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The Benefits Of Pharma 4.0 And Validation 4.0

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By Rick Ruiz

The emergence of Pharma 4.0 is bringing dramatic and positive changes to the life sciences. The advent of new and highly complex therapies presents new challenges to emerging companies, which are challenged with limited staff, a need for speed to market, and limited funding.

To manage and survive these challenges, companies need to be part of a "cyber-physical" system or ecosystem that includes partnering with service providers as part of the overall supply chain. Building on the growing need for real-time high transparency and real-time data access, with a high level of data integrity, Pharma 4.0 brings a significant move to the digitization of all components related to performing real-time business and process improvement. This change is so significant that the FDA has generated a memorandum of understanding to drive the industry to Pharma 4.0, as well as encouraging the incorporation and implementation of advanced manufacturing techniques (AMT), such as continuous manufacturing.

The most significant change is how pharma/biotech business is going to be done. These segments have increasingly complex product manufacturing and distribution requirements, which necessitate Pharma 4.0 digitalization. Pharma 4.0 is the pharmaceutical version of Industry Internet of Things 4.0 (IIoT). The life sciences industry has been recognized as lagging in the adoption of IIOT and associated capabilities relative to other industries. Some examples of Pharma 4.0 technologies include cloud computing, process analytical technology (PAT), line sensors, temperature/package smart devices, ERP applications, and AI/machine learning. The digitalization of business operations brings real-time information exchange, a high level of supply chain transparency/resiliency, better cybersecurity, and greater data quality.

VALIDATION 4.0 – CHANGING THE PARADIGM

Validation 4.0 is an innovative approach to ensuring that the new technologies of Pharma 4.0 are implemented and validated to ensure requirements related to patient safety and product quality. There are three key benefits companies can gain from Validation 4.0:

- **Decreased Costs** — Leverage Pharma 4.0 technology to drive down the number of resources needed and time needed to perform the validation in a Pharma 4.0 environment.
- **Increased Quality** —Focus on the critical thinking and risk management necessary to validate smart devices and the ecosystem. This includes the data exchange and visibility into the support networks of suppliers, CDMOs, CMOs, and other partners. Leveraging QbD, critical quality attributes, and critical performance parameters will improve business processes and performance.
- **Faster Time to Market** — Approximately 30% to 40% of validation documentation creation time is saved, decreasing time to market. Validation 4.0 is highly focused on risk management and monitoring of critical business processes.

Decreased costs and risks are provided by the enhanced transparency, resiliency, and active monitoring supported by smart devices in the supply chain. Risk identification and management are essential activities of this validation form. These activities result in fewer manufacturing and distribution errors in getting drugs to market and a better control of corrective and preventive actions. New technologies, processes, and procedures that impact the safety of patients and the quality of the drug product or that negatively impact data integrity need to be tested under a validation effort. Traditionally, the industry has employed either a computer system validation (CSV) or a computer software assurance (CSA) method. Unfortunately, neither of these approaches takes advantage of the capabilities gained from Pharma 4.0. Validation 4.0 is specifically designed to leverage the digital communications of the Pharma 4.0 components and to test the ability to capture, track, monitor, and measure the performance of business processes and the embedded smart devices.

Validation 4.0 can be a critical aspect of product quality. The focus of Validation 4.0 provides a framework and approach that ensure the validation effort concentrates on process performance qualification (PPQ). This requires leveraging and understanding what Pharma 4.0 delivers in the form of standardized technology and environment as well as the intelligent data generated and consumed by these devices. This new environment is so extensive that the approach must be integrated due to the variety and complexity of the data being collected. It needs to support a risk-based and holistic view of the exercised devices to ensure there is transparency through the supply chain. To successfully accomplish a complete validation effort, the traditional CSV/CSA paradigm needs to be inverted.

Speed to market is gained by improving the validation process. The current forms of CSV and CSA have four main parts: documentation, testing, assurance, and critical thinking. This approach tends to spend an inordinate amount of time creating voluminous documentation, with problem resolution being the last step. Validation 4.0 inverts this paradigm to critical thinking, assurance, testing, and documentation. It leverages QbD and quality risk management (QRM) techniques as well as in-depth risk analysis and assessment to focus on the components to validate. The advent of industry-specific systems, known as "low/no code"

packages, and the reliability of today's hardware platforms result in fewer large documents, such as installation qualification (IQ) and operational qualification (OQ), being created. Work is concentrated on the performance qualification (PQ) document. Validation 4.0 focuses on the risk identification, assessment, and resolution of key business processes and operations. This approach has two significant benefits: 1) it supports dynamic validation and monitoring, and 2) the work products from the validation (performance and quality metrics) are continually used to help identify and support quality assurance beyond the actual validation period. This is presenting the new norm on how companies work internally and with external partners in the cyber-physical system.

HOW TO GET TO THE NEW NORM

Incorporating and migrating to Validation 4.0 can involve leveraging components of the traditional validation approach. The main difference is where the bulk of time is spent and in the collaborative effort of the business, regulatory, and IT departments. A suggested path would:

1. Embrace the value and incorporation of the culture of quality (CoQ). This is an important FDA initiative where quality becomes one of, if not the most important, goal of any company. This is where you will incorporate QbD, as you can't test quality into a product.
2. Convene a cross functional team to ensure operational or functional business areas participate in the risk assessment.
3. Perform a complete risk assessment and an identification, prioritization, and mitigation exercise that includes the identification of potential CAPAs and feasible mitigation plans.
4. Develop or update a digital and quality maturity model for the company.
5. If internal implementation of Pharma 4.0 is not feasible, align with a CDMO or CMO that provides a Pharma 4.0 environment and services.
6. Evaluate the current validation approach taken and modify for Pharma 4.0 components.
7. Conduct the validation with the newly established Validation 4.0 documents and approach.
8. Use the output as the performance monitoring and analysis activity.

ADDITIONAL BENEFITS

It is easy to determine the business benefits derived from moving to Validation 4.0. Beyond the benefits identified in the first part of this article, some additional benefits include:

1. a higher level of data integration — standardization of performance metrics and data definitions
2. doing more with less — the validation effort will require significantly fewer resources to complete
3. decreased risk profile — gain insights and continuous monitoring of key and critical risk areas
4. an increase in supply chain visibility and resiliency — leveraging Pharma 4.0 smart devices
5. establishing a collaborative relationship with the FDA and promoting the use of Pharma 4.0 to support virtual inspections and audits. This validated environment would allow the FDA to perform virtual inspections of performance.

Validation 4.0 is a component of the new norm. It is the framework and approach that will support a proactive, efficient, effective, and dynamic method of managing risk through the new extended cyber-systems.

RICK RUIZ is a principal at Tunnell Consulting. He has over 30 years of life sciences experience in quality, manufacturing/supply chain/CXO, commercial, clinical trial/R&D, and regulatory.