
THREE STAGES OF VALIDATION

CPV begins with process validation in three stages:

Stage 1
Process Design: Demonstrate an understanding of the process. The commercial manufacturing process is defined based on knowledge gained through development and scale-up activities.

Stage 2
Process Performance Qualification (PPQ) or traditional Process Validation: Demonstrate process robustness at commercial scale. The process design is confirmed as being capable of reproducible commercial manufacturing.

Stage 3
Continued Process Verification (CPV): Demonstrate understanding of process variability at commercial scale; Verification that during routine production, the process remains in a state of control.



In Stage 3, demonstration of the ability to maintain the validated state of commercial scale includes:

- Maintaining the validated state of the facility, utilities, and equipment
- Maintaining the validated state of the process
- Performing ongoing process monitoring (CPV)
- Statistically analyzing the data as appropriate for increased understanding and proposed actions

REGULATIONS

US Food and Drug Administration (FDA) expectations for an ongoing CPV program for collecting and analyzing product and process data relating to product quality include:

- Procedures for data collection, metadata (contextualization), and trending
- Data collected can verify that the quality attributes are within specs
- Management of both intra-batch (within a batch) and inter-batch variation
- Data is collected to evaluate process stability and capability
- Data is statistically trended

TIBCO Statistica and OSIsoft PI System provide a collaborative, secure, and complimentary platform for meeting the complex needs of proving final product quality through CPV.

It is recommended that a statistician or a person with proper statistical training develop the data collection and analysis methods. A system for detecting unplanned deviations from the process is also expected, which includes:

- Evaluation of the performance of the process
- Identification of problems
- Determination of corrective and preventive actions to ensure control over the process and product

European regulatory bodies, such as the European Medicines Agency (EMA) has its own definitions quite similar to FDA's CPV. EMA calls it Ongoing Process Verification (OPV), which is described in the EMA Guideline on Process Validation for Finished Products, annex 15.

STATISTICA AND PI SYSTEM FEATURES

ACCESS DATA
Integrate all data sources, internal and external, through the lifetime of the product.

MODEL KEY PERFORMANCE INDICATORS
Model critical quality attributes (CQA), critical material attributes (CMA), and critical process parameters (CPP).

MONITOR IN REAL TIME
Monitor any attribute or parameter with alerting in multiple formats.

AUTOMATE
Automate reporting requirements.

USE AD HOC REPORTING
Enable ad hoc reporting.

MEET STANDARDS AND SECURITY REQUIREMENTS
Meet global standards for security and documentation.

MANAGE DATA
Preserve data integrity and data quality with fast and secure access to data on demand.

CONTEXTUALIZE
Rely on statistical and analytical contextualization of any data.

MANAGE COMPLIANCE
Meet cGMP requirements and validate and comply with CFR 21 part 11.

SOLUTION

TWO REQUIREMENTS

Given the challenges, the appropriate solution for CPV includes two elements that need to be carefully addressed:

- Data collection from several sources, with the ability to establish a platform or infrastructure where all data is accessible, trustworthy, and able to be incorporated into the analysis across an organization.
- Data analysis for trending and critical quality attributes (CQA), critical process parameters (CPP), and critical material attributes (CMA) provides the appropriate information in a reliable and interactive report for distribution across an organization.

Data Collection

PI System delivers the premier infrastructure for operations of 23 of the worlds' top 25 pharmaceutical companies. It can connect to more than 450 interfaces and collect high-frequency data from multiple formats, standards, or conventions, both time-series and event-based, from multiple systems or sources and translate data into a uniform structure for combining, comparing, contextualizing, and leveraging information. You capture high-quality, high-fidelity data that is accurate and complete; no data is lost by data averaging or interval sampling.

Data Analysis

Statistica simplifies the inherently complex task of implementing and maintaining a CPV solution. With Statistica, you can easily connect to PI System and the other data sources that contribute to a final product. Statistica lets you easily run the analyses needed to verify that a system stays in control. Even more important, if any parameters are going out of control, built-in Statistica processes alert you. These capabilities can all be automated to ease the burden of an already over-taxed production team.

OUT-OF-THE-BOX CAPABILITIES

Together Statistica and OSIsoft provide an out-of-the-box solution to access, cleanse, analyze, and automate data in a continued validation process for manufacturing. Statistica is different in that it's commercial and off the shelf, lifting the burden of customization. It integrates all necessary applications onto one platform that does not need to be re-validated at multiple junctures. There are no proprietary databases, data formats, or black boxes that lock you into one solution and prevent you from expanding.

PI System is scalable, open infrastructure that supports an initial small-asset deployment and easily expands, allowing you to determine and manage data trends and maintain data integrity and quality.

The OSIsoft PI System provides the data infrastructure, data management, and data integrity for fast and secure access to data on demand, and contextualization of data that is easily analyzed and visualized within Statistica.

KEY COMPONENTS

The combined solution is structured around eight key components:

Data Access

Many data sources, databases, file types, aggregation methods, and delivery techniques are used over the lifetime of producing a product. All this data is required to successfully implement a CPV solution. Statistica makes the task easier by providing out-of-the-box solutions for accessing data from practically any data source, enabling aggregation of all CPV-related activities and reporting requirements. Proven and open infrastructure that connects sensor data and operations to enable real-time intelligence is important in a controlled process, and OSIsoft makes this easy with its data capture, storage, and seamless integration with Statistica for analysis.

Data Preparation

Extracting, cleansing, and enriching data is one of the most fundamental and difficult tasks in a control process. Without cleansed and enriched data it is nearly impossible to improve a continuous process or even see what is happening throughout the manufacturing process in general. OSIsoft provides a deep set of features to extract, prepare, and enrich data that can then be passed to Statistica for analysis and monitoring.

ABOUT OSIsoft

OSIsoft develops and supports software used to capture, process, analyze, and store any form of real-time data. OSIsoft's target markets include: chemicals and petrochemicals; critical facilities, data centers and IT; federal; materials, mines, metals and metallurgy; oil and gas; pharmaceuticals, food and life sciences; power and utilities; and pulp and paper.
For more information, go to www.osisoft.com

Data Management

OSIsoft simplifies complex data management by focusing on data integrity and data quality. Its fast and secure access to data on demand, as well as deep search and analytic capabilities, provides for a contextualization of batch data, allowing you to pass the most relevant data sets across the entire manufacturing process for analysis and monitoring.

Analytics

Statistica incorporates all standard methodologies needed for analyzing data in CPV. Quality control charts with configurable parameters, process capability statistics, and over 16,000 other functions are out-of-the-box. Validation packages provide an even quicker return on investment.

Monitoring

The flexibility of the Statistica platform enables you to use any model and monitor it for any requirement needed. Monitoring can involve any quality control chart (IMR, X-bar and R, EWMA, and more), and any deviation from control limit, warning limit, or other custom specification, such as residuals from a regression model. You can even monitor misclassification rates from machine learning algorithms. OSIsoft allows for constant data monitoring across a process, plant, or enterprise.

Notification and Alerting

Once an analysis is set to be monitored, communicating when any deviation occurs or is expected allows keeping a process in control within specified limits. Alerting needs to occur in a variety of ways: in-plant, in email, or by text message. Both OSIsoft PI System and Statistica allow you the flexibility to design alerts for a variety of demanding needs.

Reporting

Within the realm of CPV, a plethora of reports are required: annual product reviews (APRs), invalid trending reports (ITRs), and internal milestone reports. These reports are most often manual and require an inordinate amount of effort to develop. Statistica enables you to automate this process and method of delivery. A differentiator of the Statistica platform is the ability to enable ad hoc reporting. Statistica makes it easy to develop data sources, analyses, and reports on the fly, without costly customizations. The PI System gives you the ability to drill down into the data for fast and reliable investigation and troubleshooting.

Security

CPV by definition assumes that strict guidelines are followed so that the results of a product lifetime analysis can be trusted. From documentation to verification of analyses, guidelines and standards must be followed so that people can rely on the quality of the product they are consuming. Statistica meets global standards for security and documentation to meet CPV requirements.

REFERENCES

FDA Guidance for Industry: Process Validation: General Principles and Practices, 2011.
Roche and Genetech definition of CPV as presented at MES & Process Minds, Berlin, Germany, 2016.

TIBCO Statistica

Global Headquarters
3307 Hillview Avenue
Palo Alto, CA 94304
+1 650-846-1000 TEL
+1 800-420-8450
+1 650-846-1005 FAX
www.tibco.com

07/31/17